THE PHILIPPINE

JOURNAL OF SCIENCE

PAUL C. FREER, M. D., PH. D.

SUCCEEDED BY

ALVIN J. COX, M. A., PH. D.
GENERAL EDITOR

SECTION B

THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

RICHARD P. STRONG, PH. B., M. D.
EDITOR

VOLUME VII

1912

WITH 54 PLATES

MANILA
BUREAU OF PRINTING
1912

CONTENTS.

VOL. VII, SEC. B, NO. 1 FEBRUARY, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

PAUL C. FREER, M. D., PH. D.
GENERAL EDITOR

SECTION B

THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

RICHARD P. STRONG, PH. B., M. D.
EDITOR

MANILA
BUREAU OF PRINTING
1912

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

REPORT OF THE INTERNATIONAL PLAGUE CONFERENCE.

Held at Mukden, April, 1911, under the auspices of the Chinese Government.

Edited by ERICH MARTINI, G. F. PETRIE, ARTHUR STANLEY, AND RICHARD P. STRONG.

483 pages, 18 plates (2 colored, 4 half-tones, 12 charts and maps).

Order No. 416. Cloth, $3.50; paper, $2.50 United States currency, postpaid.

The proceedings of this International Conference and information gained therefrom, together with the results of certain bacteriological investigations, constitute the present report.

Nothing hitherto has been published which gives such a complete and comprehensive account of the entire subject of pneumonic plague.

Delegates from America (United States of), Austria-Hungary, France, Germany, Great Britain, Italy, Japan, Mexico, the Netherlands, Russia, and China attended the Conference.

The Bureau of Science of the Government of the Philippine Islands has been appointed sole agent for the distribution of the printed proceedings of the International Plague Conference.

THE SUGAR INDUSTRY IN THE ISLAND OF NEGROS.

By HERBERT S. WALKER.

145 pages, 10 plates, 1 map.

Order No. 412. Paper, $1.25 United States currency, postpaid.

Considered from the viewpoint of practical utility, Mr. Walker's Sugar Industry in the Island of Negros is one of the most important papers published by the Bureau of Science. This volume is a real contribution to the subject; it is not a mere compilation, for the author was in the field and understands the conditions of which he writes. The following is a brief synopsis of the contents:

Tables of soil analyses, both chemical and physical; analyses of the cane, juice and bagasse; estimates based on actual information as to the costs of production and of cultivation; and estimates of the cost and location of possible central factories. The island is considered by sugar-producing districts; the area of cultivation and the production per hectare are given, and the possibility for future expansion discussed.

The plates illustrate various phases of sugar industry from the cultivation of the field to the transportation of sugar in native sailboats.

A MANUAL OF PHILIPPINE SILK CULTURE.

By CHARLES S. BANKS.

53 pages, 20 plates.

Order No. 413. Paper, $0.75 United States currency, postpaid.

The silk industry is particularly adapted to be undertaken by persons with small capital, and like the making of hats in the Philippine Islands it should thrive with a little encouragement.

In A Manual of Philippine Silk Culture we have presented the results of several years' actual work with silk-producing larvæ together with a description of the new Philippine race. Half-tone plates illustrate in natural size silkworms in different stages of development, pupæ, adult moths, samples of cloth made from eri silk, hand reel, and silk house. Other plates illustrate the various appliances used in raising silkworms and in spinning silk; hand and power reels are illustrated; working drawings are given for a silk house and for a hand reel.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

VOL. VII FEBRUARY, 1912 No. 1

THE RESULT OF THE PAST TWO YEARS' WORK IN THE STUDY OF TROPICAL SUNLIGHT.

By PAUL C. FREER.

(From the Bureau of Science, Manila, P. I.)

Two years ago, I outlined some of the problems to be solved so as to give us an intelligent appreciation of the influence of different intensities of insolation, in various parts of the globe, upon the inhabitants thereof. I then pointed out that, perhaps, the first work should be comparative measurements, undertaken during reasonably long periods, in different latitudes, of the effect produced by that section of the spectrum of the sun to which, in the major portion of the literature, the greatest effect is generally ascribed, namely, the rays of greater refrangibility in the violet and ultra-violet. In suggesting this line of investigation, I did not lose sight of the fact that measurements of the total insolation and of the effect of other portions of the spectrum might be even of greater importance.

It is necessary to resort to a photocatalytic reaction to obtain data regarding the relative influence of the rays of shorter wave length on different days and in different latitudes, and therefore members of the staff of the Bureau of Science set themselves the task of investigating and making available the photocatalysis of oxalic acid in the presence of uranyl salts, as, in the decomposition in question under the normal conditions of the reaction, there is no reduction of the uranium compound and apparently there are no side reactions to complicate the conclusions.

108845

The decomposition of oxalic acid into carbon monoxide (respectively formic acid), carbon dioxide, and water is brought about almost entirely by those rays in the spectrum of the sun extending from 550 $\mu\mu$ to 291 $\mu\mu$. The sun's spectrum does not extend below the latter point, even in the Tropics.

That the decomposition is due to these rays is shown by the following summary of data obtained by exposing standard solutions of oxalic acid and uranyl acetate[1] in equal sized (standardized) vessels to the action of the sun during equal periods of time, the vessels being covered with various U-viol glasses, as follows: (1) Without cover; (2) with U-viol 280 $\mu\mu$; (3) U-viol 289 $\mu\mu$; (4) blue U-viol No. 3653; (5) U-viol copper-ruby No. 2745, all the glasses being 5 millimeters thick. The decomposition in number 1 being placed at 1, those taking place in equal times in the others were:

Number 2 (U-viol 280)	0.888
Number 3 (U-viol 289)	0.883
Number 4 (Blue U-viol No. 3653)	0.508
Number 5 (U-viol copper-ruby No. 2745)	0.004

The ultra-violet glasses, with the limit slightly beyond the range of the sun's spectrum, exert some absorptive influence; this rapidly increases to the blue, and practical extinction occurs before the red. Similar results were obtained by Bruner and Kozak,[2] who filtered the sunlight through a cold, saturated solution of potassium dichromate of 2 centimeters thickness, and thereby brought the reaction to a standstill. The absorption bands of uranyl salt solutions, according to Deussen,[3] terminate at 487.5 $\mu\mu$, but the decomposition *by light* of our standard solution extends below this point, as the cobalt-blue practically terminates at 490 $\mu\mu$ and we had minimal decomposition in the red at about 650 $\mu\mu$. However, as we used no glasses between the cobalt-blue and ruby-red, it seems probable that the action of light in the uranyl acetate-oxalic acid solution practically terminates at about 530 $\mu\mu$, in the green.

Therefore, so far as the range of its absorption spectrum is concerned, we have in uranyl acetate-oxalic acid a most satisfactory photocatalytic reagent for carrying on the comparative measurements in question. However, although the light rays accelerating the reaction may not extend below, say 530 $\mu\mu$, nevertheless, there may be an appreciable heat factor influencing the reaction and due to other causes.

Bacon,[4] when he first studied the reaction, concluded from two experiments, in which he exposed solutions of uranyl acetate and oxalic acid, at 30° and 100° respectively, simultaneously to the sunlight, that no temperature coefficient existed over a wide range of temperature, and Bruner

[1] Five cubic centimeters of a 1 per cent solution of uranyl acetate, 5 cubic centimeters of a 10 per cent oxalic acid solution (crystallized), and 20 cubic centimeters of water.

[2] *Ztschr. f. Elektrochemie* (1911), 17, 358.

[3] *Ann. d. Phys. u. Chem.*, (Wiedemann) (1898), 66, 1128.

[4] *This Journal, Sec. A* (1910), 5, 290.

and Kozak,[5] in a range of temperature observations extending from 4° to 80°, using uranyl nitrate and oxalic acid, could observe no acceleration with increasing temperature, and observe "this is probably the first photochemical reaction with such a very small temperature coefficient, if, indeed, the latter is not equal to naught." The mixture, heated in a water-bath in the dark, shows no decomposition, and flasks containing uranyl acetate-oxalic acid solutions, when covered with thin silver foil and exposed to the full effect of the sunlight, likewise show no change even though they become markedly heated.

Therefore, it seemed safe to assume that a temperature coefficient would be negligible or nonexistent in comparative measurements, but we were once more brought back to this phase of the reaction by an observation made by Mr. M. Barrowcliff, of the Institute for Medical Research at Kuala Lumpur,[6] who, in carrying on measurements with the standard solution, called our attention to the fact that, in his opinion, a temperature coefficient in reality existed.

The entire matter was open for reinvestigation, and Mr. W. C. Holmes, of the laboratory of organic chemistry of the Bureau of Science, conducted a careful series of experiments confirming Mr. Barrowcliff's results. There is very little difference between the reaction at 30° and at the boiling point, as Bacon had shown, but between 2° and 30° there is a marked increase in the rate of decomposition with the rise of temperature, so much so, that decomposition at 2° is only 60 per cent of that at 30°, whereas that at 30° is 95 per cent of the decomposition at 75°; above this point, there is even a diminution of the rate with increased temperature. Between ordinary points of measurement in our climate, say from 25° to 35°, the temperature coefficient may, therefore, be neglected; where measurements at lower temperatures are made, the correction would need to be applied, although in comparing tropical climates with those of temperate zones this temperature coefficient would work in the direction of greater contrast and apparently lesser insolation in the latter, so that, if such contrast were *not* evident on comparing measurements, the coefficient could be neglected in drawing comparative conclusions. Wherein the difference between these results and those obtained by Bruner and Kozak lies, we have not yet determined.[7]

Other factors influencing the reaction must also be considered before the method can be used in a series of comparative measurements; these are: The nature of the background and the size

[5] *Loc. cit.*, 357.

[6] Communicated by letter.

[7] Possibly, in the dilute solutions we use, the temperature coefficient of the decomposition of oxalic acid alone becomes evident. It scarcely seems practical to use greater concentrations of uranyl acetate in cold climates.

and character of the flasks used. Uranyl acetate-oxalic acid solution exposed on a surface of glazed black paper was decomposed in a ratio of 0.73 to 1 for glazed white paper and 0.74 for a black, dull background. Although there is practically no difference between a glazed black or a dull black background, it is better to adhere to one kind; therefore, the dull paper was selected.

A much greater variation is brought about by the materials of the flasks used, as well as by their size and shape. Obviously, a quartz flask is best, as it allows the ultra-violet rays to pass with a minimum of absorption, but the difference in absorption between quartz and Jena glass is not so great as might be supposed. Of greater influence is the size and shape of the vessel, that is, of the surface of liquid exposed. Bacon [8] has already pointed out that the rate of decomposition increases with the size of the flask; but even between flasks of the same capacity a variation is found which can readily be understood when we realize that two 100-cubic-centimeter Erlenmeyer flasks of Jena glass may differ 50 per cent in weight. Two such vessels, of equal capacity, of 100 cubic centimeters or under do not vary more than 2 per cent, and standardized flasks were used in our measurements, wherever possible.

Bacon [9] showed that the concentration of oxalic acid, excepting at great dilution, does not influence that speed of the reaction, and Bruner and Kozak have confirmed this result. Obviously, when decomposition of the acid reaches a point where its concentration has diminished below the critical one, the reaction will gradually diminish in rate; however, this point, in the solutions used for comparative measurements is not reached until more than 60 per cent of the acid has been decomposed, a number rarely reached in three-hour exposures, and even then the initial diminution is small, but the fact must be taken into consideration where longer exposures are resorted to.

To sum up. The decomposition of a solution of uranyl acetate-oxalic acid by the sunlight is by no means a perfect indicator, for comparative purposes, of the total ultra-violet photocatalytic effect of the sunlight, for it suffers from the errors outlined above; but when the nature of the measurements is taken into consideration and when we consider that the object to be attained is a knowledge of the average influence of the sunlight during long periods in various latitudes, small individual errors can be

[8] *Loc. cit.*, 288. [9] *Loc. cit.*, 285.

neglected. The most serious difficulty is the temperature coefficient, which would become apparent in colder climates, thus bringing down the average during the winter months, but where the temperature is known this can be compensated for by calculation; the flasks can be calibrated, the exposure made as far as possible from disturbing influences, and so, comparative measurements conducted with a sufficient degree of accuracy to give us a relative knowledge of the total influence of the rays of the sun in the more refrangible portions of the spectrum. If there are great contrasts between various regions, they will be apparent despite any errors in the method.

The basis of investigation having been determined, in addition to arranging for the carrying on of daily observations in Manila, I asked colleagues in various parts of the world to coöperate by a series of measurements with calibrated flasks and standard solutions exposed on a dull black surface, free from buildings, between the hours of 9 and 12. Returns from all the places coöperating are not yet at hand, but, so far results [10] can be reported from Kuala Lumpur [11] (latitude 3° 10′ north); Honolulu [12] (latitude 21° 18′ north); Washington [13] (latitude 38° 59′ north); Tucson, Arizona [14] (latitude 32° 12′ north) and Khartoum, Egypt [15] (latitude 15° 36′ north).

In Manila (Table I) the average per cent of oxalic acid decomposed for one hour during one year was 12.45, with a maximum of 17.8 for the highest observed day and a minimum of 1.15. The average of all days *above* the general mean was 14.65 and below 9.64. Strange to say, the lower average in Manila did not fall during the rainy months of July to October, but occurred in November, and the clear months of January, February,

[10] The figures presented in this paper are for some of the places subject to reinvestigation with standardized flasks and solutions, but, in time, as the work progresses, a large range of latitudes will be covered by exact comparative measurements.

[11] Through the kindness of the Institute for Medical Research, Dr. Henry M. Fraser, director, Mr. M. Barrowcliff making the titrations; a quartz flask was used.

[12] Through the kindness of the Hawaiian Agricultural Experiment Station, Dr. E. V. Wilcox, in charge, Mr. W. T. McGeorge making the titrations, using a 200-cubic-centimeter Erlenmeyer flask which has been sent to this laboratory for standardization since the above was written.

[13] Through the kindness of Dr. Raymond F. Bacon, Bureau of Chemistry.

[14] Through the kindness of Dr. H. Spoehr, Desert Laboratory.

[15] Through the kindness of the Wellcome Research Laboratories, Dr. Andrew Balfour, director, Dr. W. Beam, chemist.

and March do not show as high a figure as the comparatively cloudy ones of June and July.

Kuala Lumpur (Table II) shows a slightly higher average, 15.29 as against 12.45, but its maximum is somewhat higher (18.1 against 17.8) and its minimum much higher, namely 9.0 as against 1.15 for Manila. In other words, the insolation in regard to the rays under discussion in Kuala Lumpur on average clear days is practically the same as in Manila, but the cloudy and hazy weather of our island climate shuts off such a proportion of the sunlight that the total effect is that of a climate having less insolation; in other words, the difference between two places, one practically on the equator and the other 14° north is a meteorological one, and not due to any excess *per se* of the shorter wave lengths in the former.

Honolulu (Table III) shows an average of 13.81, or 1.36 higher than Manila and only 1.48 lower than Kuala Lumpur. It had an abnormal maximum in September, 1911, of 20.77, or higher than either of the so-called tropical places and a minimum of 3.48. However, the average of days above the average mean is 15.82 as against 16.52 for Kuala Lumpur. No months in Honolulu are as low as the lowest in Manila (September, December; 10.94 and 10.03 respectively). Therefore, Honolulu (21° 18′ north) has, as regards the photocatalytic action of the sun's rays, a climate much like that of Manila (14° 36′ north) and Kuala Lumpur (3° 10′ north), and the extraordinarily high days observed at that place indicate that at times the atmosphere on Hawaii is so free from disturbances, strata of varying density, or haze, as to allow even a greater proportion of the rays having photocatalytic action to reach the surface of the earth, than is the case in the more southern places. No one will venture to state that the sunlight is more oppressive in Honolulu than in the Philippines; indeed, the general temperature is lower, the average temperature at the time of the observation was 21°.1 to 22°.6, where ours in Manila was 30° to 35°, so that, if the slight temperature coefficient for the differences were to be taken into consideration, Honolulu [16] would result even higher. The difference between these three places under discussion is

[16] The figures from Honolulu are not final as the flask used was a 200-cubic-centimeter Jena glass Erlenmeyer and has not yet reached us for standardization. This will probably make the rate high, but, on the other hand, our standard is a quartz flask, which would offset the increase due to greater surface in the Honolulu flask, so that probably but little correction will be necessary in the end.

so slight that we can say that practically the photocatalytic action in all is the same.

Unfortunately, only a few data have reached us from Tucson, Arizona (32° 12′ north) (Table IV), and these for the month of October. They show a maximum of 13.4, or 4.4 less than that of Manila, and a minimum on one day of 7.7 or 2.5 greater than the average at this place. The temperature during the observation averaged about as it does here (28°.7), and higher than at Honolulu. Doubtless, when a longer series of observations is at hand from this interesting point, we will discover many days in Tucson where the maximum is as high as, or higher than, it is here, and an average about the same.

The data from Washington (Tables V and VI) need a little more careful analysis, as the methods followed were not always identical with the ones adopted by us as a standard, the hours of insolation were not always the same and recalculations need to be made in that respect. Nevertheless, so far as they are comparable, the results show that Washington, which has a winter climate, presumably more atmospheric disturbances, and many cloudy days and possibly but few absolutely clear days, can show at times as much effect as the four places discussed and an astonishingly high average of 11.80. One day in September gave an hourly decomposition, between 8.45 and 12.15 in the morning, of 19.14 per cent, and making allowance for the greater concentration of uranyl acetate used by Doctor Bacon, it would still be close to 16.00; and, in February, between the hours of 9 and 1, a decomposition, which, making allowance for the temperature coefficient and for the concentration of uranyl acetate, would certainly in Washington show but little difference between summer months (July, August, September), 11.0, and the winter months (December, January, February), 10.0. Making allowance for the greater concentration of uranyl acetate used by Bacon, the totals in Washington are lower by about 33 per cent than in Manila, excepting the one month, November, in Manila with an average of 9.97.

The results in Khartoum, Sudan (Table VII), are extremely interesting and, perhaps, the most instructive of the series. Khartoum is close to the desert and in about the same latitude as Manila. We find here, in observations extending through the months of September, October, and November, an average of 17.6 as measured by a standard quartz flask, or as much as 5.15 higher than Manila and 2.3 higher than Kuala Lumpur,

but this average is so high because of the remarkably uniform character of the insolation, the minimum being 14.7 as against 9.0 for Kuala Lumpur and 1.15 for Manila. The maximum observed day at Khartoum was 20.8, which is higher than any observation at Manila by 3.0, and 2.7 more than the highest observed at Kuala Lumpur, only two other observed days approaching this, one of 20.7 at Honolulu and the other 20.6 at Baguio in the Philippines, at an altitude of 1,432 meters. In Khartoum, out of sixty-six days of observation, no less than fifty-two gave decompositions between 16.7 and 17.9 and eleven between 17.9 and 18.6. In Khartoum, therefore, we have a remarkably uniform, high insolation so far as the portion of the spectrum under consideration is concerned; but, nevertheless, the days of maximum illumination do not materially differ from those in the other localities, so that the absolute intensity of the ultra-violet illumination which *may* reach the earth on perfectly clear days does not materially differ, the distinction being meteorological. If we consider this uniformly high rate and its causes, it is evident that the reverse can also be true and it would be possible to have so-called tropical climates where cloud interference and other causes would bring the average illumination below that in temperate zones. The temperatures of observation at Khartoum were somewhat higher than at Manila and Kuala Lumpur, but we observe that days of maximum temperature are not necessarily days of maximum photocatalytic decomposition.

Another interesting comparison is furnished by Bruner and Kozak[17] working in Krakau (53° 40′ north) on bright, sunshiny days in the spring and summer, the solutions in test tubes being exposed between the hours of 10 and 2. The background is not stated, but as they worked before an open window it is to be presumed that reflections did not play as important a part as with flasks placed on white paper, although the buildings had to be considered. As the work was done in test tubes, we can not conclusively compare results, the variation owing to the shape of container might be considerable in amount, but still, these authors, with a solution corresponding to our standard, obtained a decomposition of 15 as the maximum in their observations, so that it is apparent that even in this latitude days occur with a photocatalytic reaction sufficiently high to be comparable with those in the Tropics.

[17] *Ibid.*, 35.

In order to compare a climate at higher altitude and but little north of Manila with that of the latter city itself, a series of observations was made at Baguio (Table VIII) (altitude 1,432 meters). The temperatures of the nights and in the shade at Baguio are so low that it is an ideal resort for recuperation from the lowland climate, yet the photocatalytic action is much the same, however, with this difference: The maximum at Baguio is higher than in the lowlands (20.6 as against 17.8), being in this respect like Honolulu (20.7). The average is 14.2, or 1.75 more than in Manila and 1.09 less than Kuala Lumpur and 0.39 more than Honolulu. The ascent of 1,432 meters has produced the same effect on the photocatalysis as a transfer to Honolulu. The black-bulb readings are practically the same. At Baguio, therefore, as we would expect, we encounter a climate in which the rays undergoing investigation are somewhat more intense than in the lowland. The average temperature in the sun during the observations was 7° to 8° lower than in Manila.

Manila and Baguio, at present, are the only places where the black-bulb thermometer readings are available simultaneously with the photocatalytic measurements, and a study of individual days demonstrates that the two figures, namely, black-bulb readings and percentage of oxalic acid decomposed are not by any means functions of each other; indeed, within reasonable limits they seem to be independent. Of course, it is understood that a certain relationship exists, because, naturally on clear, bright days both black-bulb and photocatalytic readings will be high, and both the reverse on cloudy ones. As an example of these variations, I can cite a few figures taken from daily observations:

Comparison between photocatalytic and black-bulb readings in Manila.

From 9 to 12 a. m.	Weather.	Photo-catalysis.	Black bulb (mean of 3 observations).
1910.			°C.
April 28	Clear	15.4	52.0
May 7	do	17.7	52.5
May 16	Slightly cloudy	13.4	54.0
May 18	Clear	16.4	52.0
June 9	do	14.7	54.5
July 5	Slightly cloudy	16.6	56.3

Comparisons of this kind can be extended almost indefinitely, but those given suffice to show that, in the same place and on apparently equally clear days, the relative proportions of the

rays in the various portions of the sun's spectrum may vary considerably.

So much, for the present, for the effect of the more refrangible rays of the sun's spectrum lying in the region of the blue to violet and beyond in the ultra-violet. To them, the greater part of the literature has attributed, in largest measure, the supposed untoward effects of the tropical sun, and to them have been attributed even grave morphologic changes sufficient to bring about permanent differences in races of the human family. So far as the work has gone it seems to develop that, if the so-called "actinic" rays in Manila are particularly objectionable, they are the same in Honolulu and for a certain time of the year even in Washington. However, the more we consider the ultra-violet rays of the sun's spectrum, taking cognizance of the fact that nowhere, whether in northern climates or in tropical ones, do they extend beyond 291 $\mu\mu$, understanding what a large proportion, if not all, of the direct rays are subjected to molecular scattering, reflection, and dispersion by the upper layers of the atmosphere, and noting the slight differences between the lowlands at Manila and highlands at Baguio, we are forced to the conclusion that, on clear days, when the sun is at the same angle, they are everywhere much alike in intensity. Indeed, it appears as if the greater part of these rays which reach the earth are diffused and not direct.

These considerations bring us to the much larger remainder of the spectrum which extends upward from the point mentioned into the red and infra-red and which would include the heat rays. That these are a most important factor is, of course, self-evident, and so we, in considering the subject, have not overlooked this fact, but means of direct measurement as in the case of a photocatalytic reaction are lacking. The black-bulb thermometer is variable and unsatisfactory. Better comparative data could be obtained if a series of readings of the total solar radiation per square centimeter of surface, normal to the ray of incidence, were available with the Angström pyrheliometer.

Such data as are available have been gathered by Dr. Herbert H. Kimball of the Mount Weather Observatory [18] in a summary which gives the most important figures for the present discussion. Comparisons are made of the annual maximum intensity of solar radiation at various points as follows:

[18] *Bull U. S. Mt. Weath. Obs.* (1910), 3, 100.

Station and latitude.	Intensity.
Cape Horn, 55° 31′ S.	1.47
Washington, 38° 54′ N.	1.44
Montpelier, 43° 36′ N.	1.60
Modena, 44° 39′ N.	1.37
Kief, 50° 24′ N.	1.39
Warsaw, 52° 13′ N.	1.35
Hald, 56° 25′ N.	1.32
Katherinenburg, 56° 50′ N.	1.58
Pavlovsk, 59° 41′ N.	1.48
Upsala, 59° 51′ N.	1.35
St. Petersburg, 59° 56′ N.	1.47
Treurenburg, 79° 55′ N.	1.29

These variations are not great, and such as appear, are attributed by Kimball to instrumental rather than to atmospheric conditions. Angström [19] publishes some results from Teneriffe (20° 30′ north) in which he compares Guimar (360 meters altitude) with Alta Vista (3,352 meters altitude) and obtains 1.38 at noon for Guimar and 1.618 for Alta Vista, the latter higher figure is to be expected owing to the altitude. The maximum observed by Dr. Rudolph Schneider at Vienna (48° 13′ north) [20] was 1.524 in February, and figures ranging from 1.00 to 1.455 are quite frequent; indeed, the observations for the time close to the noon hour in Vienna, although averaging somewhat lower, bear a remarkable resemblance to those in Washington, when we consider that Kimball worked only on clear days and Schneider made observations on days of partial cloud and even of fog. Mr. Harvey N. Davis, working at Providence, Rhode Island, in ten months observed a maximum of 1.328 in March, and in general his figures also bear a striking resemblance to those obtained in Vienna. Kimball, in discussing the annual march of radiation as compiled by him, states that "a rather surprising uniformity throughout the year (is shown) in the maximum intensity of radiation, the December minimum being only 8 per cent less than the April maximum." The departures by months from the average quinquennial mean show that there is a considerable variation by years, amounting to a minus quantity of as much as 18 per cent on the average for the year 1903. This diminution was widespread and such low times are periodic; the same is probably true of high periods, so that the absolute amount of insolation on the earth's surface may vary

[19] *Astrophys. Journ.* (1899), 9, 342.

[20] *Jahrb. d. k. k. Zentralanstalt f. Meteorol. u. Geodyn.* (1906), n f. 43, 12.

from year to year,[21] but such variations are not frequent enough or of great enough intensity to alter the picture as a whole.

Although the maximum radiation at the various points mentioned is very similar in all, yet if we take the annual totals, we find differences for such points as have been compared. Kimball [22] has calculated the average monthly totals for Washington and Warsaw for normal surfaces, and from them we can obtain the yearly totals, which for Washington are 254,026 and for Warsaw 216,200, so that Warsaw actually has 85 per cent of the radiation received at Washington, although it is 14° farther north.[23] Unfortunately, pyrheliometer readings for places in the Tropics are not at hand. We have ordered an Angström pyrheliometer nearly a year ago, but the instrument has not yet arrived. When it does, we will begin readings in Manila and thus obtain comparative data. Enough has been shown already to demonstrate that meteorological phenomena, percentage of possible sunshine, and varying atmospheric transmissibility have more influence than variation in the actual solar insolation on perfectly clear days, and it is evident that such factors can just as readily be introduced in the Tropics as in other regions of the earth.

Because data with the Angström pyrheliometer in the Tropics are lacking, we attempted to solve the problem, for the present, by having recourse to animal experiments.

In considering this second phase of the question, a few fundamental facts must be borne in mind. The air surrounding the earth absorbs the rays of the sun in a certain proportion, and another part is reduced by reflection, molecular scattering, and dispersion; this takes place in a greater proportion with the more refrangible than with the less refrangible rays, so that the light reaching the earth contains relatively a greater amount of the rays of the upper range of the visible spectrum and infrared than are in the sunlight before it strikes the atmospheric layer; indeed, all ultra-violet rays up to 291 $\mu\mu$ disappear. On the other hand, the dark heat vibrations of great wave length, radiating from the earth, are absorbed in great measure by the atmosphere. The coefficient of absorption of the air increases with increasing density, but it never reaches that of a solid or

[21] Kimball, *Ibid.*, 114, 115.

[22] *Ibid.*, 103.

[23] These computations for Warsaw cover the period from July 1, 1904, to December 31, 1906; the period for Washington from June, 1905, to March 21, 1910.

liquid substance, such as the soil and water which form the surface of the earth. The power of absorption of the air is influenced by such factors as humidity, actual nuclei or droplets, clouds, and other causes, just as it is by density; but moisture-laden air relatively does not absorb as great a proportion of the rays of lower refrangibility as it does of higher. It is for this reason that air temperatures at higher altitudes are lower than in the lowlands, although the effects on solid objects, such as the black-bulb thermometer, may be greater. This may be shown by a comparison of some black-bulb thermometer readings in different parts of the world, which I have gathered for other purposes. At Davos, Switzerland (altitude 1,559 meters), the average of maximum black-bulb readings for three years was 53°.8, with a highest absolute maximum of 67° in 1910. Compare this with Manila, where the maximum for one year (1910–1911) was 56°; or with Helwan, Egypt, where the highest observed was 70°.8 during a period of three years; or with Alexandria, Egypt, with a maximum of 57° during the same period. Of course, there are places on the edge of the desert, where the atmosphere is exceptionally clear and where reflected light is present in great proportion, that exceed these figures, so, for example, Cairo, in May and August, 1909, shows a maximum of 79°.5; and Aswan Reservoir, in June, 1910, of 81°. However, in contradistinction to these desert places, we have another remarkably high black-bulb reading at high altitude, in Leh (Thibet), (altitude 3,517 meters) of 101°.7 with a shade temperature of 23°.9. Of course, these figures refer to maxima only, and do not take into consideration averages, or the shade temperatures, which may be high or low, but it is evident that the occurrence of days of extreme insolation is not so much a matter of latitude as of situation, and it is evident that even in the Tropics we might come to averages decidedly lower than in certain more northern, temperate climates. It is obvious that in any one of the places mentioned, a living body might encounter days in which it would be heated by solar radiation to a much greater extent than in the Tropics, and the only question would be whether the possibility of cooling, such as is brought about by low air temperature, low humidity, wind, or other means would compensate to avoid the effects of such insolation.

A body exposed to the sun absorbs a portion of the rays and reflects a portion of them, the most perfect absorption being that of as nearly ideally black a substance as is possible. The body would go on storing the energy so conveyed to it indefinitely,

were it not to lose it by radiation or convection (conduction), and the rate of this loss increases in proportion to the energy added to the body by radiation, until an equilibrium is reached. Black bodies, while absorbing the radiations readily, also radiate readily, so that it may come about that a black surface, exposed to the sun, may become little, if any, hotter than one of lighter color under similar circumstances.

It is a well-known fact that the ultra-violet rays are promptly fatal to almost all the lower organisms, such as bacteria, amœbæ, and protozoa; the heat effect on them being much less, and only apparent in so far as above certain temperatures they can not live. As we ascend high enough in the orders of animals, devices for regulating the losses of heat begin to appear, until, in birds and mammals, they are so well developed that but little variation in blood temperature is observable under the most diverse conditions of life, and hence a study of the effects of the lower rays of the sun's spectrum on such organisms, under normal and abnormal conditions, is most promising.

Such a study was undertaken by Dr. Hans Aron of the department of physiology of the University of the Philippines in conjunction with our other sunlight work, and his first results have recently appeared.[24]

The first problem was to construct apparatus for thermometric work which could easily be handled so as to give the subdermal, rectal, and skin temperatures quickly and accurately within 0°.1. This was finally accomplished by a series of specially prepared thermocouples, temperatures being read by a tangent galvanometer.[25]

Perhaps the most instructive and interesting results were obtained with monkeys, animals which naturally are at home in the Tropics and which, we should suppose, would best be able to withstand the effects of sunlight. The system of sweat glands in monkeys is not so highly organized as in man [26] and

[24] *This Journal, Sec. B* (1911), 6, 101.

[25] *Ibid.*, 117.

[26] Aron, *Ibid.*, 110, makes the statement that monkeys have no sweat glands. During the time at his disposal, as he was going on long leave, Aron did not investigate this question completely. Doctor Shaklee of the department of pharmacology, University of the Philippines, states that monkeys do have sweat glands. See also Blaschko, *Arch. f. mikros. Anat.* (1887), 30; Wimpfelheimer, *Anat. Hefte* (1907), 34, 492. Krause, Beiträge z. Kenntniss der Haut d. Affen; Inaug. Dissertat., Berlin (1888) is not available. Sweat glands have been found by Mr. Clark of the department of anatomy, University of the Philippines, in the forehead, hands, feet, axillæ, and abdomina of our monkeys.

their physical heat regulation is to a much greater extent brought about by water evaporated from the lungs and mouth through increased respiration. The normal subcutaneous temperature of the animals, in the shade, varies from 36°.6 to 38°; the rectal from 37°.9 to 39°.4. The subcutaneous temperature, therefore, is somewhat below the rectal. However, as soon as the animal is placed in the sun, the subcutaneous temperature rises above the rectal and remains so to the end of the experiment, so that the inside of the body now receives heat from the periphery. The animals exposed to the full sun,[27] without protection or artificial means of lowering the temperature, die in from one hour to one hour and fifty minutes; the exposures being either in the morning between 10 and 11, or in some cases in the afternoon between 2 and 4, in the months of November and January. Both the skin and rectal temperatures steadily rise during these exposures, the maxima before death being 43°.5 and 42°.7 to 46°.3 and 44°.8 respectively.

Entirely different results are obtained if the animals are shaded, even by a small area of shade such as an umbrella or a board, all other conditions being similar, so that the direct rays are excluded, the diffuse rays, excepting those cut off by the shade, still being available. Under these circumstances the skin and rectal temperatures never exceed 40° and the animals remain healthy. Similar results are obtained if the animals are exposed to full insolation, but care is taken to conduct away the excessive heat increment by means of a brisk current of air from a fan. Under these circumstances the subcutaneous and rectal temperatures remain the same as when the animal is shaded, never rising above 40°.6, and the monkey remains perfectly well. In this last form of experiment the monkey is exposed to all the rays of the sun, including those of lesser refrangibility, heat waves alone being conducted away. If untoward effects are to be attributed to the absorption of the ultra-violet rays, then surely the animal is in the same condition to absorb the latter as he is when no blast of air is present, and their effect should be apparent. On absorption, a large proportion of these rays is presumably converted to heat and conducted away as such, so that it can be assumed that the effects which we observe on exposing these animals to the sun is one of heat, and these conclusions are borne out at autopsy where post-mortem exam-

[27] The proportion of the body exposed to the rays in the full sunlight, even toward noon, is the lesser part of the whole, as more than one-half of the body is in its own shade.

inations give protocols clearly pointing to heat stroke. Monkeys enclosed in tight boxes, with only the head exposed, and placed in the full sun, suffer no inconvenience, although the hair temperature on the scalp may reach 47°. The effects, therefore, are not due to penetration of the sun's rays to the brain. Of course, it must be understood that the monkey's skin is protected by fur and is not sensitive to the irritating effects of the ultra-violet rays, such as would be the skin of a Caucasian[28] who, as we all know, if exposed to the sun, would be sunburned, whether in a strong blast of air or not. This latter effect is due to the ultra-violet portion of the spectrum, and as the latter rays have but little power of penetration the skin can in time amply protect itself by pigmentation. Even though pigmented, as is the monkey's skin and hence not subject to sunburn, the heat effect would still remain and bring about the results of excessive heat exposure in exactly the same manner as in the case of the monkeys. The ultra-violet rays are easily guarded against, the heat rays not.

Experiments on man exposed to the sun are equally interesting. In man we have a subject with highly developed sweat glands, so that the means of heat regulation by evaporation are much more complete than in dogs, rabbits, or monkeys.

Skin temperatures of men in this climate in the shade under normal conditions vary, as measured by the apparatus constructed in Manila, within the extreme limits of 31° to 34°, being higher over the muscular and fatty parts of the body than over bony structures lying close to the surface. These variations must be considered and therefore measurements on the changes of temperature, when exposures are made, must be taken at various points of the body.

After ten to fifteen minutes' exposure to the sun, the skin temperature of an American subject, on the sunny side, rose to 35°.8, 35°.2, and 41°.8 on the arm, cheek, and chest in the order named, whereas on the shaded side these temperatures were 31°.5 and 31°.9 on the first two; the hair temperature rose to 46°. The corresponding temperatures in a Filipino, after thirty minutes, were 36°.9, 35°.4, and 39°.8, the shade temperatures being 32°.5, 31°.9, and 32°.5 the differences being, in regard to the brown skin, +1°.1, +0°.2, and −1°. A comparative measurement of an American and Filipino, side

[28] Aron exposed a shaved monkey. It died within one hour, with the same autopsy protocol as others. Its temperature rose more rapidly than that of the others, reaching 45°.5 and 44°.4.

by side, on the same day, after fifteen minutes' exposure was as follows: American, 35°.6 and 34°.0 on the arm and cheek; Filipino, 34°.8 and 33°.9; the difference being −0°.8 and −0°.1 in favor of the Filipino. In another series of experiments, there were compared a Spanish-Eurasian and a Filipino with dark brown skin. After one-half hour in the sun, the records were as follows: Spanish, 37°.1, 36°.5, and 35°.0 for the arm, face, and the back of the neck; whereas for the Filipino they were 36°.3, 36°.3, and 34°.6, differences of −0°.8, −0°.2, and −0°.4 in favor of the latter; and in a second series, after ten minutes, 36°.2, 35°.2, and 35°.4 as against 36°.2, 34°.1, and 34°.8; differences of −0°.0, −1°.1, and −0°.6. These differences are but slight as between the white and dark skin, the majority of observations being somewhat in favor of a lower skin temperature for the Filipino, but after fifteen minutes both the American and Spanish-Eurasian were sweating slightly, whereas this was not apparent with the Filipinos. Another series of results was obtained after longer exposures, when all of the subjects were sweating freely and only slight differences were observed, thus the Spanish-Eurasian after forty-five minutes in the sun, having performed muscular work, showed temperatures of 33°.2, 33°.0, and 33°.2 as against 33°.4, 32°.6, and 32°.8, differences of −0°.2, −0°.4, and −0°.4. At rest, lying on a cot, after one hour's exposure, the skin temperatures were 34°.6, 35°.2, and 35°.0 as against 34°.8, 34°.8, and 34°.4; differences of +0°.2, −0°.4, and −0°.6. It will be seen that the skin temperatures, at rest, do not fall as rapidly as when the subject is doing muscular exercise, but yet, after one hour, they are from 0° to 1°.6 lower than the earlier maximum, except in one observation, when the rise was 0°.7. The fifty minutes of exposure, therefore, have caused no practical rise over the temperatures after the first ten minutes, and indeed a lowering in all but one instance, the excessive heat received by radiation being taken care of by the usual means and by evaporation through perspiration, whereas in the case of the monkeys there was a steady rise up to the lethal point. In a final series of experiments, an American and a Filipino were exposed side by side for thirty minutes. In this case the final temperatures were as follows: American, 36°.9, 36°.3, and 36°.5 as against 36°.1, 35°.4, and 35°.4 for the Filipino, differences of −0°.8, −0°.9, and −1°.1 in favor of the dark-skinned man. Therefore, out of 14 observations, 12 showed a lower skin temperature for the Malay race, so that the series results slightly in favor

of the darker skin, the highest of all observations being 37°.4 in an American, on the cheek, after exposure for twenty-five minutes.

These measurements, while showing conclusively that the adaptable mechanism for heat regulation possessed by human beings is sufficient to lower the temperature and protect the individual from such fatal effects as are observed in monkeys, still did not appear sufficiently conclusive as regards the differences between the white and dark skins. Therefore, both for the purpose of comparing the effects of insolation at high altitudes with those at sea-level as well as for a further study of the possible differences between the two colors, the experiments of Aron were repeated in Baguio by H. D. Gibbs of the laboratory of organic chemistry of the Bureau of Science. The skin temperature in Baguio rose to higher points than those observed by Aron in Manila.

This may in part be accounted for by the technique employed, for Aron warmed the thermometric junction in the palm of the hand and then placed it on the part of the skin to be measured, whereas Gibbs commenced measurements a short distance from the desired spot and, as soon as the maximum deviation of the galvanometer was reached, moved the thermocouple nearer the place, and when the instrument was again at rest, placed it in the final position. However, after taking the differences in technique into consideration, the absolute values recorded for the upper altitude are still higher than those for the lower.

Comparison between an American and two dark-skinned Igorots, A and B, taken over the level of the third dorsal vertebra, the fifth dorsal vertebra, and over the upper angle of the scapula, in the order named, were as follows: The average of shade temperatures of all subjects being 30°.06, 32°.4, and 33°.52, but it must be recorded that a slight breeze affected the American's temperature. After twenty-seven minutes the American reached maxima of 37°.65, 37°.15, and 37°.95; Igorot A, after thirty-six minutes, measured 38°.05, 38°.35, and 37°.9; whereas Igorot B, after thirty-three minutes, recorded 37°.4, 37°.9, and 36°.8, or temperatures averaging +0°.73 against the dark skin of A and −0°.05 in favor of B. The thigh of A, which was steadily exposed to the sun, showed the remarkable skin temperature of 52°.7.[29]

[29] Wind screens were used to protect the subjects from the cooling effects of the breeze, but occasional eddies would reach the men in spite of all precautions.

In the first ten to fifteen minutes the temperature of the white skin rose more rapidly than the dark; namely, an average of 6°.25 as against 2°.60, but then the white skin began at a lower shade temperature; and if the difference is taken into account, the white skin rose 2°.79 as against 2°.60, so that there is but little difference in this respect. In the final temperatures, one Igorot reached 0°.73 more than the American, while the other was practically the same.

In a second series of measurements, a Canadian, a Filipino, and an American Negro were compared. The shade temperature averaged 33°.65, 33°.97, and 34°.15, or higher by 0°.63 to 3°.59 than in the previous experiment. After thirty-one minutes the Canadian reached 38°.55, 37°.40, and 38°.85; the Tagalog and Negro, after twenty-nine minutes, reached 38°.75, 38°.80, and 38°.78 and 39°.32, 38°.85, and 39°.15 respectively. Therefore, the differences were +0°.20, +1°.40, and −0°.07 against the Tagalog and +0°.77, +1°.45, and 0°.30 against the Negro. In the first seven minutes the Canadian recorded a rise of 4°.3, 3°.2, and 4°.35; the Tagalog, in eight minutes, 5°.55, 5°.40, and 5°.25; and the Negro, 3°.90, 3°.95, and 4°.50, so that the temperature of the Tagalog rose decidedly more rapidly than that of either of the others, but the Negro had an initial shade temperature higher than those of the Canadian and Tagalog by somewhat more than 1°.0. The final temperatures, therefore, are decidedly against the Negro, slightly so against the Tagalog, and in favor of the Canadian as against the other two. Taking these experiments into consideration and comparing them with the indices we use in Manila, it may be said that, as regards rise in temperature on exposure to the sun, the white and brown skins are about equal, with a slight factor in favor of the white, but that in the case of the very dark-skinned Negro, the temperature on exposure reaches a decidedly higher point than it does with either of the others.

One fact very strikingly appears from these measurements, namely, that the skin temperatures of all the subjects reach higher points in the sunlight at the high altitude of Benguet than they do in Manila, despite the lower shade temperature at the former location. However, the measurements show that perspiration begins at an earlier period in the lowlands.

In explanation of the above results, it may be taken for granted that the dark skin of the Negro will absorb heat more readily than the light ones of the American or Canadian, but

then, it will also radiate more readily, so that heat rapidly taken up on the sunny side will also rapidly be lost on the shaded one and it is the balance between the two which determines the ultimate degree of rise in temperature. This balance evidently results against the Negro. On the other hand, with the white skin we have the phenomenon of sunburn, with its resultant irritation of the nerve-endings and hyperæmia of the peripheral tissues, and this would cause a rise which, apparently, just about offsets the rise in the brown skin due to the pigmentation.

The decidedly higher skin temperature of the Negro made it of importance to investigate the behavior of animals of such decided differences in color that the contrasts would show with greater certainty. For this purpose 6 rabbits: 2 pure white, 2 gray, and 2 black, were used. These were placed in the sun, side by side, with only a few centimeters between, the subcutaneous temperature being taken through a small slit in the lower dorsal region. The first 3 animals remained in the sun for thirty-six minutes, from 9.10 to 9.46 in the morning, at which time they were returned to the shade. The white and gray rabbits soon recovered from the exposure, but the black one died at 12.30 in the afternoon.

The subcutaneous temperatures rose from 38°.6 for the white and gray and 41°.8 for the black to a final height of 41°.0, 42°.8, and 44°.2 for white, gray, and black in the order named.

In the second series the black and gray animals were strong and healthy specimens, whereas the white was much weaker.

The subcutaneous temperatures at the beginning were 38°.0, 37°.85, and 37°.7; the exposures were for one hour and thirty minutes, from 9.02 to 10.32 in the morning. The black rabbit reached a maximum of 47°.8 in thirty-one minutes and then died; the gray rabbit, a final temperature of 44°.9 in one hour and twenty-six minutes, when it died; the white rabbit a final temperature of 45°.7, and when put in the shade, it recovered although much exhausted.[30]

These experiments appear conclusive. None of the animals suffer from sunburn as does the white man, and it is evident that the darker the coat, the greater the heat absorption and the more apparent do the effects of insolation become. It appears

[30] Monkeys exposed to the sun at Baguio developed higher subcutaneous temperatures than in Manila; a maximum of 54° being reached in one case before death, and in another 48°.3 before death. Rectal temperatures were not taken.

evident when these results are compared with those observed for human beings that, all other things being equal, the Negro will suffer more from the heat effects than the lighter-skinned races.

Chamberlain,[31] in a series of observations in which he carefully compared the relative resistance to the Philippine climate of blond and brunette types of soldiers, concludes that the evidence is conflicting and that from a consideration of all the facts the blonds are quite as well able as the brunettes to withstand the Philippine climate. The effect of the rays of greater refrangibility in the violet and ultra-violet portions of the spectrum are not the important factors, except in so far as they cause sunburn and subsequent excessive pigmentation, but protection from these rays is so easily accomplished and has been accomplished so long as man has worn clothes, that skin-color can not be an important factor in determining adaptability to climate; that question is a morphologic one which takes into consideration many more factors than skin-color alone. A white cotton shirt and white trousers are sufficient to protect against sunburn, and hence against the ultra-violet rays.

Phalen [32] compared 500 troops in the Philippines, dressed in orange-red underclothing with 500 dressed in white. The experiments show that the test underclothing added materially to the burden of heat upon the system and that the white underclothes of practically the same weight were superior in this respect. In fact the lighter and whiter the clothing, the better is it adapted to protection against the sunlight; indeed, in the Tropics, were it possible, the ideal protection simply would be an umbrella. The lowering of temperature in man is brought about by evaporation of perspiration, and the better the facilities offered for this purpose, the better off will the individual be.

Consequently, relative humidity plays a most important part in the study of the influence of the sunlight. The higher the relative humidity, other things being equal, the less readily will evaporation take place and the less complete will be the result in lowering the temperature. As the lowering is brought about by the evaporation of sweat, it necessarily follows that those races with the best developed sweat glands will have an

[31] *This Journal, Sec. B* (1911), 6, 427.
[32] *This Journal, Sec. B* (1910), 5, 525.

advantage. The greater the surface for evaporation, the greater will be its effect. For this reason it seemed advisable to investigate the relative number of sweat glands developed in the white and Malay, and Mr. Elbert Clark of the department of anatomy of the University of the Philippines has pursued this subject. After many measurements on American soldiers, Philippine scouts, and persons of both colors in civil life, he has come to the conclusion that the Malay possesses from 12 to 15 per cent more sweat glands than the white. Measurements on Negroes are not yet complete enough to warrant a final statement, but the results, so far, show that the race has perhaps an excess of 7 per cent. The few counts which have been made on Negritos give 26.82 per cent excess for adults and 67.54 for youths.[33] Neither can anything be said as to the relative capacity of the individual glands in the two races.

In this respect, then, the Malay possesses a decided advantage over the white man which the latter can only offset by seeking greater shade, but, to judge from the data which have been given, ample protection at all times can be given to all races by sufficient shade, as owing to that protection the temperature does not rise, and indeed is somewhat lower, apparently, in the white. Given ample shade, and any race is adapted to resist the sun alone of tropical climates; the white man should be better able to do so than the colored. It would seem to me as if the dark skin of the Negro was not a result of excessive insolation, for it is certain that in a state of nature the Negro would seek the shade, just as monkeys do, intuitively, and in the earliest times he probably was exclusively a forest dweller. The color of his skin would, therefore, more probably be protective just as protective coloring is developed in animals other than man.

One other factor must be considered in discussing the influence of latitude upon the total heat effect throughout the year, and this factor would not in general appear as such by any of the means of measurement mentioned in the previous part of this paper, namely, the absorption of heat by the earth's surface and its radiation therefrom. This factor will naturally vary with different regions according to the color of the surface exposed,

[33] Measurements on Negroes when continued in a longer series will probably result in higher figures. The endeavor will be made to secure more Negritos.

being least in green surfaces of vegetation and greatest in rocks or red, clay soil such as is common in India under the name of laterite. The actual number of hours of insolation per year on the earth's surface, were the sky always clear, is greatest at the equator and diminishes toward the poles, the ratio between 0° and 45° being 1.83 to 1.34, although in the longer days in the temperate zone the sunshine reaching the earth when the sun is near sunrise or sunset is only a small proportion of that at midday. As a result we have in the Tropics the added factor of greater radiation from the earth's surface to augment the direct influence of the sun, so that, as it has been shown above that the influence of heat is the chief one to consider, this increment due to radiation from the earth would be of decided influence in the Tropics. In middle latitudes this factor has been determined as about 0.1 of the solar insolation at midday, but it acts during the entire twenty-four hours, whereas the sun rises and sets.[34] In northern climates the hours of insolation during the short days are so few and the hours of radiation so many during the night that the surface of the earth actually steadily cools at certain times of the year, making one of the factors which causes a winter season.

Probably, untoward effects attributed to the tropical sun, if any, are caused by the evenness of the climate rather than by the differences of insolation at any one time; the absence of severe contrasts, such as are given by the winters and the monotony having their effect. However, Chamberlain [35] investigated the systolic blood pressure and pulse rate in 6,847 readings in 1,489 individuals of varying lengths of residence in the Philippines and found that:

"Reduced to the basis of a 12.5-centimeter armlet * * * the average blood pressure for healthy white men in the Philippines (is) 115 millimeters for those between 15 and 30 years of age and 118 millimeters for those from 30 to 40 years old. These figures are little if any below those to be expected in a temperate climate when a 12.5-centimeter cuff is employed. * * * There was no progressive tendency for the pressure to increase or to decrease with continued tropical residence up to a little over three years, beyond which point our observations do not extend." This author also found that "we may * * * conclude that the mean blood pressure for

[34] Hann, Handbuch der Klimatologie (1910), 2, 23, calls attention to measurements in Chinchochro, Laoango coast, near the equator. The regular measurements of the surface of the earth exposed to the sun gave temperatures generally over 75°, often 80°, and one time nearly 85° C.

[35] *This Journal, Sec. B* (1911), 6, 437.

Filipinos during the period of 15 to 40 years of age (average about 25 years) is 115 to 116 millimeters and that it does not differ from the pressure at the same ages for Americans residing in the Philippines. For neither race is it very materially below the figure to be expected for white men residing in temperate climates."

Mr. H. D. Gibbs has endeavored in the laboratory of organic chemistry of the Bureau of Science to determine what changes are brought about in the animal economy by exposure to severe sunlight, and has obtained indications in rabbits of the formation of methæmoglobin, but the work is not sufficiently advanced to be definite. A report on these results will therefore be postponed.

From all of our observations it would seem legitimate to draw the conclusion that a climate such as we have in the Philippines, where we are surrounded by the sea which modifies the extremes of temperature and where we have such a large proportion of cloud, is not by any means deleterious to the white man if he takes ordinary precautions which are not as elaborate as those he would take in a northern climate to keep out the cold. The differences in maximum insolation as compared with temperate regions are not great, if any, and many days occur in which the effect of the sunlight is greatly modified. The individual needs only to seek the shade to avoid any deleterious results from even the greatest insolation. If individuals must be exposed to the sun, as is the case with troops on the march, they can be given adequate protection by light, preferably white, clothing and helmets, but it must be remembered, as shown above, that perspiration is a great factor in keeping the man normal under these conditions and that, during exercise in hot weather much water is lost during the day. Many of the untoward effects attributed to the sun are probably due to the rapid loss of water from the system and could be avoided if the individual were in a position to drink enough to preserve the equilibrium. Two canteenfuls per man are certainly not sufficient. The temptation to drink available water along the road, also, may become irresistible, and sickness caused by infection from such a source may be attributed to the sun as a predisposing factor. Even in places like Khartoum, where the average effect of insolation is much higher than in Manila, the results can be avoided just as they can be here, and it is only in the places where the radiation from the earth at night is so great that no relief is experienced from excessive heat, that the climate may become such as to preclude the possibility of persons unaccustomed to such conditions living in health. In the Philippines

the nights are rarely too hot for comfort and they may even be quite cool.

Before concluding, I wish to call attention to another phenomenon to which I referred two years ago in a previous paper on this subject and which, at the time, I said merited further investigation. Bacon [36] observed that the fall of the aluminium leaves in a fontanoscope, according to Engler and Sieveking, was much accelerated when the apparatus was placed in the sunlight, as compared with the dark. At that time this result was attributed to the ionization of the air by the sunlight of Manila. Since that time, we have modified the apparatus by carefully enclosing it in a glass jar which could thoroughly be dried and which avoided outside influences. Almost 2,000 readings were made both in Manila and Baguio with currents varying from 300 to 1,000 liters per hour. The data are too voluminous to quote here, but will be published by Mr. H. D. Gibbs of the laboratory of organic chemistry, Bureau of Science, at a later date. The rate varies from day to day, but with the modified apparatus the highest fall was far below those obtained by Bacon, and a careful analysis shows that the rate during sunlight does not materially differ from that during cloudy weather. Bacon's results can therefore be attributed to outside disturbing factors, as the apparatus during Mr. Gibbs's measurements was removed from outside influences. This work is being continued so as to include the total ionization of the air in Manila and will also give the data in regard to the ionization due to radio-activity, the measurements for which are being made by Dr. J. R. Wright of the department of physics of the University of the Philippines. Simpson and Wright [37] in a study of atmospheric electricity over the ocean, the series extending from the equator southward, did not observe any phenomena which would indicate any unusual ionization of the air by the ultra-violet rays of the sunlight.

Although the spectrum of the sun as shown by the spectrograph does not extend beyond 291 $\mu\mu$, still it may be possible that we receive rays the nature of which we have not yet determined and which, with our present physical technique, we can not determine and which may have an influence in the phenomena of insolation. The discovery of such rays, if they exist, will form an interesting and important chapter in the work on this subject.

[36] *This Journal, Sec. A* (1910), 5, 267.
[37] *Proc. Roy. Soc. London, Ser. A* (1911), 85, 175.

TABLE I.—*Manila. Rate for one hour.*

Month.	Average.	Maximum.	Minimum.	Mean maximum.	Mean minimum.	Average temperature.	Observatory thermometer readings.	Black-bulb readings.	Clear days.
1910.									
May	13.21	17.7	3.21	15.42	6.88	32.09	37.2	46.9	10 out of 27.
June	12.62	17.1	6.08	15.87	10.05	32.85	38.0	47.6	8 out of 25.
July	13.74	17.8	4.61	15.95	10.07	33.37	36.6	47.6	7 out of 24.
August	13.11	17.5	5.11	15.14	10.07	31.27	39.3	49.3	3 out of 25.
September	10.94	17.1	1.15	13.51	6.05	30.30	35.2	47.2	4 out of 26.
October	11.78	17.45	1.71	13.88	9.33	30.61	35.5	45.9	4 out of 26.
November	9.97	17.38	1.47	13.78	6.16	28.57	33.8	44.5	1 out of 24.
December	10.03	14.61	1.19	12.44	7.12	29.18	33.1	43.9	3 out of 22.
1911.									
January	12.69	17.64	7.99	14.91	11.20	30.51	35.1	45.3	5 out of 19.
February	11.54	16.32	4.98	14.01	7.97	30.14	34.0	42.0	5 out of 22.
March	13.13	17.35	4.64	15.24	10.45		36.6	46.0	11 out of 25.
April	13.88	17.60	10.49	15.94	12.41		37.4	48.0	6 out of 17.
May	13.27	15.09	10.28	15.48	13.06		39.1	50.3	11 out of 22.
June	14.07	16.38	12.80	15.00	13.42		37.9	49.5	6 out of 17.
July	11.83	14.06	7.11	13.18	10.22		35.7	45.1	0 out of 11.
Average	12.45	16.82	5.52	14.65	9.64	30.889	36.3	46.6	

TABLE II.—*Kuala Lumpur. Rate for one hour.*

Month.	Average.	Maximum.	Minimum.	Mean maximum.	Mean minimum.	Clear days.	Temperature.
1911.							
March	15.27	17.3	12.2	16.70	13.56	5 out of 11	31.57
April	15.21	17.5	10.4	16.76	12.79	10 out of 18	32.56
May	15.25	17.5	9.0	16.66	11.25	7 out of 23	32.42
June	15.45	17.3	12.2	16.7	13.97	5 out of 13	32.80
July	14.53	17.3	9.3	15.6	13.09	5 out of 26	32.72
August	15.39	18.1	11.6	16.2	13.62	6 out of 25	32.06
September	15.94	17.5	12.0	16.91	13.99	11 out of 21	31.76
Average	15.29	17.5	11.0	16.52	13.18		32.27

TABLE III.—*Honolulu, Hawaii.*

Month.	Average.	Maximum.	Minimum.	Mean maximum.	Mean minimum.	Average temperature.	Clear days.
1911.							
January	11.78	17.40	3.77	14.67	7.47	21.1	0.
February	13.49	16.71	6.29	15.57	10.72	21.1	7 out of 21.
March	13.82	17.76	3.48	16.26	9.48	21.6	15 out of 25.
April	14.30	17.99	5.46	16.04	10.83	22.8	13 out of 24.
May	13.85	17.64	7.89	15.87	10.62	21.1	9 out of 26.
June	13.64	17.41	6.62	15.46	11.34	21.1	14 out of 25.
July	12.45	16.85	5.53	14.53	9.35	21.1	3 out of 25.
August	14.58	18.51	9.08	16.28	11.92	21.6	10 out of 23.
September	15.30	20.77	6.57	17.07	12.02	21.1	12 out of 20.
October	14.96	18.37	8.24	16.46	12.47	21.1	14 out of 24.
Average	13.81	17.94	6.29	15.82	10.62	21.1	

TABLE IV.—*Tucson, Arizona.*

Date.	Decomposition for one hour.	Temperature.	Remarks.
1910.			
October 24	12.0		
October 25	7.7	32	Thin clouds.
October 26	10.5	23	Overcast, sun 11 to 12.
October 27	13.4	30	Clear, slight cirrus.
October 28	13.2	28	Dust storm.
October 29	12.9	30	Very thin clouds.
October 30	11.1	29	Clear.
Average	11.5	28.7	
Maximum	13.4		
Minimum	7.7		

TABLE V.—*Washington, D. C.*

Months.	Average.	Maximum.	Minimum.	Mean maximum.	Mean minimum.	Remarks.	Clear days.
1910.							
June	9.91	12.70	6.54	11.55	7.18		5 out of 8.
July	11.19	15.60	1.70	12.80	7.19		10 out of 14.
August	10.37	15.75	1.85	12.75	6.81		8 out of 10.
September	11.38	19.14	3.83	13.49	8.37		10 out of 18.
October	12.91	16.66	4.37	15.05	10.16		14 out of 16.
November	9.18	15.33	2.66	11.55	6.35	Without temperature coefficient.	4 out of 9.
December	8.01	11.11	3.50	9.85	6.49		8 out of 11.
1911.							
January	9.08	11.50	6.66	10.34	8.07		8 out of 9.
February	12.60	14.24	9.66	13.88	10.68		4 out of 5.
March	11.96	12.63	11.29	12.63	11.29		2 out of 2.
April	13.09	13.48	12.32	13.48	12.32		3 out of 3.
Average	10.88	14.37	5.85	12.48	8.63		
May	7.21	8.21	5.72	7.92	6.27	With our solution.	7 out of 7.

TABLE VI.—*Washington, D. C.*

Months.	Average.	Maximum.	Minimum.	Mean maximum.	Mean minimum.	Remarks.	Clear days.
1910.							
June	9.91	12.70	6.54	11.55	7.18		5 out of 8.
July	11.19	15.60	1.70	12.80	7.19		10 out of 14.
August	10.37	15.75	1.85	12.75	6.81		8 out of 10.
September	11.38	19.14	3.83	13.49	8.37		10 out of 18.
October	12.91	16.66	4.37	15.05	10.16		14 out of 16.
November	11.29	17.33	3.54	14.38	8.82	With temperature coefficient.	4 out of 9.
December	11.51	15.85	5.00	14.15	9.27		8 out of 11.
1911.							
January	12.97	16.42	9.52	14.77	11.53		8 out of 9.
February	15.01	20.34	9.66	20.07	11.64		4 out of 5.
March	11.96	12.63	11.29	12.63	11.29		3 out of 3.
April	13.09	13.48	12.32	13.48	12.32		
Average	11.96	15.99	6.33	14.10	9.50		
May	7.21	8.21	5.72	7.92	6.27	With our solution.	7 out of 7.

TABLE VII.—*Khartoum, Egypt.*

Months.	Average.	Maximum.	Minimum.	Mean maximum.	Mean minimum.	Maximum temperature.	Clear days.
1911.							
September	17.4	19.6	14.8	17.8	16.5	40.2	12 out of 22.
October	17.8	20.8	16.1	18.7	17.3	38.9	22 out of 31.
November	17.4	17.8	16.7	17.7	17.0	35.4	10 out of 13.
Average	17.5	19.4	15.8	18.1	16.9	38.1	

TABLE VIII.—*Baguio. Rate for one hour.*

Months.	Average.	Maximum.	Minimum.	Mean maximum.	Mean minimum.	Observatory thermometer readings.	Black-bulb readings.	Clear days.
1911.								
March	12.5	18.7	6.9	16.2	8.2			5 out of 13.
April	16.1	20.6	8.3	17.9	12.1	27.3	51.2	3 out of 19.
May	16.2	19.4	11.1	17.7	14.0	27.5	51.4	
June	11.9	16.7	7.1					
Average	14.2	18.8	8.3	17.1	11.4			

MUCOCELE AND DIVERTICULUM OF THE VERMIFORM APPENDIX OF INFLAMMATORY ORIGIN.

By B. C. Crowell.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

While cystic dilatation of the vermiform appendix is in all probability not as rare an occurrence as the literature on the subject would suggest (Kelly, 68 cases), the scant attention accorded it in most text-books on pathology and the paucity of accurate microscopic descriptions which would enable one to form an idea of its pathogenesis amply justify further reports. Feré, in 1887, was the first to apply the term retention cyst, hydrops, or mucocele to that portion of the appendix in which dilatation had occurred, although the condition was first recognized by Virchow, who considered his case as one of colloid degeneration of the appendix.

When the lumen of the appendix becomes occluded at any point, the sequelæ in the distal portion depend upon various factors:

1. If it occur during the course of an acute appendicitis, the remainder of the appendix being also the seat of inflammation, it may result in healing, in perforation, or in gradual general diminution of the lumen of the appendix; that is, the ordinary obliterative appendicitis.

2. If, on the other hand, it occur as the result of a gradually progressing process, a mucocele may result and diverticula may form, the contents being at first mucoid, later clear and watery, and, perhaps, later more viscid and inspissated. For the production of the cystic dilatation, or mucocele, the necessary factors *a priori* are:

(*a*) *Gradual occlusion of one part.*—The cause of this may be a tumor, cicatricial stenosis such as occurs in the healing of ulcers, or angulation produced by peritoneal adhesions, and one case has been reported in which the appendicectomy wound broke down and rapidly healed under antisyphilitic treatment (Lilienthal).

(*b*) *Absence of infection with pyogenic organisms.*—If pyogenic organisms be present at the time of occlusion, or enter

through an incompletely occluded lumen, an empyæma rather than a mucocele may result.

(*c*) *A mucosa able to secrete faster than it can resorb.*—This predicates a functionating mucosa, that is, one in which too extensive pathological changes have not been produced by the causative factor upon which the occlusion depends, and unless secretion proceed more rapidly than resorption, dilatation will not occur. Bierhoff is of the opinion that dilatation is wanting when the mucosa is still able to resorb in the usual way. This latter point has been emphasized by several authors, whereas it would seem that in order to prevent dilatation, resorption through the mucous membrane must proceed more rapidly than under normal conditions, inasmuch as the normal outlet into the cæcum is occluded.

The relative infrequency of mucocele in comparison with other lesions of the appendix is thus seen to be accounted for by the stringency of the requisites for its production or the multiplicity of the factors which must be properly coördinated.

Occlusion under these conditions having been produced, the changes occurring in the distal portion follow in fairly definite order. The accumulation of retained secretion leads to dilatation and degenerative or atrophic changes in the mucosa and submucosa, along with a replacement fibrosis of the tunica muscularis, the fibrosis originating from both the subserous and submucous layers. Some muscular hypertrophy may take place, and if one or more portions of the wall have been unduly weakened by previous disease, for example, ulceration, a diverticulum, or diverticula may result. The changes in the character of the contents depend upon those in the mucosa. A mucoid degeneration of the epithelial elements of the mucosa is a comparatively early feature, leading to over-production of mucus and desquamation of epithelial elements. At this period the contents are thick and mucoid. As the result of the increasing distension, the mucosa undergoes atrophic changes which may involve all or a part of the mucosa according as the previous weakening of the wall has been uniform or otherwise. At the same time the submucosa becomes replaced by fibrous tissue and the contents become clearer and more watery and of the character of a transudate, which may become turbid and more or less viscid from the admixture of cellular elements from the blood and the desquamated epithelium of the mucosa. The pressure may also lead to degeneration of a hyaline or myxomatous character in the fibrous tissue.

The various phases as here depicted form but different stages

in one process, and the result, in whatever stage encountered, has been termed a retention cyst, hydrops, or mucocele. The term retention cyst indicates the origin and is, therefore, correctly applicable to all stages, but it would appear rational to differentiate between a hydrops and a mucocele as being different stages. Where the overproduction of mucus or even definite myxomatous changes predominate, the term mucocele seems more appropriate, while that stage in which the mucosa is destroyed and the cyst filled with a transudate would more appropriately be denominated a hydrops.

It is to be remembered that, according to the position of the occluded portion, the whole or any part of the appendix may be converted into a cyst. Probably the largest described is that of Guttmann, which was 14 centimeters long and 21 centimeters in circumference.

The peculiar character of the contents of a true mucocele along with some unusual features in the epithelial changes have suggested in some cases the possibility of tumor formation. As already mentioned, Virchow considered his case as one of colloid degeneration, and Stengel has reported a case in which he considered the possibility of colloid carcinoma. He also mentions the cases of Rokitansky, Draper, Vimont, and Baillet as possessing histological features suggestive of neoplasms. No case, however, has been recorded, as far as I can ascertain, with indubitable neoplastic features. The extreme mucoid degeneration of the mucosa with desquamation of the epithelium and the myxomatous degeneration of the fibrous tissue form a picture readily mistaken for a tumor, without the actual presence of tumor formation. I believe it to be a retrogressive rather than a progressive metamorphosis.

Congenital diverticula of the appendix have been described, especially by Hedinger, but the chance of as rare a lesion as a mucocele occurring in an appendix with a congenital diverticulum seems remote; on the other hand, in a mucocele all the factors necessary for the formation of acquired diverticula may be at hand.

The case here to be reported (number 1403) was discovered in the necropsy of a male Filipino, 40 years old, who had died of pulmonary tuberculosis, and in whom there was no evidence of abdominal tuberculosis.

The vermiform appendix was 4.5 centimeters long, occupied its normal position, and there were no surrounding adhesions. At its origin from the cæcum on the side opposite the mesentery

was a globular swelling 2 centimeters in diameter and raised 1.5 centimeters above the surface of the appendix. This swelling was covered with peritoneum continuous with that clothing the appendix, its surface was perfectly smooth, and the mass was slightly fluctuating. The tip of the appendix seemed to have a somewhat thinner wall than the remainder of the organ, and the intermediate portion was thicker than normal. These features are illustrated in Plate I, fig. 1, a photograph taken after opening the appendix and removal of some of the contents, thus accounting for the shrunken appearance of the cyst. The appendix, cyst, and adjacent portion of the cæcum were preserved *in toto.* On opening the appendix longitudinally (after fixation), the picture as seen in Plate I, fig. 2, was disclosed. The hypertrophic base of the appendix projected a few millimeters into the lumen of the cæcum much as the cervix uteri projects into the vagina; its orifice was practically occluded, allowing the passage of only a very fine strand of catgut. The proximal and distal thirds of the appendix were dilated, while the middle third was almost obliterated by the approximation of its walls. External to the proximal half of the appendix was the cyst, the inner wall of which was formed by the muscular tunic and the outer wall by a thin membrane covered by peritoneum. No direct communication of this cyst with the lumen was discovered on gross examination. The cyst and the proximal and distal thirds were distended by a thick, pearly-white, translucent mucoid material of about the consistence of gelatine, showing flecks of a whiter substance embedded in it.

Description of the microscopic details must include a study of practically the entire appendix, and for the purpose of clear orientation the different localities will be studied separately.

1. The proximal portion of the appendix. This shows a marked inflammatory hypertrophy which has led to the projection of the appendix into the cæcum, and the practical obliteration of the lumen of this part of the appendix. The inflammatory condition is manifested by fibrosis with round-celled infiltration and a muscular atrophy, along with a marked mucoid degeneration of the mucosa. The glandular tubules of the mucosa are separated by masses of round cells and are probably diminished in number, whereas the individual epithelial cells of the glands are almost entirely transformed into large goblet cells with basal nuclei surmounted by large cup-shaped cavities just emptied of their mucus contents. This condition exists for about 4 millimeters within the appendix.

2. Just distal to this there is a considerable dilatation of the lumen for a distance of from 7 to 8 millimeters. This area shows some thickening of the wall of the appendix on the mesenteric side, the thickening being accounted for chiefly by an increase of the fibrous elements of the submucosa along with some muscular hypertrophy and slight increase of the subperitoneal fibrous tissue. The mucosa here has largely disappeared, and in places the fibrous submucosa shows a myxomatous degeneration.

On the side opposite the mesentery, however, the wall is much thinner, and it is from this portion that the cyst has arisen. From within outward, the mucosa is largely destroyed, the submucosa fibrous, the muscularis is much atrophied, and one portion of the subperitoneal fibrous tissue is slightly thickened. At one point the mucosa, submucosa, muscularis, and a portion of the subperitoneal fibrous tissue have undergone a solution of continuity, and the cyst has formed as a hernial protrusion of the peritoneum, lined internally by a thin part of the outer layer of subperitoneal fibrous tissue. Direct connection exists between the cyst and the lumen of the appendix at this point, which is 15 millimeters from the base of the appendix. The fibrous tissue lining this cyst has undergone extensive myxomatous degeneration.

3. Distal to this, the lumen of the appendix is reduced to a minimum, the reduction being caused by a much thickened and fibrous submucosa and muscularis encroaching upon the lumen. Here the mucosa is represented by only an occasional remnant of a glandular tubule.

4. Beyond this the distal third of the appendix is dilated and its walls are thin. Here remnants of mucosa remain in a state of mucoid degeneration with abundant round-celled infiltration, the lymphoid elements of the submucosa are replaced by fibrous tissue, the muscularis is atrophied, and the subperitoneal fibrous tissue is somewhat thickened. The extreme apex is formed by a thin wall of fibrous tissue containing only a few muscular bundles.

The contents of the cyst and appendix are of a myxomatous character, the white flakes mentioned corresponding to masses of exfoliated epithelium and cells which have exuded from the vessels. These masses do not take the form of definite glandular structures, but in places do suggest that they are portions of the mucosa which have become exfoliated. They are prob-

ably of the same nature as those described in Stengel's case and do not, to my mind, furnish evidence of tumor formation. The number of leucocytes associated with the exfoliated epithelium is remarkable. In no place in the appendix is there anything suggesting invasion of the muscularis by epithelial elements. In the appendix where the mucosa is lacking, the lining fibrous tissue has undergone a myxomatous transformation, being represented by but few cells and abundant transparent, homogeneous, intercellular substance. In the wall adjacent to the point of formation of the cyst there is evidence of an old hæmorrhage.

This case exemplifies one mode of formation of both mucoceles and diverticula. The preexisting inflammation, upon which the occlusion of the orifice depended, was also responsible in all probability for some of the destruction of the mucosa as well as for the almost complete destruction of the wall at one point which made possible the formation of the cyst. The degenerative and atrophic changes were natural sequelæ. Had the constriction in the middle third been more nearly impermeable, then a second cyst would have developed involving the distal third. Had the condition persisted for a greater length of time, the character of the contents would have been changed, the wall would have become thin and transparent, and the cyst much larger.

Plate 2 is a semidiagrammatic drawing of a section stained by Van Gieson's method, designed to show the method of formation of the diverticulum as well as the mucocele.

SUMMARY.

1. A mucocele of the appendix is a retention cyst, the requisites for the production of which are:

a. Gradual occlusion of the lumen.

b. Absence of infection with pyogenic organisms.

c. A mucosa able to secrete faster than it can resorb.

2. The infrequency of the association of these factors accounts for the rarity of mucoceles.

3. They are of inflammatory origin, no case indubitably of intrinsic tumor formation having been recorded.

4. The terms hydrops and mucocele are used interchangeably, but it would seem preferable to apply the terms to different stages of the same process.

5. Diverticula of the appendix not infrequently occur in the formation of mucoceles.

REFERENCES.

1. Bierhoff. *Deutsches Arch. f. klin. Med.* (1880), 27, 248.
2. Guttmann. *Deutsche med. Wchnsch.* (1891), 17, 260.
3. Hedinger. *Virchow's Arch.* (1904), 178, 25.
4. Kelly. *Ann. Surg.* (1909), 49, 524.
5. Lilienthal. *N. Y. Med. Journ.* (1903), 77, 233.
6. Stengel. *Journ. Am. Med. Ass.* (1906), 46, 495.
   Idem. Osler's Modern Medicine (1908), 5, 433.
7. Virchow. Die krankhaften Geschwülste, 1, 350.

For a more complete bibliography, the reader is referred to the articles of Kelly and Stengel.

ILLUSTRATIONS.

Plate I.

Fig. 1. Appendix and diverticulum after incision and partial removal of contents. Portion of cæcum also shown. (Photograph by Cortes.)

2. Opened appendix and diverticulum. (Photograph by Cortes.)

Plate II.

Semidiagrammatic drawing of a section of appendix stained by Van Gieson's method.

1. Oblique section of practically occluded lumen at origin.
2. Wall of cæcum.
3. Peritoneum.
4. Diverticulum.
5. Subserous fibrous tissue.
6. Submucous fibrous tissue.
7. Muscularis.
8. Remnants of mucous membrane.
9. Point immediately adjacent to opening of diverticulum.

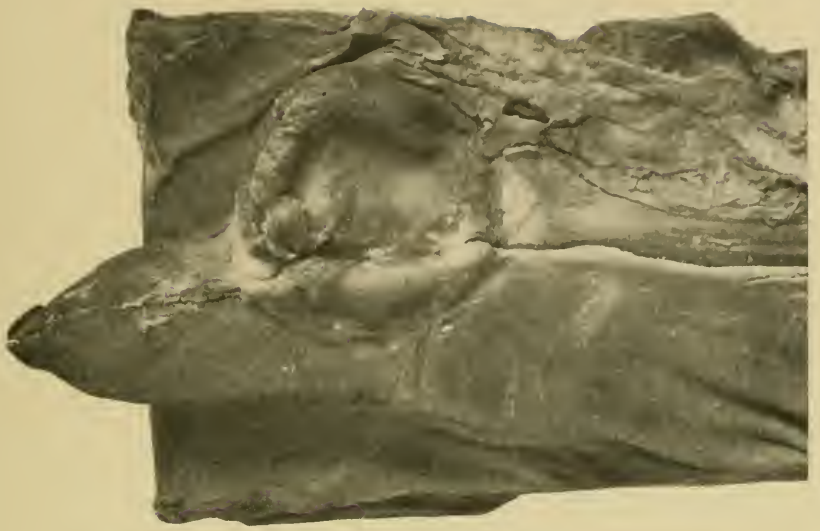
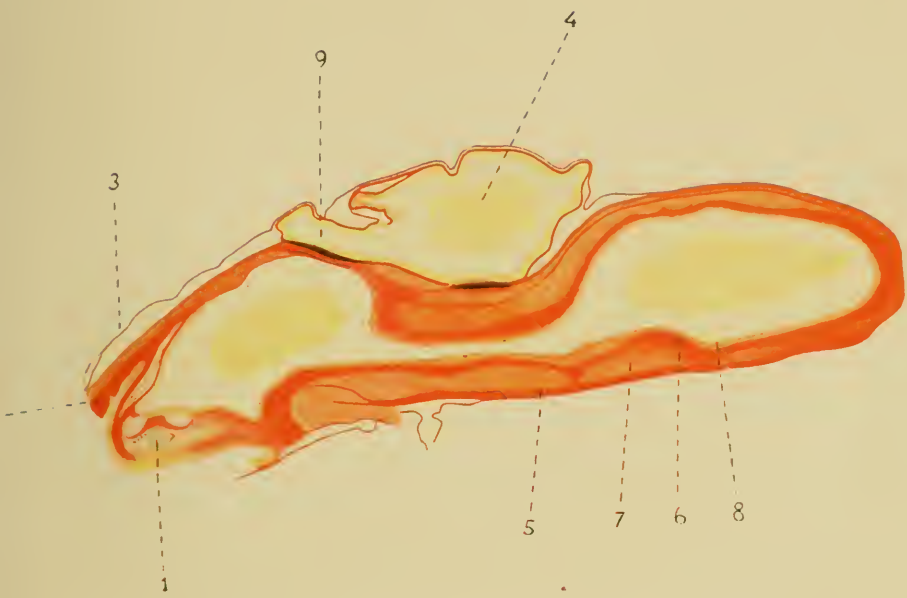


Fig 1. Appendix and diverticulum.

Fig. 2. Opened appendix and diverticulum.

PLATE I.



SECTION OF APPENDIX STAINED BY VAN GIESON'S METHOD.

PLATE II.

A THIRD CONTRIBUTION TO THE ETIOLOGY OF BERIBERI.[1]

By

WESTON P. CHAMBERLAIN and EDWARD B. VEDDER.

(From the United States Army Board for the Study of Tropical Diseases.)

AND

ROBERT R. WILLIAMS.[2]

(From the Laboratory of Organic Chemistry, Bureau of Science, Manila.)

In previous communications (1) (2) Chamberlain and Vedder showed that the substance in rice polishings which prevents polyneuritis gallinarum was present in an extract of the polishings having the composition shown in Table I.

TABLE I.—*Analysis of a neuritis-preventing extract of rice polishings.*

Constituents.	Per cent.
Total solids	1.34
Ash	0.03
Phosphorus pentoxide	0.00165
Nitrogen	0.0406
Sucrose	0.88

It was further proved that the neuritis-preventing principle was soluble in cold water, cold 95 per cent alcohol, was dialyzable, and was adsorbed by bone black or animal charcoal. By experiments on fowls the phosphorus, the inorganic salts, and the sucrose of this extract were excluded from further consideration as regards the prevention of neuritis.

We had hoped that the problem could next be attacked by direct chemical analysis, but a preliminary examination showed that the extract was of so complex a nature as to render a direct search for the neuritis-preventing substance impracticable. Therefore a further study of the nitrogenous constituents of this extract was begun.

For this purpose a fresh supply of extract of rice polishings

[1] Published with permission of the Chief Surgeon, Philippines Division.

[2] W. P. Chamberlain, major, Medical Corps, United States Army, and E. B. Vedder, captain, Medical Corps, United States Army, members of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands. R. R. Williams, chemist in the Bureau of Science, Manila, P. I. The chemical work relating to amido-bodies was performed by Mr. Williams. This paper was submitted for publication in September, 1911.

was prepared according to the method previously described (1), except that the polishings were extracted by three successive macerations with fresh 95 per cent alcohol and that the residue obtained by this extraction of 10 kilograms of polishings was redissolved in 1 liter of distilled water instead of the usual 10 liters. These two changes of method were made in order to obtain a more concentrated extract which would be better suited for chemical analysis. The extract used in the following experiments, therefore, is several times stronger than that previously used. The results of its analysis are shown in Table II.

TABLE II.—*Analysis of a neuritis-preventing extract of rice polishings, made more concentrated than that shown in Table I.*

Constituents.	Per cent.
Specific gravity	1.0437
Total solids	12.517
Sucrose [a]	6.33
Reducing sugars	0.52
Total nitrogen	0.161
Amido-nitrogen	0.156
Phosphorus pentoxide	0.006
Ash	0.27
Undetermined	5.23

[a] The determination of sucrose was not accurate because of the presence of other optically active substances.

Nonproteid nitrogenous substances are commonly found in seeds and in other parts of plants. Thus, in *Lupinus luteus*, Schulze (4) found asparagin, phenyl-alanin, amido-valeric acid, arginin, cholin, and xanthin-like substances; in *Cucurbita pepo*, glutamin, asparagin, leucin, tyrosin, arginin, cholin, vernin, and xanthin-like substances; in *Vicia sativa*, asparagin, phenyl-alanin, leucin, amido-valeric acid, guanidin, cholin, and betain. Of these, asparagin, glutamin, and arginin occur most widely and plentifully.

The amount of amido-nitrogen present in rice, rice polishings, beans, and *mongos* was found to bear a very close relation to the amount of phosphorus pentoxide present in those substances, as may be seen from Table III.

TABLE III.—*Relationship between percentage of nitrogen and amido-nitrogen in rice and beans.*

Article.	Total nitrogen.	Amido-nitrogen.
	Per cent.	*Per cent.*
Highly milled rice, No. 1	1.43	0.03
Highly milled rice, No. 2	1.22	0.00
Rice polishings, No. 1	5.40	0.96
Rice polishings, No. 2	5.10	0.504
Navy beans	4.13	1.23
Mongos	3.71	0.616

The amido-nitrogen is low in the highly milled rices which are always low in phosphorus pentoxide; and high in rice polishings, beans, and *mongos* which contain a considerable proportion of phosphorus pentoxide. This is an interesting parallel to the work of Parrozzani(3) who showed that the amido-nitrogen and total nonproteid nitrogen in many grains commonly used as food are both proportional to the content of organic phosphorus. The fact is also interesting in the consideration of a suitable index of the beriberi-preventing character of certain rices. The amount of phosphorus pentoxide has hitherto been used as such an indicator with general satisfaction, but we have recently examined samples of undermilled rices which retained almost the entire pericarp and which undoubtedly will prevent beriberi, and yet these rices on analysis were shown to contain a percentage of phosphorus pentoxide as low or lower than that in some specimens of highly polished rice which have been analyzed by the same chemists. There can be no doubt that the character of the soil may effect very materially the phosphorus content of rices as it does in the case of other grains. Chamberlain, Bloombergh, and Kilbourne(5) have shown that the percentage of potassium present in a rice is satisfactory as an indicator, and it now appears that the amount of amido-nitrogen may also be equally reliable.

These observations pointed to the possibility that some nonproteid nitrogenous substance, like arginin or asparagin, might be the neuritis-preventing substance which is present in rice polishings. As is well known, Takaki considered the disappearance of beriberi from the Japanese navy to be due to the increase in nitrogenous constituents in the ration. Although this theory of nitrogen starvation has long been discredited, the possibility that there might be a deficiency in a particular nitrogenous compound, such as amido-nitrogen, has not to our knowledge been considered. This possibility was further emphasized by a study of two dietaries used in Bilibid prison in Manila(6). The first ration (Table IV) was in use from about December 1, 1901, until October, 1902, during which time there were 5,448 cases of beriberi with 229 deaths. Beriberi completely disappeared after the institution of the second ration (Table V). The two rations are given in full, together with their proximate principles, and it will be seen that while there was no appreciable change in the amount of albuminates in the two dietaries, the amount of amido-nitrogen, calculated as asparagin, was only 5.84 in the first ration and was increased

to 12.26 in the second. Aside from the increase in amido-nitrogen there was no marked change perceptible except that the amount of carbohydrate was greatly reduced in the second ration.

TABLE IV.—*Ration for convicts at Bilibid from December 1, 1901, to October, 1902; 5,448 cases of beriberi occurred in this period.*

Ration.		Proximate principles.[a]					
Components.	Amounts.	Non-proteid nitrogen.	Albumin-ates.	Proteid nitrogen.	Fats.	Starches.	Salts.
	Grams.	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*
Sugar	28.35					27.35	0.14
Bread	151.20	0.38	12.09	1.55	2.26	74.39	1.96
Rice	453.60	0.09	35.43	5.58	3.12	377.40	2.26
Beef	226.80	0.27	48.52	7.49	11.77		3.62
Potatoes	85.05	0.34	1.13	0.18	0.09	11.90	0.50
Onions	28.35	0.28		0.09			
Pepper	0.50						
Vinegar	10.00						
Salt	18.00						18.00
Ginger root	28.35						
Total		1.36	97.17	14.89	17.24	491.04	26.48

Total vegetable amids, calculated as asparagin, 5.84 grams.

[a] The proximate principles as given in the tables are taken from the tables in the article by Fales(6), except the proteid and nonproteid nitrogen, these having been estimated by Mr. Williams.

TABLE V.—*Ration for convicts at Bilibid introduced in October, 1902. Beriberi disappeared after this change.*

Ration.		Proximate principles.					
Components.	Amounts.	Non-proteid nitrogen.	Albumin-ates.	Proteid nitrogen.	Fats.	Starches.	Salts.
	Grams.	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*
Sugar	28.35					27.35	0.14
Bread	302.40	0.76	24.18	3.11	4.53	148.78	3.93
Rice	255.15	0.05	17.71	2.78	1.56	188.70	1.13
Beef	226.80	0.27	48.52	7.49	11.77		3.62
Dried fish	56.70	0.15	7.08	0.97	0.85		0.28
Potatoes	119.07	0.48	2.38	0.37	0.14	25.00	1.19
Onions	102.06	1.00	1.84	0.29	0.50	5.90	0.70
Pepper	0.50						
Vinegar	10.00						
Salt	18.00						18.00
Ginger root	28.35						
Total		2.71	101.71	15.01	19.35	395.73	29.99

Total vegetable amids, calculated as asparagin, 12.26 grams.

The extract of rice polishings considered in Table II was, therefore, submitted to chemical treatment in order to divide the amid substances into classes and to enable us to test each class by means of experiments on fowls. The following is the process which was employed.

In order to remove noncoagulable proteids and other colloidal substances, the extract obtained from 3 kilograms of rice polishings was treated with an excess of basic lead acetate, the precipitate was removed by filtration, washed with water, and redissolved in 40 cubic centimeters of 10 per cent sodium hydroxide solution. The lead in this solution was precipitated with sulphuretted hydrogen and filtered. The filtrate was rendered slightly acid with hydrochloric acid (whereupon the substances originally precipitated by the basic lead acetate were once more thrown down), was allowed to stand over night in order that the excess of sulphuretted hydrogen might be dissipated, and the following day was rendered slightly alkaline for the purpose of again dissolving the precipitate. The solution was then diluted to 3 liters so that each cubic centimeter of solution represented the substances precipitated by basic lead acetate from the extract of 1 gram of polishings. Ten cubic centimeters of this solution were given to fowls daily, and it was denominated Extract Number 24.

The filtrate remaining after the lead acetate precipitate had been removed was treated with a slight excess of sulphuric acid to remove the lead. The lead sulphate thus formed was filtered. A saturated solution of phospho-tungstic acid was added to the filtrate until precipitation was complete. (About 10 grams of phospho-tungstic acid were required.) The rather bulky, orange-yellow precipitate was removed and mixed with freshly slaked lime and barium hydroxide. The lime unites with the phospho-tungstic acid leaving in solution free bases of the histon group, including arginin. The excess of lime and baryta was removed by precipitation with carbon dioxide and the solution was neutralized with hydrochloric acid, a few drops of sulphuric acid being added to precipitate any barium salt remaining. The filtrate was diluted to 3 liters. The solution thus prepared represented the free bases of the histon group, chiefly arginin and histidin, extracted from the rice polishings, each cubic centimeter being equivalent to 1 gram of polishings. Ten cubic centimeters were given daily to fowls, and it was denominated Extract Number 25.

The filtrate remaining after the separation of the phospho-tungstic acid precipitate contained amino-acids and other substances. In order to remove the excess of phospho-tungstic acid, barium hydroxide was added to slight excess and barium phospho-tungstate filtered off. Sulphuric acid was added until the solution was slightly acid and the barium sulphate removed. The filtrate, containing amino-acids and amino-acid amids, was likewise diluted to 3 liters and fed to fowls as Extract Number 26.

Experiment 10.[3]—Four fowls were fed on polished rice plus a daily dose of 10 cubic centimeters of Extract Number 24,

[3] Experiments 1 to 9, inclusive, are recorded in the two previous articles referred to under references (1) and (2).

containing the precipitate obtained by basic lead acetate and dissolved after removing the lead with hydrogen sulphide.

One fowl developed neuritis in twenty-five days, 1 in twenty-eight days and 1 in twenty-nine days, after which the experiment was discontinued.

Experiment 11.—Four fowls were fed on polished rice plus a daily dose of 10 cubic centimeters of Extract Number 25, containing the histon bases.

One fowl developed neuritis in twenty days and 1 in twenty-eight days, after which the experiment was discontinued.

Experiment 12.—Four fowls were fed on polished rice plus a daily dose of 10 cubic centimeters of Extract Number 26, containing amino-acids.

Two fowls developed neuritis in twenty-six days and 1 in thirty-one days, after which the experiment was discontinued.

In order to check these experiments we also fed fowls with pure chemical substances of the amino-acid group and with amids. Glycocoll, asparagin, and succinamid were chosen as representing the general classes of amino-acid and amid substances likely to be present in the extract of rice polishings. Thus glycocoll or amino-acetic acid contains an amino radical attached to a carbon atom. Asparagin or amino-succinamic acid contains 1 amino and 1 amid group (NH_2), while succinamid contains 2 amido groups.

Experiment 13.—Four fowls were fed on polished rice plus a daily dose of 10 cubic centimeters of a 0.5 per cent suspension of glycocoll in water.

One fowl developed neuritis in thirty days and 1 in thirty-five days, after which the experiment was discontinued.

Experiment 14.—Four fowls were fed on polished rice plus a daily dose of 10 cubic centimeters of a 0.5 per cent solution of asparagin in water.

One fowl developed neuritis in thirty-two days and 1 in thirty-three days, after which the experiment was discontinued.

Experiment 15.—Four fowls were fed on polished rice plus a daily dose of 10 cubic centimeters of a 0.5 per cent solution of succinamid in water.

One fowl developed neuritis in twenty-nine days and 1 in thirty-one days, after which the experiment was discontinued.

The doses of these substances used in the above experiments were selected because it was certain from the chemical analysis that the amount of rice polishing which is known to be sufficient

to protect a fowl from polyneuritis could not contain more than these quantities of amido substances.

It will be seen that all of the experiments were negative, and showed that none of these substances possessed any protective power. Although these experiments do not exclude all such substances which are present in the extract of rice polishings, it seems improbable that the remaining ones can be of importance.

An objection may be raised to part of these experiments because of the fact that the extract was treated with alkaline reagents. Fraser and Stanton(7) have shown that treatment with sodium hydrate destroys the neuritis-preventing substance. We have repeated this experiment and have found that treatment of the extract with sodium hydrate does remove its protective action. However, it should be remembered that the chemical procedure which we followed, as described above, is the recognized method for the isolation of the histon bases; therefore, whatever effect the alkaline reagents may have had on the neuritis-preventing substance, they could not have affected such substances as arginin or histidin. That the neuritis-preventing substance may be destroyed by such treatment is simply another argument against the possibility that any protective action is possessed by the compounds in question.

Since the extract used in the above experiments was a different lot from that employed in the work previously reported by us(1) (2), a control experiment was performed in order to be certain that the extract would prevent neuritis before it was put through the chemical processes already described. For this purpose the concentrated extract was diluted in such proportion that 1 cubic centimeter represented the substances dissolved from 1 gram of rice polishings. Four fowls were then fed on polished rice with a daily dose of 10 cubic centimeters of this diluted extract. These fowls all remained well for fifty days, when they were released. This definitely shows that the neuritis-preventing substance was present in the extract previous to its chemical treatment.

We now considered that it might be of interest to determine exactly what dose of this extract was required in order to prevent neuritis and for this purpose performed Experiment 16.

Experiment 16.—Four fowls were fed on polished rice plus a daily dose of 5 cubic centimeters of the extract of rice polishings. These 4 fowls also remained well for fifty days when they were released. Four fowls were then fed on polished rice plus a daily dose of 2.5 cubic centimeters of the extract of rice

polishings. Two fowls developed neuritis on the fortieth day and 1 developed neuritis on the forty-first day. The fourth fowl remained well for fifty days when he was released.

It is, therefore, obvious that 2.5 cubic centimeters of our extract, equivalent to 2.5 grams of the rice polishings, is insufficient to protect the majority of fowls as long as fifty days, although delaying the onset of symptoms of neuritis for about ten days, but that 5 cubic centimeters is sufficient to afford complete protection for at least fifty days. The fact that a definite dose of this extract is necessary to protect fowls, while a smaller dose delays the onset of the disease, is an additional argument in favor of the assumption that polyneuritis gallinarum is a disease due to the absence of some essential nutritive principle. This work with reduced doses of extract agrees quantitatively with the results obtained by Fraser and Stanton, who found that 5 grams of rice polishings were sufficient to prevent neuritis when fowls were subsisting on polished rice.

We have long been convinced that polyneuritis gallinarum is due to a nutritive deficiency, but apparently some others are not, since Kohlbrugge has recently published an article maintaining that this disease is caused by the acid produced during the fermentation of rice which results from the action of a number of acid-producing bacteria contained in the rice itself. There are many possible criticisms of Kohlbrugge's work, but we will limit ourselves to the following:

Kohlbrugge states that he has produced beriberi in fowls in four or five days by feeding polished rice mixed with agar cultures of the acid-producing bacteria isolated from rice. However, he did not demonstrate the existence of nerve degenerations, and gave few details of his experiment. From what we know of beriberi and polyneuritis gallinarum it seems to us impossible that he could produce this disease in four or five days, and it appears that his fowls must have died of toxæmia or infection, and not of beriberi. He further states that the disease is prevented by large amounts of acid in the food, maintaining that excessive acidity inhibits the growth of the bacteria. Thus rice polishings, beans, etc., are preventive because they contain a great amount of acid. This is certainly incorrect, because we have prevented neuritis in fowls by means of an extract of rice polishings that had been *neutralized* with sodium carbonate. It may be possible that some particular acid, or its salt, is the neuritis-preventing substance, but we have tried phosphoric acid, sulphuric acid, and lime juice with negative results. Since

these three acids failed to prevent neuritis and since a neutral extract added to polished rice did prevent the disease, it is quite obvious that acidity *per se* can be of no importance.

The following points are of interest with reference to Kohlbrugge's view that a culture of his rice bacillus, obtained from fermented rice, was capable of producing neuritis of fowls in four or five days.

Shiga(9), in endeavoring to test the validity of the intoxication theory, performed the following experiment: He fermented an undermilled rice in the incubator for about a week and fed fowls on this fermented material, but they remained healthy for two hundred days, when the experiment was discontinued. We have repeated this experiment with the same result. We have, also, fed fowls on a highly milled rice, fermented in a similar way, and have found that these fowls do not develop neuritis any sooner than fowls fed on the same rice when perfectly fresh and dry. These facts seem to us absolutely to disprove Kohlbrugge's theory.

On comparing the two rations used in Bilibid prison (Tables IV and V), it will be seen that in the latter dietary (which led to the disappearance of beriberi) one of the most obvious changes was the very great increase in the amount of onions prescribed. Onions are very rich in amido-nitrogen compounds, and the oil of onions is composed almost entirely of allyl sulphide $(C_3H_5)_2S$. In order to determine whether the increased consumption of onions could have been responsible for the disappearance of beriberi, Experiment 17 was performed. Two kilograms of onions were ground up finely in a meat cutter, mixed with 2 liters of water, and allowed to macerate for twenty-four hours in the ice-box. The mixture was then filtered. The clear filtrate contained the greater bulk of the onions, very little solid matter being left on the filter.

Experiment 17.—Four fowls were fed on polished rice plus a daily dose of 10 cubic centimeters of extract of onions.

One fowl developed neuritis in twenty-one days, 1 in twenty-two days and 1 in forty-three days, after which the experiment was discontinued.

Since the neuritis-preventing substance is soluble in water, it should have been contained in this extract if it were originally present in the onions. As the experiment was negative, we are forced to conclude that onions will not prevent polyneuritis gallinarum, and therefore are not likely to prevent beriberi.

The only other differences that are apparent between the second and first rations at Bilibid are (*a*) an increase in potatoes from 85.05 grams to 119.07; (*b*) a decrease in rice from 453.60 grams to 255.15 grams; and (*c*) an increase of bread from 151.20 to 302.40 grams. It seems improbable that the small increase in potatoes could have been of importance. However, the amount of rice consumed was decreased about one-half, and the amount of bread consumed was doubled, and this simple change was, in our opinion, the one that put an end to the very serious epidemic of beriberi.

A number of instances where similar slight changes have resulted in the prevention of beriberi are on record in the literature of the subject, among which we may mention the following:

> Beriberi was very prevalent among the Japanese soldiers at Port Arthur during the Russo-Japanese war. They received a daily ration of 30 ounces of rice and 5 ounces of meat. The Japanese sailors on the other hand, serving on shore and living under similar circumstances except as to their diet, did not have beriberi. They received a daily ration of 20 ounces of rice, 10 ounces barley, and 1 pound of meat. In this case, therefore, beriberi was prevented by the reduction in the amount of rice consumed, the addition of barley, and an increase in the meat component. By the simple change involved in the reduction of the amount of rice consumed, and the addition of a legumen to the diet, beriberi was reduced in the Philippine Scouts (native) from an average of 600 cases a year to *nil*. The instances where beriberi has been prevented by the substitution of undermilled (or cured) rice for highly milled (or polished) rice are too well known and numerous to mention. Although the discovery of the actual neuritis-preventing substance is of the greatest scientific interest and importance, we consider, in view of the facts already known and referred to above, that the hygienic problem of the prevention of beriberi is already solved.

In the further chemical analysis of the extract of rice polishings, a substance thought to be cholin was isolated. This also seemed worth testing, since cholin is an important constituent of nerve tissue, combined with phosphorus and fatty acids in the form of lecithin. Moreover, cholin fulfils the chemical and physical requirements which we have experimentally determined that the neuritis-preventing substance possesses. On account of the difficulty in obtaining pure cholin we used lecithin made from eggs (Merck's preparation).

Experiment 18.—Four fowls were fed on polished rice plus a daily dose of 0.3 gram lecithin.

One fowl developed neuritis in eighteen days and 1 in twenty-four days, after which the experiment was considered negative and discontinued. Since in chemical character lecithin is a salt containing cholin as its base, we conclude that this experiment

excludes cholin and lecithin from further consideration as the neuritis-preventing substance of rice polishings.

While our observations had led us to believe that the neuritis-preventing principle in rice polishings was insoluble in ether, there was no conclusive evidence with regard to this point. To settle the matter, polishings were extracted with ether as follows:

Two kilograms of polishings were mixed with 6 liters of ether and, after macerating for twenty-four hours, the ether extract was filtered off. The extraction was repeated with fresh ether for a second twenty-four hours, the filtrates combined, and the ether evaporated by the current from an electric fan. Three hundred cubic centimeters of residue, consisting chiefly of fat, were obtained from 2 kilograms of polishings.

Experiment 19.—Four fowls were fed on polished rice plus a daily addition of 2 cubic centimeters of the ethereal extract of rice polishings. One fowl developed neuritis in twenty-one days, 1 in twenty-nine days, and 1 in thirty days. From this experiment we concluded that the neuritis-preventing principle is insoluble in ether.

We have never seen œdema in any of the fowls that have developed polyneuritis, although this symptom has been noted by several other observers, including Shiga(9). The influence of a salt-free diet in reducing the œdema of nephritis has been much emphasized of late. Since the fowls fed on highly milled rice receive practically no salt, it seemed possible that the addition of a considerable quantity of sodium chloride to the food might produce this symptom. In order to test this hypothesis Experiment 20 was performed.

Experiment 20.—Four fowls were fed on polished rice, and in addition were given a daily dose of 1 gram of sodium chloride diluted in 10 cubic centimeters of distilled water. This would be equivalent to a dose of 50 grams daily for a man. The 4 fowls developed neuritis on the twenty-third, twenty-sixth, twenty-seventh, and thirty-third days, respectively, but at no time did they show any signs of œdema. Therefore, we concluded that the presence or absence of sodium chloride is of no importance with regard to the development of œdema in polyneuritis gallinarum and probably in beriberi.

In a previous paper(2) we reported an experiment demonstrating that the neuritis-preventing principle was adsorbed when the extract of rice polishings was passed through an animal charcoal filter, and that a portion of the neuritis-preventing element was recovered when the bone black from the filter was washed with distilled water. Unfortunately, the charcoal used

in the above experiment was not chemically pure. Consequently we were unable to obtain any information as to the chemical nature of the substances removed from the extract of rice polishings by this method.

Experiment 21.—Therefore, a second experiment was performed in the following manner: The extract obtained from 10 kilograms of polishings was dialyzed, according to the method described in our previous paper, and the diffusate was then filtered through animal charcoal (Kahlbaum I). The filtrate was clear and colorless. This filtrate was then administered to 4 fowls that were being fed on polished rice. Two of these fowls developed neuritis on the twenty-fifth day, 1 on the twenty-eighth, and 1 on the thirty-fifth day. This showed conclusively that the neuritis-preventing substance remained behind in the charcoal, thus confirming the results obtained in our previous experiment.

The charcoal was then transferred from the filter to a flask and was mixed with 500 cubic centimeters of ether. The mixture was allowed to stand in the ice box for two days, being repeatedly shaken during this time. The ether was then filtered off and evaporated, and the ethereal extract so obtained was redissolved in water. Four fowls were fed on highly milled rice and given in addition a daily dose of this extract. One fowl developed neuritis on the twentieth day, 1 on the twenty-third day, 1 on the thirty-eighth day, and 1 on the forty-second day. Therefore, it was apparent that the neuritis-preventing principle was not removed from the charcoal by the ether.

The charcoal was then treated in a similar manner with 1 liter of absolute alcohol. The alcoholic extract obtained was of a yellowish tinge and distinctly acid to litmus. The alcohol was evaporated and the residue redissolved in water as in the case of the ethereal extract. Four fowls were fed on highly milled rice plus a daily dose of this extract removed from the charcoal by alcohol. One fowl developed neuritis on the twenty-third day, 1 on the thirty-second day, 1 on the thirty-seventh, and 1 fowl remained well for sixty-one days. As a result of this experiment it is clear that the neuritis-preventing substance was not removed from the charcoal by absolute alcohol.

The charcoal was then washed with 3 liters of distilled water, shaking the charcoal up with successive portions of water and permitting the extraction to last for ten days. The water recovered from the charcoal was also acid to litmus. Four fowls were fed on highly milled rice plus a daily addition of this

watery extract from the charcoal. One fowl developed neuritis in twenty-three days, 1 in twenty-six days, 1 in thirty-six days, and 1 remained well at the end of forty-eight days. Therefore, it appeared that the neuritis-preventing principle was not removed, by extraction with water, from the pure charcoal used in this experiment.

The charcoal was next suspended in 500 cubic centimeters of distilled water, and 2 cubic centimeters of this mixture fed daily to 4 fowls subsisting on higly milled rice. Since the charcoal rapidly sinks to the bottom, the flask was shaken just before giving the mixture. The water was used simply as a vehicle for the administration of the charcoal. These 4 fowls all remained well at the end of sixty days. Therefore, we concluded that the neuritis-preventing principle was still retained by the charcoal in spite of the repeated extractions to which it had been subjected. This experiment differed from the one reported previously in that water completely failed to remove the neuritis-preventing principle, while in the former experiment (Number 6) this principle seemed to be in part removed, and the watery extract conferred partial protection. We attribute this difference in results only to the fact that in the first instance we used an impure charcoal, while the second time we used a pure product which apparently possessed a greater adsorptive power for the unknown neuritis-preventing substance.

Experiment 21 fully confirms our former observation that the neuritis-preventing principle in rice polishings is adsorbed by animal charcoal and this knowledge perhaps will be the basis for a method of isolating the substance in comparative purity, provided a means can be discovered for extracting it from the charcoal.

CONCLUSIONS.

1. These experiments all substantiate the theory that polyneuritis gallinarum and beriberi are caused by the deficiency of some as yet unknown substance in the food. We have shown previously that this substance is not phosphorus.

2. Kohlbrugge's theory that beriberi is caused by an acid intoxication, which is due to the fermentation of rice by various saprophytic bacteria contained in the kernel, must be regarded as untenable.

3. To the list of substances which we have shown in previous papers to be of no importance in preventing neuritis of fowls there may now be added the following: Nitrogenous compounds

such as arginin, histidin, asparagin, and various amino-acids; lipoids of the lecithin group and cholin; extract of onions.

4. The neuritis-preventing principle is insoluble in ether.

5. The neuritis-preventing principle is adsorbed by animal charcoal and the filtrate through the charcoal will not prevent neuritis. After adsorption the active principle can not be removed from the charcoal by maceration with water, absolute alcohol, or ether.

6. The administration of large quantities of sodium chloride failed to produce œdema in fowls suffering from polyneuritis.

7. Five cubic centimeters of our extract (equivalent to 5 grams of rice polishings) is sufficient to protect fowls subsisting upon polished rice. Two and one-half cubic centimeters (equivalent to 2.5 grams of polishings) is insufficient to confer complete protection against polyneuritis.

REFERENCES.

(1) CHAMBERLAIN and VEDDER. A Contribution to the Etiology of Beriberi. *Phil. Journ. Sci., Sec. B* (1911), 6, 251.

(2) CHAMBERLAIN and VEDDER. A Second Contribution to the Etiology of Beriberi. *Phil. Journ. Sci., Sec. B* (1911), 6, 395.

(3) PARROZZANI. *Rend. soc. chim. ital.* [2] 1, No. 14. Through *Chem. Abstracts* (1910), 2492.

(4) SCHULZE. *Ztschr. f. phys. Chem.* (1886), 2, 44.

(5) CHAMBERLAIN, BLOOMBERGH, and KILBOURNE. A Study of the Influence of Rice Diet and of Inanition on the Production of Multiple Neuritis of Fowls, and the Bearing Thereof on the Etiology of Beriberi. *Phil. Journ. Sci., Sec. B* (1911), 6, 177.

(6) FALES. Beriberi, its Etiology and Prevention. *Journ. Am. Med. Ass.* (1907), 48, 776.

(7) FRASER and STANTON. The Etiology of Beriberi, Studies from the Institute for Medical Research, Federated Malay States, No. 12, page 74.

(8) SCHAUMAN. Die Ætiologie der Beriberi unter Berücksichtigung des Gesammten Phosphorstoffwechsels. *Arch. f. Schiffs- u. Trop.-Hyg.* (1910), 14, No. 8.

(9) SHIGA und KUSAMA. Über die Kakke-ähnliche Krankheit der Tiere. *Arch. f. Schiffs- u. Trop.-Hyg.* (1911), 15, No. 3.

THE SCHIZOGONY OF TRYPANOSOMA EVANSI IN THE SPLEEN OF THE VERTEBRATE HOST.

By Ernest Linwood Walker.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

There have been in recent years observations by several investigators that indicate a more complicated developmental cycle of trypanosomes in the vertebrate host than has hitherto been suspected.

Salvin-Moore and Breinl, in 1907, described the development of round bodies from the trypanosomes in the lungs of rats infected with *Trypanosoma gambiense*. These bodies are formed at or near the maximum of the multiplication of the trypanosomes in the circulating blood. In their development, there is, according to these authors, first an interaction between the blepharoplast ("extra-nuclear centrosome") and the nucleus of the trypanosome in the form of a stainable band that grows out from the blepharoplast and becomes connected with the nucleus. This band later becomes broken up and disappears, but it is believed that during the process a part of the blepharoplast becomes united with the nucleus. The protoplasm of the trypanosome then becomes separated from the nucleus which lies in a vaculoid space. This vesicle, containing the nucleus and surrounded by a thin layer of protoplasm, becomes detached from the body of the trypanosome which disintegrates. These bodies are stored chiefly in the spleen and bone marrow, and are considered by Salvin-Moore and Breinl as a resistant stage of the trypanosome which persists when the parasites disappear from the peripheral blood and which give rise by development to the new generation of motile trypanosomes that reappear in blood after the lapse of a variable period of time. For this reason these bodies are designated by these authors as "latent bodies."

Chagas, in 1909, published an account of a new trypanosomiasis of man in Brazil, South America, which is transmitted by a biting bug (*Conorhinus megistus*), and of which the etiologic

factor, for reasons that will be apparent later, is named *Schizotrypanum cruzi*. This trypanosome is said not to multiply by simple division in the peripheral blood, but instead to undergo schizogony in the capillaries of the lungs of the infected animal. This reproductive process takes place at the time of the increase of the trypanosomes in the blood, especially at five to six days after inoculation of the animal and, also, during the great increase of the parasites which occurs just previous to the death of the infected animal. The trypanosome sheds its flagellum and undulating membrane, bends upon itself, and becomes fused into a round or oval body. In some of these bodies, the blepharoplast is shed with the flagellum, in others it is retained. By division of the nucleus in the first form and of the nucleus and blepharoplast in the second form, and by a differentiation of the protoplasm there are developed from these bodies schizocysts containing 8 small club-shaped merozoites. The merozoites escape from the cyst and penetrate red blood-corpuscles, where they develop into trypanosomes. When fully developed, they leave the blood-corpuscles and live free in the plasma. The blepharoplast-less merozoites develop into female trypanosomes, having a small blepharoplast derived from the nucleus through heteropolar division, a round nucleus, and a broad body; the merozoites having a blepharoplast develop into male trypanosomes having a large blepharoplast, an elongated nucleus, and a slender body.

Hartmann, in 1910, found in a section of the lung of a guinea pig infected with *Schizotrypanum cruzi* Chagas, greatly hypertrophied endothelial cells containing large numbers of more or less pyriform, binucleate bodies. Similar intracellular stages, Hartmann states, were subsequently found by Chagas in the heart musculature and in the brain of a man dead from schizotrypanosomiasis. He believes that this intracellular multiplication represents the true schizogony, while the extracellular schizogony with a sexual differentiation of the products of division, previously described by Chagas, is considered a gametogony. Carini (1911) has described a similar so-called schizogony of *Trypanosoma leptodactyli* in endothelial cells in the blood from the heart of an infected animal (*Leptodactylus ocellatus*).

Fantham (1911) has recently studied the life history of *Trypanosoma gambiense* and *Trypanosoma rhodesiense* in relation to the number of trypanosomes in the peripheral circulation, making use of the thick film method of Ross to determine accurately the number of trypanosomes in the blood from day to

day. He has confirmed the observations of Salvin-Moore and Breinl that small round bodies are developed in the lungs of the vertebrate host at or near the maximum of the multiplication of the trypanosomes in the circulating blood, and that these "latent bodies" persist in the spleen and bone marrow during the period when the trypanosomes are absent from the blood. However, Fantham does not agree with Salvin-Moore and Breinl as to the method of development of these bodies. He was unable to observe the interaction between the blepharoplast and nucleus of the trypanosome described by the latter authors. In the process as described by Fantham in the living trypanosome from the circulating blood under the microscope, the anterior end of the trypanosome disintegrates, the blepharoplast migrates near the nucleus and the posterior end of the trypanosome with the remnant of the flagellum is cast off. The round body, consisting of the nucleus and blepharoplast surrounded by a thin layer of protoplasm, constitutes the "latent body." Fantham was also able to observe the metamorphosis of the "latent bodies" into trypanosomes by mixing infected spleen pulp with fresh blood of an uninfected rat and observing it on a warm stage under the microscope. Finally, he claims to have demonstrated the infectiousness of this stage of the trypanosome by inoculating animals with spleen pulp found by microscopic examination to be free from motile trypanosomes but to contain the "latent bodies." Fantham, like Salvin-Moore and Breinl, is of the opinion that these bodies are a more resistant stage of the trypanosome and he believes that consideration should be taken of them and of the time of their development in the chemotherapeutic treatment of trypanosomiasis.

On the other hand, Laveran (1911), who has recently studied these round bodies of *Trypanosoma gambiense* in guinea pigs, has come to the conclusion that they are involution forms of the trypanosome, which are naturally very numerous in the spleen and bone marrow at the crisis of the infection.

Buchanan (1911) has observed some of the forms described by these other authors in the internal organs, bone marrow, and axillary glands of the gerbil (*Gerbillus pygargus*) infected with *Trypanosoma brucei* (*pecaudi*). This author describes and gives illustrations of round binucleate bodies found in smears from the lungs of animals killed on the sixth day of infection which correspond to the "latent bodies" of *Trypanosoma gambiense* and *Trypanosoma rhodesiense*. The development of these bodies, as observed by Buchanan, differs from that described

by either Salvin-Moore and Breinl or Fantham. The trypanosome bends upon itself ventrally and becomes fused into a round, binucleate body, around the border of which the flagellum remains for a time attached, but is later cast off. This method of development, therefore, corresponds more nearly with the formation of the schizonts of *Schizotrypanum cruzi.* In the spleen, bone marrow, and axillary glands round, ring, and coiled forms were found on the fourth to sixth day, usually surrounded by a clear area which gave the impression that the protoplasmic mass was lying in a vacuoloid space that was surrounded by a limiting membrane. In these forms the blepharoplast frequently appeared to lie detached from the protoplasmic mass in the clear area. Buchanan also found in smears of the spleen ring-form parasites and all stages in the development of these to the fairly mature trypanosomes within the red blood-corpuscles, which appear to be similar to the intracorpuscular stages of *Schizotrypanum cruzi* described by Chagas.

In the development of *Trypanosoma evansi* in guinea pigs, round nonflagellated forms are found in the spleen and bone marrow that correspond to the "latent bodies" described by Salvin-Moore and Breinl in *Trypanosoma gambiense* and by Fantham in *Trypanosoma gambiense* and *Trypanosoma rhodesiense.* These bodies of *Trypanosoma evansi,* however, appear to be not "latent," but developmental, forms which undergo a schizogony comparable to that taking place in *Schizotrypanum cruzi.* While all of the relations of this reproductive process to the life-cycle of the parasite have not been worked out, nor the process studied in the natural host of this trypanosome, it has seemed advisable to publish a preliminary account of it. The hope is expressed that it may lead to a more careful study of what appears to be early stages of the same reproductive process in *Trypanosoma gambiense* and other species of *Trypanosoma,* and to a further investigation of the relation, if any, of the different stages of this process to latency in trypanosomiasis and to relapses after chemotherapeutic treatment.

Two strains of *Trypanosoma evansi,* one from a horse and the other from a carabao, have been studied. These two strains have been propagated by subcutaneous inoculations from guinea pig to guinea pig, and the development herein described is based upon the study of the blood and organs of these animals.

The blood, taken from the ear veins, and the internal organs of guinea pigs killed at different periods of the infection, have been studied fresh, in dried smears, in smears fixed wet, and

in paraffine sections. These preparations have been stained with Giemsa's stain, aqueous alum hematoxylin, Mallory's ferric choloride hematoxylin, and Seidlin's iron hematoxylin. Air-dried smears of both the blood and organs, stained twelve to twenty-four hours with Giemsa's stain, have given the best results. The sections of the organs have been useful in determining the relation of the stages of development of the trypanosome to the tissues.

Trypanosoma evansi, when inoculated subcutaneously into guinea pigs, has an incubation period that varies from five to seventeen days, depending upon the strain of the virus, the number of trypanosomes inoculated, and the susceptibility of the animal. The disease runs a more or less chronic course in these animals, usually of from one to several months' duration. The course of the disease is marked by alternating phases of increase and decrease of the parasites in the peripheral blood. The trypanosomes will increase to a maximum and often swarm in the blood for several days; they will then decrease, and may wholly disappear from the peripheral circulation for several days, only to reappear and repeat the cycle. Sometimes one or more smaller crests of multiplication will intervene between two larger crests. Occasionally the infected guinea pig will die at the summit of the first crest of multiplication of the parasites in its blood.

Guinea pigs have been killed at different periods in the multiplication curve of the parasites in the blood and preparations from the different internal organs examined. It has been found, corresponding to the observations of Salvin-Moore and Breinl on *Trypanosoma gambiense* and of Fantham on *Trypanosoma gambiense* and *Trypanosoma rhodesiense*, that at or near the maximum of the increase of the trypanosomes in the blood large numbers of round, binucleate bodies are developed in certain of the internal organs. Guinea pigs inoculated intraperitoneally and killed from the fifth to eighth day, according to the directions of Chagas for finding the schizonts in *Schizotrypanum cruzi* and followed by Buchanan in studying the development of *Trypanosoma brucei* (*pecandi*) in the internal organs of the gerbil, showed only a few of the round forms. Guinea pigs, killed during the decrease or the absence of the trypanosomes from the peripheral blood, showed few or no round forms in the organs.

The place of development of these round forms of *Trypanosoma evansi* does not correspond to that of the development of the "latent bodies" *Trypanosoma gambiense* and *Trypanosoma*

rhodesiense or to that of the development of the schizonts of *Schizotrypanum cruzi.* According to Salvin-Moore and Breinl, Fantham, and Chagas the round forms of these trypanosomes are developed in the capillaries of the lungs of the infected animals. In *Trypanosoma evansi,* on the other hand, the round forms are developed chiefly in the spleen and to a lesser extent in the bone marrow. A few of them can sometimes be found in the lungs and other internal organs, where they have probably been carried by the circulating blood. This corresponds to the observations of Buchanan on *Trypanosoma brucei.* The spleen is always more or less enlarged, congested, and dark in color. Sections of the organ show that the round forms are developed extracellularly in the small capillaries, which are often occluded by them.

Furthermore, the development of these round forms of *Trypanosoma evansi* is different from that described in *Trypanosoma gambiense* and *Trypanosoma rhodesiense.* Salvin-Moore and Breinl and also Fantham disagree as to the details of the development of these bodies, but both agree that a large part of the trypanosome degenerates and is cast off, and that the round body consists only of the nucleus, blepharoplast, and a small remnant of the protoplasm of the trypanosome. According to my observations the round form of *Trypanosoma evansi* is made up of the whole trypanosome, with the exception of the flagellum which is cast off. The trypanosome bends upon itself ventrally (Plate I, fig. 2) until the anterior and posterior ends are apposed, the halves then fuse to form a round or oval body, around the border of which the flagellum remains for a time attached (fig. 3). Sometimes by the fusion of the two ends of the coiled-up trypanosome, ring-shaped bodies are developed which later become fused into a solid mass. The flagellum attached about the border of the rounded trypanosome soon becomes detached, leaving the nonflagellated, binucleate body. Therefore, the development of these bodies in *Trypanosoma evansi* corresponds more nearly to the development of the forms described by Buchanan in *Trypanosoma brucei* and to the development of the schizonts described by Chagas in *Schizotrypanum cruzi.*

These bodies in *Trypanosoma evansi* (fig. 4) are round or oval, 2 to 5 microns in diameter, stain pale blue, and contain a nucleus and a blepharoplast that stain red with Giemsa's stain. The nucleus may be situated centrally, but more often eccentrically. The blepharoplast is usually eccentrically placed, often at the side opposite to the nucleus; sometimes it is adjacent to

the nucleus. They bear a resemblance to the Leishman-Donovan bodies. I have not been able to distinguish a blepharoplast-less variety corresponding to the female type of schizont described by Chagas in *Schizotrypanum cruzi*. Sometimes the blepharoplast lies closely applied to or over the nucleus, where it is distinguished with difficulty. These bodies do not appear to be surrounded by a definite wall or limiting membrane, but are probably bounded by the periplast of the trypanosome.

In the spleen of guinea pigs killed when the blood is swarming with trypanosomes, a further development of these bodies is evident. The round binucleated body increases in size, and concomitantly a multiplication of both nucleus and blepharoplast takes place. The first evidence of these nuclear changes is seen in forms like that shown in fig. 5 which contains one nucleus but in which the blepharoplast has divided. Succeeding stages containing 2, 4, 6, and 8 nuclei, and blepharoplasts are shown in figs. 6 to 10. The fully developed schizonts are round in optical section and measure 10 to 15 microns in diameter. The average number of nuclei and blepharoplasts appear to be 8, but the number varies from 4 to 16. Some of the large schizonts (fig. 11) show evidence of fission of the protoplasm, and others (fig. 12) show a complete division and differentiation of the merozoites, surrounded by a thin cyst wall. In schizocysts that are not ruptured or deformed the merozoites appear to be arranged like the segments of an orange, but with a slight spiral twist. The merozoites are elongated, sickle-shaped bodies, 6 to 10 microns long and 1 to 1.5 microns broad, are without undulating membrane and flagellum, and have a nucleus situated near the center and a blepharoplast near one end.

The merozoites of *Schizotrypanum cruzi*, according to Chagas, escape from the cyst and penetrate red blood-corpuscles of the host where they develop into adult trypanosomes. Buchanan, also, observed ring-form, binucleate parasites and all stages of the development of these to adult trypanosomes in the red blood-corpuscles from the spleen of the gerbil infected with *Trypanosoma brucei*. Forms, corresponding to these intra-corpuscular stages of Chagas and Buchanan, are frequently seen in the smears from the spleen of guinea pigs infected with *Trypanosoma evansi*, but in no case have I been able to convince myself that the parasite lay within the red corpuscle. In spreading a smear of the spleen pulp containing many trypanosomes it must frequently happen that a parasite will lie over, under, or around a red corpuscle; and in drying such a smear the

parasite may be pressed more or less into the surface of the plastic corpuscle and appear as if intracorpuscular in the stained preparation. The merozoites of *Trypanosoma evansi,* so far as my observations show, develop extracorpuscularly and directly into adult trypanosomes.

No sexual process has been observed preceeding or during the formation of the round bodies from the trypanosomes, nor during the development of the multinuclear cysts. Moreover, the sexual reproduction of trypanosomes should, according to the accepted theory, take place in the invertebrate host. The merozoites of *Trypanosoma evansi* do not show the dimorphism described by Chagas in *Schizotrypanum cruzi,* nor have I observed any evidence of a sexual differentiation in the adult trypanosomes. Therefore, I shall provisionally designate this reproductive process in *Trypanosoma evansi* as a schizogony. The occurrence of the young schizont (round or "latent") stage in *Trypanosoma gambiense, Trypanosoma rhodesiense, Trypanosoma brucei* (*pecaudi*), and *Trypanosoma leptodactyli* indicates that this schizogony is a general reproductive process in the *Trypanosomata.*

The genus *Schizotrypanum* established by Chagas for the parasite of South American trypanosomiasis of man may have to be abandoned. Its chief differential character from the genus *Trypanosoma* appears no longer to exist. The so-called intracorpuscular stages of *Schizotrypanum cruzi* have been observed, also, in *Trypanosoma brucei* and in *Trypanosoma evansi.* In the last species the parasites, although apparently within the corpuscle, are really extracorpuscular. The schizogony of *Schizotrypanum cruzi* described by Hartmann in the endothelial cells of the lung has been observed in *Trypanosoma leptodactyli* by Carine in endothelial cells in the blood from the heart of an infected animal. This so-called schizogony consists in both cases of hypertrophied endothelial cells containing a large number of the round or "latent" forms of the trypanosome. It appears to be a case of phagocytosis of the young schizonts by an endothelial macrophage. Phagocytosis of the trypanosomes, of the round forms, and occasionally of the large schizonts by the macrophages appears to be a common phenomenon in trypanosomiasis; indeed, this is the fate of most of the trypanosomes when they disappear from the blood in the latent phase of the disease. The absence of multiplication by simple division in the peripheral blood would appear to be distinctive of *Schizotrypanum cruzi;* but, in view of the fact that this parasite appears to

multiply by simple division in the gut of the invertebrate host (*Conorhinus megistus*) and in cultures on Novy and McNeal's medium, a suspicion is raised of the accuracy of the observation that it is absent in the peripheral blood of the vertebrate host.

The significance of this schizogony in the life-cycle of the trypanosome is uncertain. Fantham as well as Salvin-Moore and Breinl consider the round form of *Trypanosoma gambiense* and *Trypanosoma rhodesiense* to be a resistant stage of the parasite which persists during the latent phase of trypanosomiasis when the parasites are absent from the peripheral blood. Salvin-Moore and Breinl designate them as such by the name "latent bodies," and Fantham suggests, although he does not definitely state, that these latent bodies may be resistant to drugs used in the treatment of trypanosomiasis and may be responsible for the relapses that occur after chemotherapeutic treatment. If these so-called latent bodies are, as my observations have indicated, only an early stage in the development of the schizonts, it would seem more probable that the mature schizocysts might be the resistant stage of the trypanosome. However, an examination of the spleen and other internal organs of guinea pigs killed during the decrease of the trypanosomes in the blood, or during the latent phase of the infection, has shown no schizocysts but only a very few flagellated trypanosomes and round forms (schizonts). It is possible, therefore, that some of the young schizonts persist through the latent period and undergo schizogony at the beginning of the relapse, giving rise to the new generation of trypanosomes. It is also possible that it is unnecessary to assume the existence of a special resistant stage of the trypanosome to account for latency and relapse in trypanosomiasis. Further morphological and experimental investigation is necessary to decide those questions.

CONCLUSIONS.

In the developmental cycle of *Trypanosoma evansi* a schizogony takes place in the spleen of the vertebrate host.

The observations of Salvin-Moore and Breinl, Fantham, and Buchanan that forms similar to the young schizonts of *Trypanosoma evansi* occur in the internal organs of animals infected with *Trypanosoma gambiense*, *T. rhodesiense*, and *T. brucei* make it probable that schizogony is a reproductive process common to the trypanosomata.

The validity of *Schizotrypanum* Chagas as a genus distinct from *Trypanosoma* Gruby appears to be doubtful.

Further investigation is necessary to determine the significance of this schizogony in the life-cycle of the trypanosomata and its relation, if any, to latency in trypanosomiasis and to relapses after chemotherapeutic treatment.

LITERATURE REFERRED TO IN THE TEXT.

BUCHANAN, S. Note on developmental forms of *Trypanosoma brucei* (*pecaudi*) in the internal organs, axillary glands, and bone marrow of the gerbil (Gerbillus pygargus). *Proc. Roy. Soc. London, Ser. B* (1911), 84, 570, 161–164, Pl. 3.

CARINE, A. Über Schizogony bei Trypanosomen. *Arch. f. Protistenkunde* (1911), 24, 80–83, 2 text figs.

CHAGAS, C. Ueber eine neue Trypanosomiasis des Menschen. Studien über Morphologie und Entwicklungszyklus des *Schizotrypanum cruzi n. gen., n. sp.* Erreger einer neuen Krankheit des Menschen. *Memorias do Instituto Oswaldo Cruz* (1909), 1, 159–218, Taf. 9–13.

FANTHAM, H. B. The life-history of *Trypanosoma gambiense* and *Trypanosoma rhodesiense* as seen in rats and guinea pigs. *Ann. Trop. Med. & Parasit.* (1911), 4, 465–485, Pl. 27.

HARTMANN, M. Notiz über eine weitere Art der Schizogonie bei *Schizotrypanum cruzi* Chagas. *Arch. f. Protistenkunde* (1910), 20, 261–363, 1 text fig.

LAVERAN, A. Les trypanosomes ont-ils des formes latentes chez leurs hôtes vertèbres? *Compt. rend. Acad. des Sci.* (1911), 153, 649–652.

SALVIN-MOORE, J. E., and BREINL, A. The cytology of the trypanosomes. *Ann. Trop. Med. & Parasit.* (1907), 1, 441–480, Pl. 38–42.

ILLUSTRATIONS.

(From water-color drawings by Teodosio S. Espinosa.)

PLATE I.

The figures in Plate I were drawn with the camera lucida at a uniform magnification of 2,000 diameters.

FIG. 1. Motile form of *Trypanosoma evansi* from the blood of an infected guinea pig.

2. A trypanosome coiling up to form a schizont ("latent body"), from the spleen of an infected guinea pig.

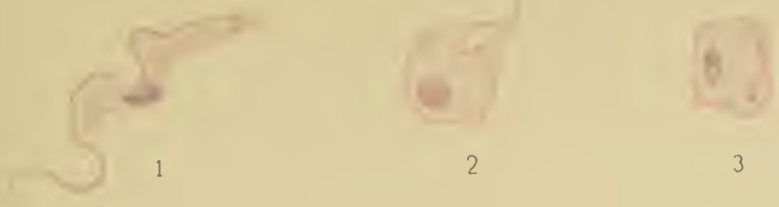
3. A schizont ("latent body") with the flagellum still attached, from the spleen of an infected guinea pig.

4. A schizont ("latent body") of *Trypanosoma evansi*, from the spleen of an infected guinea pig.

FIGS. 5 to 10. Schizonts showing successive stages of division of the blepharoplast and nucleus, from the spleen of an infected guinea pig.

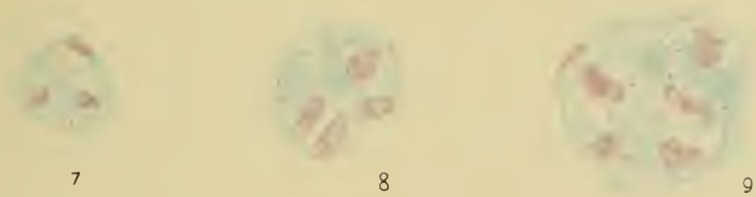
FIG. 11. A schizont showing the beginning of the formation of the merozoites, from the spleen of an infected guinea pig.

12. A mature schizocyst containing 8 merozoites (semidiagrammatic), from the spleen of an infected guinea pig.



1 2 3

4 5 6



7 8 9

10 11 12

FORMS OF TRYPANOSOMA EVANSI.

PLATE I.

REVIEW.

Pathology and Bacteriology of the Eye. An International System of Ophthalmic Practice. By E. Treacher Collins, F. R. C. S., and M. Stephen Mayon, F. R. C. S. Edited by Walter L. Pyle, A. M., M. D., Philadelphia, Pa.

Both authors are well known; their extensive experience, coupled with unusual laboratory opportunities, enabled them to write a treatise excelling anything that has been published heretofore on the same lines. The book is unsurpassed in compactness and clearness, and incorporates the most recent views. Chapters I and II describe aberration in development and neoplasms with description of their origin; Chapter III takes up derangements of the circulating fluids of the eye and of the vessels in which they are contained, and toxic amblyopia and glaucoma; Chapter IV contains a complete treatise upon injuries of the eye, foreign bodies in the eye, burns and injuries with caustics, and also, last but not least, injuries from exposure to bright light, electric shocks, lightning, and the X-rays. The subject of Chapters V and VI is inflammation due to systemic, extrinsic, and parasitic causes. Degeneration is dealt with in Chapter VII. The appendix is devoted to the practical methods of obtaining material for examination, methods of fixing and hardening, mounting macroscopic and microscopic specimens, collecting blood, film-making, preparation of vaccines, and Wassermann and agglutination tests.

The book is well illustrated with about 250 figures in the text and 3 colored plates.

REINHARD REMBE.

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

THE SUBANUNS OF SINDANGAN BAY.

By Eaton B. Christie.

121 pages, 1 map, 29 plates.

Order No. 410. Paper, $1.25 United States currency, postpaid.

Sindangan Bay is situated on the northern coast of Zamboanga Peninsula. The Subanuns of this region were studied by Mr. Christie during two periods of five and six weeks, respectively.

The following is an abstract from the contents of Mr. Christie's report on the Subanuns: Habitat and history; relations with the Moros; material culture; houses, industries; trade; agriculture; family life; social customs; administration of justice; religion; the medicine man; ceremonies; tales; word-lists; physical measurements.

The 29 plates illustrate the Subanuns at work and at play; their industries, houses, altars, and implements; and the people themselves.

THE HISTORY OF SULU.

By Najeeb M. Saleeby.

275 pages, 4 maps, 2 diagrams.

Order No. 406. Paper, $0.75 United States currency, postpaid.

In the preparation of his manuscript for The History of Sulu Doctor Saleeby spent much time and effort in gaining access to documents in the possession of the Sultan of Sulu. It is fortunate that these records have now been translated and preserved in permanent form. This book is a history of the Moros in the Philippines from the earliest times to the American occupation.

STUDIES IN MORO HISTORY, LAW, AND RELIGION.

By Najeeb M. Saleeby.

107 pages, 16 plates, 5 diagrams.

Order No. 405. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

This volume deals with the earliest written records of the Moros in Mindanao. Doctor Saleeby was fortunately able to obtain exact copies of carefully preserved early records written in the Magindanao dialect with Arabic characters. The author presents translations of these as well as 16 half-tone illustrations of certain pages from the originals. The names of the rulers of Magindanao are recorded in five folding diagrams.

NEGRITOS OF ZAMBALES.

By William Allan Reed.

83 pages, 62 plates.

Order No. 402. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

The introductory chapter deals with the general distribution of Negritos and with the distribution of the Philippine branch of the race. The succeeding chapters deal with the various industries, amusements, and social relations of these little men.

Plates from photographs, the greater part of which was taken for this publication, show ornaments, houses, men making fire with bamboo, bows and arrows, dances, and various types of the people themselves.

CONTENTS.

The "Philippine Journal of Science" is issued as follows:	U. S. currency.
Section A. Chemical and Geological Sciences and the Industries	$2.00
Section B. The Philippine Journal of Tropical Medicine	3.00
Section C. Botany	2.00
Section D. General Biology, Ethnology and Anthropology (Section D began with Volume V)	2.00
Entire Journal, Volume II, III, IV, or V	5.00
Entire Journal, beginning with Volume VI	7.00
Single numbers	.50
Volume I, 1906 (not divided into sections)	10.00
Supplement to Volume I (botany)	3.50
Volume I (without supplement)	6.50

Each section is separately paged and indexed.

Publications sent in exchange for the Philippine Journal of Science should be addressed: Library, Bureau of Science, Manila, P. I.

Subscriptions may be sent to the BUSINESS MANAGER, Philippine Journal of Science, Bureau of Science, Manila, P. I., or to any of the agents listed below:

AGENTS.

The Macmillan Company, 64–66 Fifth Avenue, New York City, U. S. A.
Wm. Wesley & Son, 28 Essex Street, Strand, London, W. C., England.
Martinus Nijhoff, Nobelstraat 18, The Hague, Holland.
Mayer & Müller, Prinz Louis Ferdinandstrasse 2, Berlin, N.W., Germany.
Kelley & Walsh, Limited, 32 Raffles Place, Singapore, Straits Settlements.
A. M. & J. Ferguson, 19 Baillie Street, Colombo, Ceylon.
Thacker, Spink & Co., P. O. Box 54, Calcutta, India.

Entered at the post-office at Manila, P. I., as second-class matter.

VOL. VII, SEC. B, NO. 2 APRIL, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

PAUL C. FREER, M.D., PH.D.
GENERAL EDITOR

SECTION B

THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

RICHARD P. STRONG, PH. B., M. D.
EDITOR

MANILA
BUREAU OF PRINTING
1912

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

REPORT OF THE INTERNATIONAL PLAGUE CONFERENCE.

Held at Mukden, April, 1911, under the auspices of the Chinese Government.

Edited by ERICH MARTINI, G. F. PETRIE, ARTHUR STANLEY, AND RICHARD P. STRONG.

483 pages, 18 plates (2 colored, 4 half-tones, 12 charts and maps).

Order No. 416. Cloth, $3.50; paper, $2.50 United States currency, postpaid.

The proceedings of this International Conference and information gained therefrom, together with the results of certain bacteriological investigations, constitute the present report.

Nothing hitherto has been published which gives such a complete and comprehensive account of the entire subject of pneumonic plague.

Delegates from America (United States of); Austria-Hungary, France, Germany, Great Britain, Italy, Japan, Mexico, the Netherlands, Russia, and China attended the Conference.

The Bureau of Science of the Government of the Philippine Islands has been appointed sole agent for the distribution of the printed proceedings of the International Plague Conference.

THE SUGAR INDUSTRY IN THE ISLAND OF NEGROS.

By HERBERT S. WALKER.

145 pages, 10 plates, 1 map.

Order No. 412. Paper, $1.25 United States currency, postpaid.

Considered from the viewpoint of practical utility, Mr. Walker's Sugar Industry in the Island of Negros is one of the most important papers published by the Bureau of Science. This volume is a real contribution to the subject; it is not a mere compilation, for the author was in the field and understands the conditions of which he writes. The following is a brief synopsis of the contents:

Tables of soil analyses, both chemical and physical; analyses of the cane, juice and bagasse; estimates based on actual information as to the costs of production and of cultivation; and estimates of the cost and location of possible central factories. The island is considered by sugar-producing districts; the area of cultivation and the production per hectare are given, and the possibility for future expansion discussed.

The plates illustrate various phases of sugar industry from the cultivation of the field to the transportation of sugar in native sailboats.

A MANUAL OF PHILIPPINE SILK CULTURE.

By CHARLES S. BANKS.

53 pages, 20 plates.

Order No. 413. Paper, $0.75 United States currency, postpaid.

The silk industry is particularly adapted to be undertaken by persons with small capital, and like the making of hats in the Philippine Islands it should thrive with a little encouragement.

In A Manual of Philippine Silk Culture we have presented the results of several years' actual work with silk-producing larvæ together with a description of the new Philippine race. Half-tone plates illustrate in natural size silkworms in different stages of development, pupæ, adult moths, samples of cloth made from eri silk, hand reel, and silk house. Other plates illustrate the various appliances used in raising silkworms and in spinning silk; hand and power reels are illustrated; working drawings are given for a silk house and for a hand reel.

Paul C. Freer.

OBITUARY

Paul Caspar Freer

DIRECTOR OF THE BUREAU OF SCIENCE OF THE GOVERNMENT OF THE PHILIPPINE ISLANDS
DEAN OF THE COLLEGE OF MEDICINE AND SURGERY AND PROFESSOR OF
CHEMISTRY OF THE UNIVERSITY OF THE PHILIPPINES, AND
FOUNDER AND EDITOR-IN-CHIEF OF THIS JOURNAL

We are deeply grieved to announce the death of Doctor Freer at Baguio, Philippine Islands, on April the seventeenth, in his fifty-first year, from arterio-sclerosis and acute nephritis.

In an effort formally to express our sorrow and to honor his memory a memorial meeting of the members of the Staff of the Bureau of Science, the Council of the University of the Philippines, and the members of the Philippine Islands Medical Association will be held on July 1, 1912. The proceedings of this memorial meeting will be published in a future number of this Journal.

At a meeting of the members of the Staff of the Bureau of Science, held on the eighteenth day of April, the following resolutions were adopted:

Whereas it has pleased Almighty God in His Wise and Inscrutable Providence to remove from our midst Paul Caspar Freer, M. D., Ph. D., Director of the Bureau of Science of the Government of the Philippine Islands, since the time of its organization as the Bureau of Government Laboratories in the year 1901, Dean of the College of Medicine and Surgery, and Professor of Chemistry, University of the Philippines, and Founder and Editor-in-Chief of the "Philippine Journal of Science," who, for many years, has been our Leader, Counselor, and Friend; and

Whereas at best we can do little to indicate at this time our real appreciation of him as a man and as a worker for the general good: Therefore be it

Resolved, That we, the Members of the Staff of the Bureau of Science in Manila, Philippine Islands, do hereby express our deepest sorrow and keen feeling of personal loss in the death of Doctor Freer; and be it further

Resolved, That he holds a place of highest respect, admiration and appreciation both officially and personally in the hearts of all of us, and especially of those who were most intimately associated with him in scientific work; and be it further

Resolved, That it is the sense of the Members of this Institution that the Bureau of Science has suffered a very great loss and that the cause of Science in these Islands has been deprived of one of its most zealous and conscientious advocates; and be it further

Resolved, That we extend our sincere sympathy and condolence to his Widow in her overwhelming grief, to his Sister, Brother and other Relatives; and be it further

Resolved, That copies of these resolutions be engrossed and sent to the bereaved Widow and Brother of Doctor Freer, and that they be filed in the Archives of the Bureau of Science, transmitted to the Bureau of Civil Service, published in the forthcoming Number of each Section of the "Philippine Journal of Science," in the newspapers of Manila, in a paper in the City of Chicago, Doctor Freer's birth-place, and in "Science," the Official Organ of the American Association for the Advancement of Science, of which Doctor Freer was a Fellow.

For the Staff of the Bureau of Science:

RICHARD P. STRONG,
CHARLES S. BANKS,
E. D. MERRILL,
ALVIN J. COX,
OSCAR TEAGUE,
A. E. SOUTHARD,
Committee.

[L. S.]

At Manila, Philippine Islands, this eighteenth day of April, in the year of our Lord one thousand nine hundred and twelve.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

VOL. VII APRIL, 1912 No. 2

INFANTILE BERIBERI.[1]

By VERNON L. ANDREWS.[2]

(From the Department of Pathology and Bacteriology, College of Medicine and Surgery, University of the Philippines.)

Of all the so-called tropical diseases, beriberi probably enjoys the distinction of having the largest literature associated with it, of having been the subject of the most extensive discussion, and of having had the most diverse opinions expressed concerning its etiology, symptomatology, and pathology. Nor is this to be wondered at when we consider the number of years the condition has been recognized, its protean manifestations, and the destruction of human life it has wrought.

Beriberi is world-wide in distribution and, although tropical countries have been more extensively ravaged by it, climate seems to exert little or no influence upon the course of disease. The condition has always been considered a disease of adults and adolescents and not until within the last decade and a half has attention been called to a possible manifestation of the malady in earlier life.

[1] Preliminary report presented before the Manila Medical Society, January 8, 1912.

[2] Associate professor of pathology and bacteriology and chief of the department, College of Medicine and Surgery, University of the Philippines.

Clark of Hongkong,(1) in 1900, wrote of an epidemic of beriberi in the Berlin Foundling Home of that place. There was nothing of particular interest in the outbreak except the early age of the patients affected which varied from 4 to 7 years.

The fact that the disease may attack still younger patients apparently escaped the notice of the older writers on the subject. Hirota first described the condition in infants. Although it has been a number of years since his first contribution on the subject was published, still in only two countries (Japan and the Philippine Islands) has infantile beriberi, as an entity, been recognized and studied. In 1888 Hirota observed a peculiar condition in some infants that were brought to his clinic. From 1888 to 1891 he reported 30 of these cases at a meeting of the General Association of the Medical Society of Tokyo.(2) At this time he noted the close similarity between the clinical findings of beriberi in adults and the symptoms observed in these infants and made a tentative diagnosis of "beriberi." Between 1891 and the latter part of 1897 he observed 38 more infants suffering from the same condition.(3) He again noted the similarity of clinical findings in beriberi in adults and the condition he had described in infants and unconditionally called the disease from which the infants were suffering "infantile beriberi."

In 1900(4) he reported additional cases and again affirmed the diagnosis of "infantile beriberi." Later, other workers(5) performed necropsis upon similar cases and observed changes in accord with Hirota's clinical findings. However, they did not make sections of the nerves. But still other Japanese workers(6) have amply confirmed Hirota's diagnosis by clinical and necropsy findings, including the sectioning of nerves.

Because of the high death rate among infants in the Philippines, the subject of infant mortality has always been one of great interest here. It has claimed the attention of many members of the medical profession as well as of laymen from time to time. As early as 1886 a medical symposium(7) was held in Manila on the subject of infant mortality. Seven papers were presented at this meeting, and the one which won the prize considered *taon* or *suba* as a synonym of infantile convulsions and eclampsia. It may be mentioned that the sickness which carries off so many infants here is called *taon, taol,* or *suba* by the native laity.

Some years later, Manuel Gomez Martinez(8) attributed this sickness of infants to a nervous breakdown due to gastralgia and intestinal colic produced by digestive disturbances.

In 1904, M. S. Guerrero,(9) in an article on The Etiology, Symptomatology, Clinical Forms, Diagnosis, and Pathogenesis of Beriberi in Children, based his observations on 103 clinical cases of *taon*. He came to the conclusion that *taon* was similar to a disease described by Hirota as occurring in Japan in children nursed by mothers suffering from beriberi and called by Hirota "infantile beriberi." This paper was read before the Colegio Medico-Farmaceutico de Filipinas and, although it was received with considerable skepticism, nevertheless, it produced a complete revolution of ideas concerning *taon*. Guerrero performed no necropsies and his conclusions were based solely on his clinical observations. In the following year, 1905, the native doctors, without attempting to confirm Guerrero's conclusions by necropsy, began attributing death to "infantile beriberi," and the number of such death certificates has gradually increased to the present time.

Four years later, in 1908, José Albert(10) described the clinical and pathological findings in a case of infantile beriberi. So far as I have been able to ascertain this was the first attempt in the Philippine Islands to confirm the clinical diagnosis in these cases by necropsy. In this case the pathological findings amply confirmed the clinical observations, degeneration of the nerves even being demonstrated.

In the latter part of 1909, the Bureau of Health attempted to confirm, by necropsy, the clinical diagnoses appearing upon the death certificates of infants in Manila. In examining the death certificates of infants of 1 year of age and under, it was found that in a large majority of them death was attributed to "convulsions," "congenital debility," "beriberi," "acute bronchitis," "acute meningitis," or "enteritis." At first, necropsies were performed in all cases in which death had been attributed to "acute meningitis;" later with regard to congenital debility, convulsions, beriberi, acute bronchitis, and enteritis. The results were startling and appeared in a paper by McLaughlin and the writer(11) which was presented at the first biennial meeting of the Far Eastern Association of Tropical Medicine held in Manila in March, 1910, and was published in July, 1910. In this paper, we presented the pathologic findings observed at necropsy of 219 infants under 1 year of age. Of this number, we found 124, or 56.6 per cent, to have died of a condition which we called infantile beriberi. Neither of us had been able to see the cases clinically and the history obtained by the medical inspector was quite meager.

Three months later M. S. Guerrero and Joaquin Quintos(12)

in a monograph upon beriberi of infants due to breast feeding, reported 176 clinical cases with 2 necropsies which were performed twenty-two and thirty-two hours respectively after death. Their clinical studies are quite detailed and complete. The necropsies having been performed so long after death and the bodies not having been placed in ice boxes, post-mortem changes undoubtedly rendered their pathologic findings, especially the microscopic ones, questionable or obscure. They concluded that death of the infants was due to infantile beriberi and that this disease was caused by a toxin in the mother's milk.

In spite of the large amount of work that had been done on this subject, the evidence was considered by the writer insufficient to establish the cause of the high infant mortality in the City of Manila. In the past the different papers by different men have been almost entirely clinical or entirely pathological and not a combination of the clinical and pathological study of a large number of cases by the same worker. Hence the present work was undertaken with the idea of studying a series of cases clinically and subjecting those that died to necropsy.

It was planned to carry out the following procedures:

1. A clinical study of infant and mother.
2. Analyses of the milk of mothers whose infants had died of the disease.
3. In case of death of the infant to secure a quick necropsy and material for histological study.
4. To determine the etiology of the condition, if possible.

Instead of taking the cases one at a time, it was thought best to study a number at the same time so that comparisons could be made and differences in clinical symptoms would be more striking. To accomplish this an assistant was sent into the Tondo district, which furnishes the largest number of cases of all districts of the city, to find the patients, and to observe them from day to day. Sick infants are met with on almost any street of this district. If one of them is suffering from beriberi it will nearly always be found to be a plump, apparently well-nourished baby. The face is full, sometimes presenting an almost swollen appearance. Frequently œdema may be elicited by deep pressure on the lower extremities. The little one is invariably breast-fed and is usually about 2 months old. Nine-tenths of the deaths occur between the ages of 1 and 3 months, but it is not unusual for the infant to be 4, 5, 6, or even 7 months old. I encountered the disease once or twice in infants that were 10 months of age.

Unless the infant is seriously ill and the disease far advanced,

it would not be considered at the first glance to be sick, for it smiles and plays as a normal infant should. Closer inspection, however, will change this opinion. The onset of symptoms is insidious; they come so gradually that the mother does not notice them till they become prominent. There is cyanosis around the mouth and nose, slight dyspnœa, periodic restlessness, insomnia, rarely a slight cough, occasionally vomiting, and possibly a change in the child's voice. As a rule one of these symptoms is more pronounced than the others and this is the one the mother notices first and for which she seeks relief, although several of the others may be present at the same time. Possibly the mother has noticed nothing wrong with the child, yet it may manifest several of these symptoms. When once the condition is present the tendency is to increase in severity and seriousness. Aphonia and oliguria appear, as a rule, late; this is especially true of the oliguria. Patients not infrequently exhibit repeated attacks of the disease with eventual recovery. On the other hand, well-authenticated cases are on record where the infant has been apparently well (at least the mother has noticed nothing wrong) when suddenly the child is seized with a fit of crying without any apparent cause; the crying increases in severity, the infant finally goes into convulsions and dies in a few hours. The child evidently suffers great pain, as the crying continues until death. Clinically, I have never seen such a case, but I have observed cases at necropsy in which the attending physicians gave such a history and have found the typical pathologic picture of beriberi to be present. I do not doubt that cases with such clinical histories occur, but the child probably had been sick for some time and the mother had noticed nothing abnormal, and not until an acute heart attack set in was the real condition of affairs revealed. Possibly the child began crying for other reasons and the exertion thus produced precipitated an acute attack of heart failure. This form of the disease is spoken of by the Filipino doctors as the *acute pernicious type.*

CLINICAL OBSERVATIONS.

This study includes a series of 27 infants, 8 of which came to necropsy. Several died in which necropsy was not permitted.

Circulatory system.—The pulse is rapid, ranging from 130 to 170, or more, per minute. The latter rate is not unusual. It is usually of good volume. There is an increase of dullness both to the right and the left in the præcordial area. The second pulmonic sound is accentuated. The apex beat is usually clear,

but is muffled sometimes. In one or two cases I thought I obtained a distinct heart murmur when the infant was sleeping. This could not be located.

Respiratory sytem.—As a rule dyspnœa is present, and this increases in intensity the longer the condition exists, until at the end it seems that all the accessory muscles of respiration are called into play. While a certain amount of dyspnœa is nearly always present, periodic attacks come on in which it seems that the child will die the next minute. In one such case the attack came on at 5 o'clock in the evening and lasted until 9 o'clock that night. I watched the child during this time. It was moaning and sighing and very restless and its face became cyanotic. It seemed almost impossible for it to get any air. Apparently all the accessory muscles of respiration were called into play. The intercostal and abdominal muscles were depressed with every inspiration. A slight manifestation of Cheyne-Stokes' respiration was present. At 9 o'clock the attack wore off and the child, exhausted, sank into peaceful slumber. The next morning my assistant reported that the child was smiling and apparently well. That evening shortly after 5 o'clock another attack came on somewhat severer than the former. I remained with the child from 5 o'clock until 11 that night. Its suffering was intense. During these attacks the respirations were 112 per minute and the pulse from 160 to 180. It remained in this condition until 3 o'clock the next morning when it died. Auscultation showed that considerable œdema was present in both lungs and an increase of fluid in the pleural cavities. Acute attacks of dyspnœa, which are apparently due to acute attacks of heart failure, are not uncommon in these cases. They may appear every few days, or weeks may intervene between attacks. In some a form of Cheyne-Stokes' respiration is present; coughing is never a marked symptom, but does occur. The normal bronchial breathing is present and râles of any kind are unusual, unless œdema of the lungs is marked. I have seen one or two cases in which there was apparently little or no dyspnœa.

Fever.—There is *no fever* in an uncomplicated case. Indeed the temperature is slightly subnormal.

Digestive system.—The abdomen may be distended and tympanitic, or it may be flat. Constipation is present in the majority of cases; in some, slight diarrhœa is present; in others, the bowels are normal. The child has a normal appetite and takes the nipple greedily.

Muscular system.—The child is apparently well nourished. There is no paralysis or paresis. An attempt was made to elicit the reaction of degeneration in the muscles of the calves of the legs of two infants by the Faradic and Galvanic currents, but, owing to the early age of the patients and consequent unsatisfactory result, it was abandoned.

Cutaneous system.—The skin is anæmic, soft, and almost velvety in touch. In many cases a general œdematous condition is present. It may be well marked or only slight.

Kidneys.—In many cases oliguria or even anuria is a late symptom. When this makes its appearance the child has been suffering for some time, although this is occasionally one of the symptoms which first attracts the mother's attention. In several cases the urine was examined during life and in a few others was obtained from the bladder at necropsy, but in all instances albumen was absent by the nitric acid and heat tests.

Nervous system.—In many cases the child manifests periods of restlessness and moaning; its sleep is disturbed.

Voice.—Aphonia may be present for several weeks or it may come on late. There may be complete loss of voice or only a slight weakness. In many cases the voice has a peculiar shrillness or whining tone which manifests itself soon after the disease begins and remains till aphonia develops or till death takes place.

Sex.—Both sexes are susceptible.

Age.—The condition is most common between the ages of 1 and 3 months, although cases of 4, 5, and 6, and even 10 months of age are noted.

Social condition.—The disease is most common among the extremely poor, but is occasionally found among the fairly well-to-do classes.

Season of prevalence.—According to the statistics of the Bureau of Health, infantile beriberi is most common in the months of September, October, and November, gradually decreasing in numbers with the approach of the hot season (April, May, and June) and then increasing as the rainy season advances.

History of the mother.—In nearly all cases the mother shows some symptoms of beriberi; numbness and pains in the legs, anæsthetic areas on the legs, formication, tachycardia, dyspnœa on slight exertion, lack of coördination in walking, palpitation, possibly distinct heart murmurs, loss of knee jerks and other reflexes. In two cases we found the mother suffering from such pain in the legs that she could not walk, but sat on the floor and shuffled herself along. On inquiring as to the

mother's diet we found that it consisted entirely of white rice, and fish or meat; rarely were any vegetables or fruit eaten.

The disease is just as apt to manifest itself in the first infant of a girl 18 years old as in the infant of an older woman with her third or later pregnancy. Indeed one of the severest cases we saw in both mother and child was exhibited in a girl barely 18. The child died when 6 weeks old and at this time the mother could hardly stand. She sat on the floor and pushed herself along as best she could. The pains in the legs were severe. Areas of anæsthesia, numbness, and formication were present.

It is not unusual to obtain the history that the first and second children have died each at about 2 months of age from *taon.* With the third child the doctor advises artificial feeding, and if the little one escapes the gastro-enteritis which usually follows, it survives. With the fourth child the mother resumes the breast-feeding with the result that the infant dies of *taon* in about 2 months. Occasionally the mother starts the infant on artificial feeding. In about a month, gastro-enteritis has become severe, and she returns to breast feeding; two months later the child dies of beriberi.

Several families were found in which the first and second children were born in the country and showed no evidence of *taon.* On moving to Manila the subsequent children were carried off by this disease. In the country the daily rice is pounded out by the family and a large part of the pericarp remains. Furthermore, both vegetables and fruit form a part of the diet, whereas in Manila only polished rice is obtainable.

Analysis of milk.—In the past attempts have been made to analyze the milk of women with beriberi. In all such attempts the diagnoses were based only on clinical findings in the child or mother or both. The amount of milk secured was small and the number of cases very limited. It is evident that analyses under such conditions are unsatisfactory and perhaps misleading. In the present cases the milk was obtained from women the death of whose infants from beriberi had been confirmed by necropsy. Results obtained from such cases are obviously more reliable than those obtained from cases based only on clinical symptoms; then, too, the amount of milk secured was larger. The mother was visited as soon after the funeral of the child as possible. She was given a sterile flask containing a few drops of formalin and was told to milk into the flask all she could from time to time. The next day at about the same hour the flask was called for. In this way we secured a twenty-four-hour

specimen of milk. In some cases we did not obtain much but it represented portions secured during different periods of the twenty-four hours. On the whole the analyses show the milk of these cases to be very poor, but some are quite normal so far as proteid, fat, and, carbohydrate are concerned and one or two are exceedingly rich.

TABLE OF MILK ANALYSES.

Date.	Case No.	Volume.	Specific gravity.	Water.	Fat.	Sugar.	Proteid.	Ash.	Calcium oxide CaO (parts per 1,000 of ash).	Phosphorus pentoxide P_2O_5 (Parts per 1,000 of ash).
				Per ct.	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*		
Normal human milk			1.02834	87.30	4.00	7.00	1.50	0.20	.328	.473
August 5, 1911	1		1.032	88.26	2.82	7.70	0.92	0.30	1.603	.946
September 25, 1911	1	215	1.032	88.95	2.29	7.16	1.50	0.10		
September 17, 1911	2		1.032	89.75	1.76	7.53	0.85	0.11		
September 23, 1911	3	255	1.041	85.75	4.05	8.36	1.50	0.34		
September 26, 1911	3	195	1.029	88.27	3.52	5.22	2.70	0.29		
October 1, 1911	4	88	1.029	90.37	1.76	6.51	1.30	0.06		
October 11, 1911	5	120	1.036	89.43	1.06	7.71	1.70	0.10	1.072	.323
October 11, 1911	6	46	1.020	90.52	3.52	4.98	0.90	0.08		
October 20, 1911	7	130	1.033	89.03	2.11	7.61	1.15	0.10	.742	.471
October 24, 1911	3	107	1.034	88.39	2.46	7.44	1.50	0.21	1.312	.626
October 27, 1911	8	149	1.033	90.14	1.06	7.64	0.90	0.26	1.502	.663
November 10, 1911	9		1.038	88.10	1.76	8.54	1.50	0.10		
November 15, 1911	10	51	1.029	88.27	3.52	6.66	1.40	0.15		
December 15, 1911	11		1.034	87.12	3.52	7.60	1.50	0.26		

The first line of figures in the table shows the percentage of the various constituents of milk of the average normal woman as given by Holt. The calcium oxide and phosphorus pentoxide, however, are taken from Hammerstein's Physiological Chemistry and represent the parts per thousand parts of milk. In studying the table it is seen that with the exception of four cases, Nos. 3, 6, 10, and 11, the amount of fat is greatly below the the normal. However, it is evident that the lessened amount of fat is not the cause of the disease, as the analysis which shows the largest percentage of fat was from one of the most marked cases we had.

The amount of calcium oxide is increased from three to four times the normal.

The amount of phosphorus pentoxide is in one instance almost double what it should be. This is interesting when taken in con-

nection with the work of Schaumann(13) and Aron.(14) They claimed to have demonstrated that the polyneuritis of fowls fed on white rice results from a lack of phosphorus in the food. Later work, however, by independent investigators(15) has shown, I think, conclusively that phosphorus is not a factor in the etiology of the disease. The analysis of the mother's milk just given confirms the view taken by these latter writers.

The analyses were made in the division of organic chemistry of the Bureau of Science.

From the table it will be noticed that the milk from some of the cases has been analyzed at different times. In case No. 1 the first analysis was made August 5, a day or so after the death of the child. The second analysis was made seven weeks later after the death of two puppies which she had nursed (see below). In case No. 3 the first analysis was made on September 23 and showed the milk to be very rich—so rich that I thought perhaps a mistake had been made and obtained another sample for analysis September 26. This was quite similar to the first. Her milk was again analyzed on October 24 after she had nursed the puppies. At this time the fat content was considerably lower.

NECROPSY FINDINGS.

In this series there were 18 necropsies in 8 of which the infants were seen during life. The other cases were referred to us by the various health stations of the city. The submitting of the body for necropsy was voluntary on the part of the parents. As we did not wish to antagonize the relatives the body was dissected as little as possible; hence the cranium was opened in only a few cases.

In those cases that were not seen during life, the parents were visited immediately after the necropsy; and, with either Doctor Calderon or Doctor Hilario acting as interpreter, the history of the child's sickness was obtained. In all instances this agreed with the clinical findings of those cases we had observed.

The macroscopic findings in these 18 cases agreed in all particulars with those examined two years ago. At that time we did not report on the histologic findings, because the cadavers were not fresh. In this series several of the bodies were autopsied a few hours (four to six) and most of them within fourteen hours after death. The condition encountered in these necropsies may be outlined as follows:

The body is that of an apparently well-nourished infant, that is, plump; the skin is usually pale and anæmic. The face is full with almost a swollen appearance. The flesh of the thighs and

legs is soft and flabby, and, as a rule, pits on deep pressure. Occasionally the skin has a tough, leathery feel, a leaden color, and a slight goose-flesh appearance.

Subcutaneous fat is present, apparently in good amount, grayish-white and very moist; the muscles are anæmic. Owing to the œdema, one is apt to overestimate the amount of fat present and hence the bodies may not be as well nourished as they appear. Generally there is an increase of peritoneal fluid which is distinctly yellowish.

Heart.—The pericardial sac contains a clear, greenish fluid. Probably the most striking and constant change is found in the right heart. Its musculature is coarse and firm and forms much the larger part of the organ including the contour of the apex. Its trabeculæ and papillary muscles are prominent and its cavity is enlarged. The wall of the right ventricle equals or exceeds that of the left. In many cases the foramen ovale is still patulous but is apparently competent. The ductus arteriosus, when not closed, is represented by a very minute opening. In this series it was entirely closed in half the cases. The circumference of the pulmonary ring exceeds that of the aortic by 4 millimeters on an average. The circumference of the tricuspid ring exceeds that of the mitral by 6 millimeters. The musculature of the left heart is soft and flabby, and darker than that of the right. The blood vessels of the heart are congested and prominent, and frequently a few hæmorrhages are seen along the auriculoventricular junction.

Lungs.—These organs are light pinkish-gray anteriorly and light purplish-gray posteriorly. They fill the pleural cavities and crepitate throughout. The anterior part of the lung is lighter and more fluffy than the posterior. Few or many petechial hæmorrhages may show beneath the visceral pleura, especially along the junction of the lobes. Occasionally there is a slight increase of the pleural fluid. In two cases in this series bronchopneumonia was present. It was not marked and was clearly a terminal affair.

A cut section shows a pinkish-gray surface which may or may not exude some blood. Air can be expressed from all portions of the lung and usually also a slight amount of œdematous fluid. The posterior part of the lung is darker in color and is heavier than the anterior, and more fluid can be expressed from it than from the anterior part. The bronchi do not appear to be hyperæmic, but contain more or less frothy material and mucus. Sometimes this can be expressed from the smaller bronchi.

Spleen.—This organ is usually very hyperæmic and the normal markings are partially obliterated.

Kidneys.—The kidneys are reddish-gray; fœtal lobulations are prominent. A cut section is very moist and a considerable amount of blood oozes from it. Striations of the cortex are plainly seen. Except for congestion, the kidneys, in the greater number of cases, present a normal appearance. Occasionally a slight degree of albuminous degeneration or a few subcapsular hæmorrhages occur. The adrenals show congestion.

Liver.—The liver is dark reddish-brown and firm. Section shows congestion and rarely a slight "nutmeg" appearance. The liver is frequently slightly enlarged due to the intense congestion. Here, also, we may find some albuminous degeneration.

Stomach and duodenum.—The stomach nearly always contains some curdled milk and mucus. The mucosa is smooth and anæmic. *No rice or other artificial food was found in the stomachs of any of the cases;* sometimes there is a trace of fæcal material present. Not infrequently the duodenum is congested and even a few minute hæmorrhages may be seen in the mucosa.

Intestines.—They are normal in appearance. The intestinal contents are yellow, semi-liquid, and apparently digested. The mesenteric glands may be slightly enlarged and soft. Occasionally a few petechial hæmorrhages show in the mucosa.

Urinary bladder.—It may or may not contain urine. In a number of cases the urine was examined for albumen by the nitric acid and heat tests and found negative.

Throat organs.—Except for some froth and mucus present in the larynx and trachea, these organs are normal.

Thymus.—The thymus is usually of normal consistency and full. Some milky fluid can frequently be expressed from the cut surface.

Meninges and brain.—In those examined the meninges were congested and œdematous and there was usually an increase of the cerebrospinal fluid. The brain substance was of normal consistency or soft and very moist.

In two cases evidence of rickets was present, indicated by the slight formation of a rickety rosary. This was not marked and there was no other evidence of the disease.

There was no evidence of scurvy in any case. The periosteum of the femurs was not examined for hæmorrhages, since it was desired to mutilate the body as little as possible.

The anatomic findings just described correspond very closely with those of moist beriberi in adults. Indeed, throughout the

description, organ by organ, the findings are identical; or, if any difference exists, it is of degree only.

In these cases there are four points of special interest: first, the dilated and hypertrophied right heart; second, the congestion of the viscera; third, anasarca; fourth, the *absence of other findings* to account for death. I have relied on these points in making the diagnosis of infantile beriberi. In several cases I have seen a hypertrophied right heart in which I could account for the condition by a patent foramen ovale, which was not competent, or by an imperfect interventricular septum. All these cases have been excluded. Whenever death could be attributed to causes other than beriberi, this has been done.

Since the description of the gross findings corresponds with that of moist beriberi of the adult, the question has often occurred to me: Is there an atrophic form of infantile beriberi corresponding to the atrophic form in the adult? One such case, I think, occurred in the present series. The infant was 10 months old and was *greatly emaciated.* The condition was undoubtedly chronic. The baby developed fever a couple of days before death and at the necropsy there was a slight bronchopneumonia present. The right heart was greatly hypertrophied and dilated. The calves of the legs and the dorsum of the feet were slightly œdematous. Such cases are not common.

MICROSCOPICAL FINDINGS.

In the paper of two years ago we gave no microscopical description of tissues for fear the post-mortem changes would render the lesions obscure. In the present cases this difficulty was overcome, and the microscopical findings are as follows:

Heart.—The muscle fibers of the right heart are hypertrophied and the muscle nuclei are apparently increased in number. In nearly all cases the cross striations are distinct without any appearance of degeneration. In a few cases there is a slight clouding of some of the fibers. The fibers of the left heart are of normal size, cross striations are distinct and no clouding of fibers is present. Congestion is present.

Lungs.—The lungs present the picture of extensive hypostatic congestion and more or less œdema. The vessels are greatly congested, and the alveoli in the dependent portions of the lungs contain more or less granular débris. A few epithelial cells are scattered here and there in the alveoli and sometimes a few red cells. There is no evidence of fibrin by the hematoxylin and eosin stain and only a few leucocytes are to be seen. The

bronchi present absolutely no evidence of inflammation. In the anterior portions of the lungs there is more or less evidence of emphysema as shown by the thinned and broken alveolar walls.

Spleen.—The spleen shows intense congestion. In many places hæmorrhages have taken place in the splenic tissue as shown by the almost solid mass of red cells present. There is no increase of splenic tissue.

Liver.—Besides the congestion, the other changes are slight albuminous degeneration and fatty infiltration. The fatty deposit is scattered through the liver substance, but is probably more prominent around the portal-spaces. In some cases considerable hæmorrhage is present beneath the capsule.

Adrenals.—Other than congestion, they present nothing abnormal.

Thyroid.—The sections of some cases show the presence of more colloid material than do the sections of others. Congestion is present.

Parathyroids.—Aside from congestion they are apparently normal. The nuclei are deeply staining and are surrounded by a clear protoplasm. The cell membrane is clearly defined.

Thymus.—In some cases there is possibly an increase of the cellular elements. Hassel's corpuscles appear normal. Congestion is present.

Kidneys.—These organs are intensely congested. Albuminous degeneration of the convoluted tubules is shown in a number of the cases and a few show fatty degeneration in addition. The endothelial cells of the glomeruli seem to be increased in number and in many cases there is a slight granular detritus in Bowman's capsule. There is *no infiltration of leucocytes.* There is apparently no difference between the sections of the kidneys in which oliguria was present and those in which it was absent. It is probable that the condition of the glomeruli and Bowman's capsule is due to the intense congestion present.

Nerves.—Sections from various nerves (vagi, phrenic, intercostal, and anterior tibial) were taken for staining. These were stained by Marchi's method and show degeneration of some of the fibers. The degeneration is not as extensive as is found in cases of adult beriberi but is clearly defined.

EXPERIMENT ON PUPPIES.

Since in infants sick of this disease, improvement rapidly follows a change in diet, it seems evident that the mother's milk bears some causal relation to the condition. The disease is evidently not due to bacteria in the milk, for in that case, im-

provement would not so quickly manifest itself on simply changing the food of the infant or the mother. It is highly probable also that it is not due to toxins in the milk, for the reason, that the anatomic and histologic findings reveal nothing to substantiate such a basis for the disease.

In the paper written two years ago McLaughlin and the writer stated that the mother's milk "is probably deleterious by reason of what it *lacks* rather than because of any harmful constituent." If this were true, it seemed highly probable that the condition could be reproduced in laboratory animals, for example, young puppies by feeding them with the mother's milk.

The majority of the infants die when 1 to 2 months old. Hence it would be expected that the puppies would show some symptoms after nursing one to two months.

For these experiments I secured young puppies 2 to 14 days old. When it had been demonstrated by necropsy that an infant had died of beriberi I called on the mother and persuaded her to nurse two puppies. After explaining to the mothers the object in view, most of them were willing to comply with the request without any recompense whatever. In all, 16 puppies were used, but for various reasons (some died, for others the women did not have sufficient milk, and, in one or two cases after nursing them a while the women were unwilling to proceed further with the experiment) only 7 were nursed for a period of one month or longer. These were nursed by cases 1, 3, 8, and 10. (See table of milk analyses.)

In case 1 the woman lived near the Medical School. The puppies were kept in the laboratory and the woman came here every day, remaining from 7 in the morning to 6 in the afternoon, and nursed the puppies every two hours. The puppies were weighed every day or two. The other cases occurred on the other side of the city and the puppies were taken to the women's homes. They were kept warm and comfortable and were fed every two hours. I visited them every day or every other day, weighed them, and noted the changes taking place in them.

EXPERIMENT NO. 1.

The two puppies were 3 days old and the woman began to nurse them August 12, just one week after the death of her child of typical infantile beriberi. The woman had numbness and areas of anæsthesia in her legs. It was with some difficulty that she could walk and any exertion produced palpitation of the heart. She suffered from shortness of breath. Her knee jerks were absent. During the first four days the puppies lost in weight; they then gained continuously until two days before death when

a slight drop occurred. They nursed for six weeks and died within twenty-four hours of each other, September 22 and 23.

Although the puppies gained in weight they never became fat and were in fact rather lean-looking. Nothing of importance occurred until the fourth week when it was noticed that they had some difficulty in walking or standing. The ankles of the front feet turned under them; they swayed from side to side, and apparently could not control the muscles so as to go just where they desired. As time passed, all these phenomena were augmented and other symptoms appeared. The hind legs became more seriously affected than the forelegs. The puppies sat on their haunches and moved their legs as little as possible. On getting up they fell to one side or the other and stumbled on their noses; apparently they had lost control of most of the muscles of locomotion. This condition continued to grow worse until death. During the fifth week it was noticed that they were becoming anæmic. Also during the last two weeks the front feet became œdematous.

Necropsy was performed about ten hours after death. The bodies of the puppies were emaciated and the subcutaneous tissues were anæmic and œdematous throughout. The peritoneal cavity contained a slight increase in fluid. The heart was neither hypertrophied nor dilated. All the internal organs were anæmic and œdematous. The intestines contained a large number of ascaris and hookworms. The fæces were dark colored and in a few places in the mucosa of the intestines hæmorrhages had taken place.

EXPERIMENT NO. 2. (PLATE II.)

Two puppies, 4 days old, were given to Case III to nurse on September 26. The 1-month-old child had died one week previously of typical infantile beriberi. The woman showed marked symptoms of beriberi; numbness, anæsthesia, and formication of legs; shortness of breath, distinct heart murmur, and loss of knee jerks and other reflexes.

For the first three days the puppies lost weight. They then continued to gain until the end. One died October 19 after nursing twenty-three days, and the other October 22 after nursing twenty-six days.

Both these puppies became plumper and apparently fatter than the first two. Nothing of importance was noticed in either of them until the 14th of October when both began to show symptoms of weakness in the legs. This grew worse until it seemed that the hind legs were practically paralyzed. The puppies would rise up on their front feet and then fall over. Their feet and legs became œdematous. The first one, which died on the 19th, developed no further symptoms; but the second, living three days longer, developed *marked dyspnœa*, and the legs became greatly œdematous. It made no attempt to move its hind legs but dragged them along. Toward the last it could not raise itself on its front feet.

Necropsy. Puppy which died October 19.—The body tissues are œdematous, and the muscles are pale. The heart is apparently normal. The lungs are congested and œdematous. The spleen and liver are dark colored, firm, and congested. The kidneys are pale. The intestines contain a few hookworms. All tissues are very moist.

Necropsy. Puppy which died October 22. (*Plate II.*)—The subcutaneous tissues showed marked œdema. The muscles are pale. Increase of fluid in the peritoneal and pericardial sacs. *The right heart is dilated*

and hypertrophied. The lungs are congested and œdematous. The spleen and liver are dark colored and congested. The kidneys are pale. Intestines contain a few worms.

EXPERIMENT NO. 3.

In this instance the woman, Case VIII, objected to nursing a puppy whose eyes were closed. To overcome this difficulty I had to give a puppy that was 14 days old and this fact may have had an influence on the effect produced in the puppy. The woman did not exhibit marked symptoms; slight shortness of breath and numbness of legs were most noticeable. She was given two puppies, but one was soon taken away because she had not sufficient milk for both. She began nursing the puppies October 30, about one week after the death of her child from typical infantile beriberi, and continued nursing one of them till December 29, when it died. During the first three weeks the puppy gradually lost in weight. It also vomited occasionally after nursing and had a number of convulsions. These attacks lasted from five to seven minutes, the woman said. They would begin with whining and frothing at the mouth, and then the muscles would become rigid. I never saw the puppy in one of these attacks. They were said to occur at night as well as in the day time. Altogether it had 6 convulsions that the woman noticed.

At the end of third week it was somewhat emaciated, but began to gain in weight and continued to gain until the last week of life. During the third week of nursing it was noticed that its front feet were becoming œdematous. This condition became worse, and later the hind feet began to swell. The puppy became very weak and staggered about while walking, but it never lost complete control of its muscles and was always able to move about. It died December 29, after it had been nursed by the woman for two months.

Necropsy.—Body of an emaciated puppy. Subcutaneous tissues are œdematous and anæmic. Twenty cubic centimeters of fluid in the peritoneal cavity. The heart is pale, otherwise apparently normal. Lungs are slightly congested and œdematous. No increase of fluid in pericardial or pleural sacs. Spleen dark colored, normal markings. Kidneys pale, moist. Liver dark red, apparently normal. Stomach normal. Intestines show the presence of hookworms and several minute areas in which small hæmorrhages have apparently taken place.

EXPERIMENT NO. 4.

The puppies were 7 days old when the woman, Case 10, began to nurse them on November 15, 1911, five days after the death of her infant from typical infantile beriberi. The woman had loss of knee jerks. She easily became tired on exertion, and her legs were weak. There was no numbness or areas of anæsthesia in the legs.

Puppy which died December 14, 1911.—This puppy lost in weight for the first five days, then gradually increased until death.

At the end of the first two weeks it was noticed that its feet were beginning to swell and were becoming œdematous. From this time on it exhibited symptoms of weakness. Its front ankles turned under it when it attempted to stand. In walking it staggered from side to side

and fell over easily. As time passed these symptoms became more marked. There was never paralysis.

Necropsy.—Apparently a fairly well-nourished puppy. Feet œdematous. Subcutaneous tissues very œdematous and anæmic. Slight increase of fluid in the peritoneal cavity. Heart firm, normal. Increase of fluid in the pericardial sac. Lungs congested and œdematous. Spleen normal. Kidneys apparently normal. Liver dark red, normal. Stomach normal. Intestines show a very few hookworms.

Puppy which died December 31, 1911.—The puppy lost weight the first two weeks but was sick and nursed but little several days of this time. During the third week it gained in weight and its feet began to swell. As the fourth week came on the œdema of the feet increased in amount and the legs became weak, the ankles of its front feet turning under it when it stood up. It staggered first to one side and then to the other, stumbled on its face, and in other ways exhibited a weakness or loss of control of its muscles. It lost its footing easily. This condition continued through the fifth and sixth weeks until the puppy died December 31, having nursed six weeks.

Necropsy.—Body of an apparently well-nourished puppy. Feet and ankles œdematous. Subcutaneous tissues œdematous and anæmic. Increase of fluid in the peritoneal cavity. Pericardial sac shows slight increase of fluid. Heart apparently normal. The lungs are congested and œdematous. Spleen normal. Kidneys apparently normal. Liver dark-red, normal. Stomach normal. Intestines contain a few hookworms.

In all these necropsies the vagi, sciatic and intercostal nerves were preserved and stained for degeneration. In all those examined a few fibers were found in which degeneration was present.

To summarize, all of these puppies showed incoördination and weakness of the extremities, particularly of the hind legs. In all slight degeneration of the peripheral nerves by the Marchi method was demonstrated. All showed œdema and anæmia of the subcutaneous tissues. These findings agree entirely with those of the infants dying of beriberi. However, only one of the puppies showed the dilation and hypertrophy of the right heart which I have regarded as a constant finding in infantile beriberi. In my opinion these experiments furnish, therefore, additional evidence that the condition described as infantile beriberi is due simply and solely to the ingestion of the mother's milk.

DISCUSSION.

Without doubt in these infants we are dealing with cases of infantile beriberi. The clinical picture and the anatomic findings all point to this. In all cases the child is breast fed, and with the manifestation of symptoms in the infant the mother likewise shows some symptoms. Occasionally the symptoms in the mother are not apparent on the first examination, but will appear later if the child continues nursing. Infrequently we

find a mother showing symptoms of the disease and the child apparently free, but with continued watching, sooner or later, symptoms will appear in the infant.

The history of the mother shows that invariably her diet consists of white rice and fish or meat; rarely of a vegetable or any fruit. When taken for a sufficient length of time such a diet leads to beriberi according to the present ideas that obtain as to the etiology of beriberi in the adult.

The woman before pregnancy probably exhibited symptoms of beriberi, as many of the natives do. When the necessity arises for providing the material for a new being, as she is called upon to do in pregnancy, the strain becomes too great. The latest works on the etiology of adult beriberi consider this disease not as an infection or toxæmia, but as the result of an improperly-balanced diet. Further proof that this condition is not due to an infection or toxæmia is afforded by the recent work of Chamberlain and Vedder in which they made an extract of *tiqui tiqui* (rice polishings), and by feeding this extract to chickens prevented the development of polyneuritis in them. They(16) also treated infants suffering from *taon* or infantile beriberi with this extract, and the improvement in the symptoms was prompt and striking. In one suffering from this disease there is something lacking in the diet which is essential to the normal growth and development of the nerves. When this substance is deficient in the mother's diet it is highly probable that it will also be deficient in her milk, and hence both the mother and child will suffer. Probably with a deficiency in her diet the mother draws on her own store-house for this substance for her child, thus diminishing her own supply and producing the disease in herself. This probably accounts for the variation in time in the development of symptoms in the infant and its mother.

In the records of the Bureau of Health the death certificates show that infantile beriberi is more prevalent in the wet season. I think this is due, not to the effect of the season *per se* on the child, but to the relation it has to the growing crops. After the rainy season, usually in November, vegetables and fruits begin to come into the market in increasing quantity. These commodities decrease in price and they are available as food to a larger number of people. These foods become scarcer with the beginning of the rainy season; prices go up with a consequent shutting off of the supply to the poorer classes.

It has been recognized for some time among Filipino physicians that the ordnary medication in these cases of infantile

beriberi does little good. However, with a change of diet to artificial feeding, the child rapidly improves unless the disease is too far advanced. The dyspnœa disappears, the heart becomes quiet, restlessness ceases, and peaceful slumbers follow. If aphonia has been present, it remains usually for several weeks but eventually subsides. Because of poverty a wet nurse is impossible, and it is usually hard in the Philippines to find one who does not show some symptoms of beriberi. Even with artificial feeding the child is not safe; although it has escaped death from beriberi it is likely to contract an acute gastro-enteritis. Because of poverty and ignorance, artificial feeding is practically impossible at the present time by these people. Furthermore, unless the condition is too far advanced, a change in the mother's diet with the child still nursing will bring about a cure in both mother and child. One such case came into the wards of the University Hospital on December 20. The mother, a primipara, was 20 years old and her infant 6 weeks old. The mother was suffering from such pain and numbness in the legs that she could hardly stand and it was with considerable difficulty that she could walk. Areas of anæsthesia and numbness with formication were present in both legs. Knee reflexes were lost. The child was cyanotic in the face and very restless, and while dyspnœa was constantly present there were periodic attacks in which it was *more marked.* The second pulmonic sound was accentuated. The child had no fever. The temperature was taken every three hours for six days and the maximum registered was 37°.2 C, the minimum 35°.8 C. On entrance of the child into the hospital, the pulse, was 140 per minute; the respiration, 50 per minute. The mother was placed in the ward and given the usual hospital diet, except that undermilled rice was substituted for the white rice and *mongos* were given in addition. Both mother and child made an uninterrupted recovery and were discharged from the hospital cured, January 9, 1912.

As there seems to be a relation between the disease and the mother's milk and as the artificial feeding of the infant is attended with so much danger, the Filipino doctors have recognized the importance of changing the mother's diet and making it as nearly a balanced ration as the poverty of the people will permit. As the undermilled rice is not available in the open market, they advise the use of *mongos,* a leguminous vegetable very similar to the cow peas of the United States.

In our paper written two years ago we showed that the death rate of infants of 1 year of age and under was practically 50 per

cent of the total death rate of Filipinos. Further, we showed that this was more than two and one-half times higher than the death rate of such infants in the United States or in European countries. We stated that in Manila practically 75 per cent of the deaths of infants occurred among the breast fed, while in Germany the breast-fed infants numbered from 12 to 15 per cent of the total. In this same paper [3] we stated further:

> In the Philippines the mortality is greatest among breast-fed children, possibly because of the poor quality of the mother's milk. The latter is probably deleterious by reason of what it lacks rather than because of any harmful constituent. The average Filipino mother is in poor physical condition, many of them are beriberic and subsist upon a diet favorable to [the production of] beriberi. It seems probable that there is an intimate relation between beriberi of infants and a mother's milk poor in quality and lacking certain necessary elements which are not included in the mother's dietary. * * * A possible solution of the problem lies in improving the quality of the mother's milk and encouraging the continuance of the custom of breast-feeding so general among the Filipino poor. The improvement of the physical condition of the Filipino mother and of the quality of her milk is an economic question. Her condition is the result of poverty and therefore insufficient and unsuitable food, especially during the periods of pregnancy and lactation.

In this connection I want to emphasize again that "the improvement of the physical condition of the Filipino mother and of the *quality* of her milk *is an economic question*" of the highest importance to Manila. Fifty per cent of the total number of deaths of Filipinos in Manila is of infants 1 year of age and under. Over fifty per cent of these is due to infantile beriberi. Since the recent advances in our knowledge of the etiology of beriberi indicate that this appalling condition may be stopped or at least checked by the substitution of undermilled rice for white rice in the daily diet of this people, it certainly behooves us to become active in some measures of relief. Just the *modus operandi* for bringing this about would have to be determined. It might be possible, perhaps, to require all dealers handling rice to keep a stock of the undermilled variety on hand, and then, by the introduction of a campaign of education among the people with especial reference to pregnant women, it may be possible to do considerable to relieve the situation.

The mothers are crying for relief. They realize that they are begetting children only for them to be seized after one or two months by the scourge *taon* or *suba*. Time after time we obtain the history that the mother has had 3, 5, or 6 children all of whom have died of this disease.

[3] p. 159.

CONCLUSIONS.

1. The high infant mortality in Manila is due to infantile beriberi.

2. This high death rate of infants is due primarily to the quality of the mother's milk.

3. The mother's milk lacks something which is essential for the growth and development of the nerves of the child.

4. The disease is not due to an infection or toxæmia of either the mother or the child.

5. Another link has been added in the chain of evidence showing that beriberi is a nutritional disturbance.

6. As a prophylactic measure, the dealers handling rice should be required to keep on hand the undermilled variety, and a campaign of education should be carried on for the purpose of enlightening the poorer classes, especially the pregnant women.

The writer considers it a privilege, as well as a duty, to extend his thanks to Doctor Hilario, his assistant in the department, and to Doctor Calderon, professor of obstetrics, who with their knowledge of the people and their customs have made the work possible. He also wishes to express his thanks to the Bureau of Health for all assistance given.

BIBLIOGRAPHY.

(1) CLARK. *Brit. Med. Journ.* (1900), 1, 1152.
(2) HIROTA, Z. *Ztschr. d. med. Ges.*, Tokyo (1891), 5.
(3) IDEM. *Zentralbl. f. innere Med.* (1898), 19, 385.
(4) IDEM. *Zentralbl. f. innere Med.* (1900), 21, 273.
(5) MIURA, M. *Arch. f. path. Anat. u. f. klin. Med.* (1899), 155, 316.
(6) TANAKA. *Wien. klin. Wchnsch.* (1910), No. 48, 1710.
(7) BURGOS, M. X. This was the result of a contest authorized by the Municipal Board among the Municipal physicians for the best paper as to the cause of the excessive death rate of children and the best means of diminishing the high infant mortality. So far as I know the paper was not published.
(8) MARTINEZ, M. G. Cronica de Ciencias Medicas de Filipinas, Año III, No. .
(9) GUERRERO, M. S. This paper was not published.
(10) ALBERT, J. *Phil. Journ. Sci. Sec. B* (1908), 3, 345.
(11) MCLAUGHLIN, A. J. and ANDREWS, V. L. *Phil. Journ. Sci. Sec. B* (1910), 5, 149.
(12) GUERRERO, M. S. and QUINTOS, J. Beriberi of Infants Due to Breast Feeding. Manila, 1910.
(13) SCHAUMAN. *Arch. f. Schiffs. -u. Trop. Hyg.* (1910), 14, Beihefte.
(14) ARON, HANS. *Phil. Journ. Sci. Sec. B* (1910), 5, 81 and 98.
(15) EIJKMAN. *Arch. f. Schiffs- u. Trop. Hyg.* (1911), 15, Heft 21.
(16) CHAMBERLAIN, W. P., and VEDDER, E. B. *Bull. Manila Med. Soc.* (1912) 4, 26.

ILLUSTRATIONS.

PLATE I.

Enlarged right heart of infant with displacement to the right and to the left.

PLATE II.

Dilated and hypertrophied right heart of dog. Experiment No. 2; puppy which died October 22.

PLATE III.

Degenerated nerve from a case of infantile beriberi.

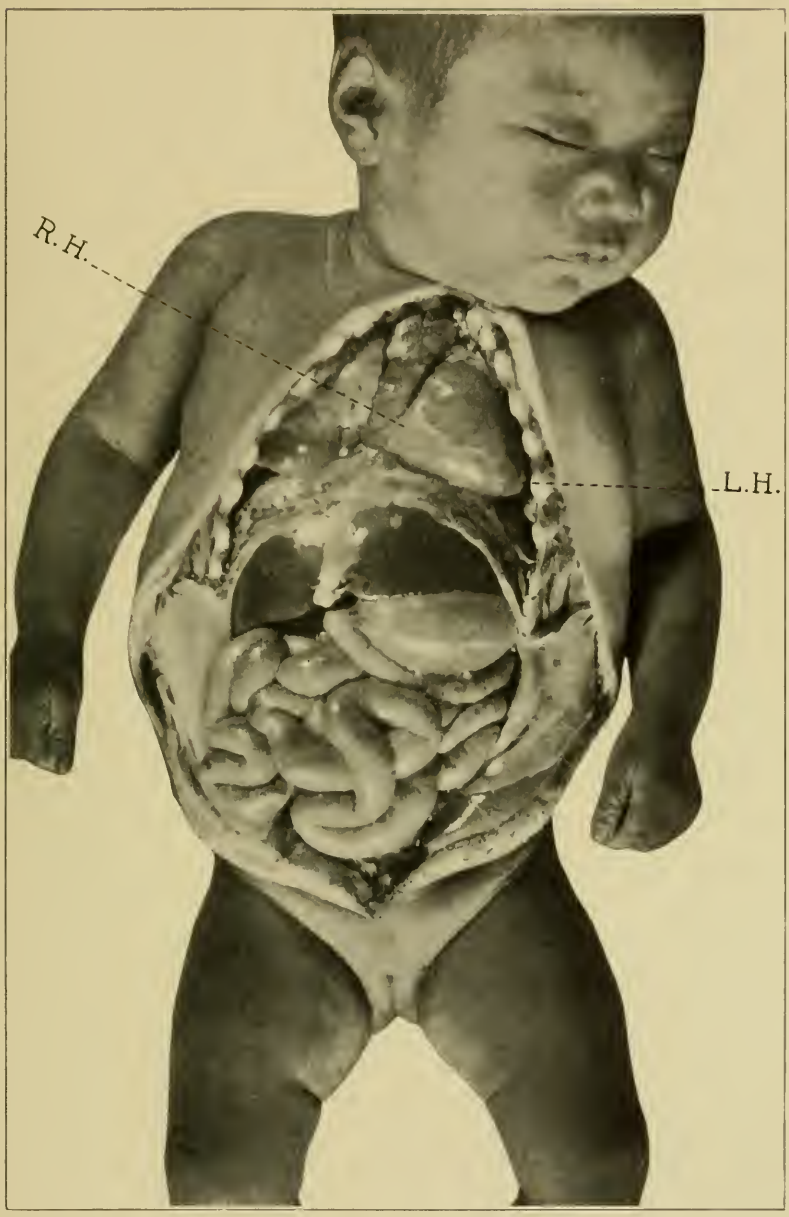


PLATE I. ENLARGED RIGHT HEART WITH DISPLACEMENT.

PLATE II. DILATED AND HYPERTROPHIED RIGHT HEART IN DOG.

PLATE III. SHOWING DEGENERATED NERVE IN INFANTILE BERIBERI.

A STUDY OF THE EFFECT OF TROPICAL SUNLIGHT UPON MEN, MONKEYS, AND RABBITS AND A DISCUSSION OF THE PROPER CLOTHING FOR THE TROPICAL CLIMATE.[1]

By H. D. Gibbs.[2]

(From the Laboratory of Organic Chemistry, Bureau of Science, and the Department of Chemistry, University of the Philippines, Manila, P. I.)

INTRODUCTION.

The literature which treats of tropical sunlight as distinct from sunlight in other parts of the world is very voluminous, and tends throughout to show that the sunlight shining upon tropical regions is different from that encountered in other latitudes. It is true that the sunlight which reaches the surface of the earth is different not only in various localities, but also in the same localities on different days and at different times of the same day. The character of the light and its intensity are subject to variations, and these two factors are regulated by the media through which the light passes; namely, the gases of the atmosphere and suspended matter. Any absorption in the space beyond the atmosphere of the earth does not, of course, enter into this consideration.

The light which reaches the surface of the earth is composed of the ultra-violet rays about as far as 291 $\mu\mu$,[3] the rays of the visible spectrum, and the infra-red. Every region of this spectrum may be altered in the passage of the rays through the atmosphere due to absorption, reflection, molecular scattering, and refraction; and thus, it is seen that at any one place the sunlight which reaches the surface of the earth is influenced

[1] This paper was submitted for publication in November, 1911.

[2] Associate professor of chemistry, University of the Philippines

[3] I have taken a large number of photographs of the sun's spectrum at sea level and at an elevation of 1,512 meters in the Philippines, and the results will be ready for publication shortly.

not only by latitude and longitude, but also by altitude and local meteorologic conditions, the last varying from season to season, from day to day, and during different hours of the day.

Excluding these conditions, I do not believe that when the normal intensities are compared, the light of the Tropics is different from the sunlight of any other region. This statement is, perhaps, more revolutionary than it seems at first thought for it conveys the idea that many of the conditions which have been treated as being peculiar to the Tropics and many of the effects attributed to tropical sunlight can be reproduced in regions outside of the Tropics. This I know to be true in some cases, and no doubt it will be proved for others upon due experimentation.

Nevertheless, the effect of sunlight *per se* upon life in the Tropics can not be ignored to the same extent that it can be in the Temperate and Arctic Zones even though the light values are taken as equal, or with differences too small to be of great account; for, in the Tropics, other factors increase the ill effects of light so that the organism is not so able to resist. In other words, during days of equal length the individual in the Tropics is not only affected by the sunlight practically to the same degree as his brother in the Temperate Zones, but in addition he is subject to unfavorable or disagreeable conditions of temperature; the factor of monotony, due to the small variation in the daily duration of sunshine; and other things which influence health.

Peculiar conditions which have often been attributed by many writers to tropical sunlight I believe to be due, not to the fact that the character of the light is different from that of the temperate regions, but to other meteorologic modifications which go to make up climate; namely, duration of sunshine, clouds, rainfall, winds, and humidity, all of which affect the air temperature; the last is probably the most important factor and depends to a large extent upon the duration of sunshine.

It has been realized from earliest times that different races are more or less adapted to certain different climates.[4] How the changes in racial characteristics and the changes in the individual which produce acclimatization have been brought about are not well understood. It has long been believed that

[4] Woodruff has considered the question involved in his works: The Effects of Tropical Light on White Men. New York (1905); and Expansion of Races. New York (1909).

the dark-skinned races can withstand the sunlight better than those of lighter skin and experimental evidence bearing on this fact, is introduced in the experimental part of this paper. Since man has at his command means such as clothing, artificial heat, refrigeration, and dwellings to aid him in uncongenial climates, transported individuals survive where many of the lower animals perish; moreover, the temperature-regulating devices of human beings are more sensitive than those of most animals.

In the sun of this region, at least, the skin temperature of men rises above the normal blood temperature, the subcutaneous temperatures of monkeys and rabbits rise more rapidly and to a much higher figure and death ensues. Since the skin characteristics are probably the most important in determining the survival of individuals and races, the measurements on skin temperatures so far made will be considered first.

Aron [5] has summarized the prior work and by means of thermocouples has extended the observations to a number of subjects in Manila. I have continued his work in much the same way in Baguio, employing as subjects a number of men, monkeys, and several differently colored rabbits, with striking results.

With men, higher skin temperatures were obtained than any yet recorded.

The lighter-colored skins reach a maximum in a shorter time than the darker, but the darker skins finally attain maxima higher than those of the lighter color. The protective value of the darker skins would seem to be somewhat nullified by these observations, but I believe this can be explained by the greater radiating power of the darker colors. In full sunlight the proportion of the body which is exposed to the rays of the sun is the lesser fraction of the whole, and while the part in the sun is absorbing heat rapidly, the radiation from the parts in the shade is correspondingly rapid. Moreover, counts now being made by Mr. Elbert Clark of the department of anatomy, College of Medicine and Surgery of the University of the Philippines, results to be published latter, show that the darker skins contain a larger percentage of sweat glands than the lighter. Another advantage which the darker skins have over the lighter, is that the former are not so subject to irritation by the rays of the sun, and the consequent effect upon the nerves and blood vessels, which is so pronounced in the case of white

[5] *This Journal, Sec. B* (1911), 6, 101.

people, is absent. Moreover, it has been shown that oxyhæmoglobin is transformed into methæmoglobin by ultra-violet light, and while no blood examinations were made upon the subjects described in this paper, later examinations made in Manila indicate that this effect may be produced in the living body by sunlight. I have found methæmoglobin in two cases where a series of animals were exposed in Manila. The difficulties encountered in positively detecting small quantities of methæmoglobin in presence of oxyhæmoglobin have delayed the completion of this work and any further statement of results or conclusions at this time would be premature.

With animals the skins of which are practically devoid of sweat glands, death comes upon exposure to the sun; and even monkeys having a considerable number of sweat glands,[6] but with a dark protective covering of hair, die in less than one hour, in our observations with temperatures of almost 50° in one case and over 50° in another, measured directly under the skin. Rabbits with black hair died in about thirty minutes showing temperatures between 40° and 50° measured directly under the skin; those with lighter-colored hair survived a longer time, but were unable to resist continued exposure.

The striking advantages in lower rate of heat absorption which the white hair has over the darker colors is very suggestive in the consideration of the question of clothing which will be taken up later.

EXPERIMENTAL.

The thermocouple employed by Aron and described by him was used. His measurements were made by warming the thermometric junction in the palm of the hand and then placing it on the part of the skin to be measured. He states:

> "The metal leaf must lightly touch the skin, and must be kept at one place until the galvanometer just reaches its maximum deviation; with my apparatus twenty seconds were almost more than sufficient for this purpose."
>
> It is evident that if the skin temperature is lower than the blood temperature, too long a contact with the measuring apparatus will give too high values, while if the skin temperature is higher than the blood temperature the reverse will be the case. I found that the most accurate results were obtained by commencing the measurements a short distance

[6] Doctor Shaklee, of the department of pharmacology, University of the Philippines, has investigated this question, and will report upon it.

away from the spot the temperature of which was desired; and, so soon as the maximum deviation of the galvanometer was reached, the thermocouple was very quickly moved a centimeter or two nearer the desired spot and when the galvanometer was again at rest, the operation was repeated until no fluctuation was noted on moving the couple. Care must be observed to avoid throwing shadows upon the spot finally to be measured. It is clear that in proceeding by this method the thermocouple is heated exactly to the skin temperature. The contact with the skin at the final point of measurement will be only of two or three seconds' duration.

The series of measurements recorded in Table II, while giving fairly accurate comparisons, are not the true temperatures. I believe the results in Tables I and II to be too low for the reason that the above described technique was not adopted until later. Measurements recorded in Tables III and IV are far more accurate. The higher skin temperatures which I obtained in Baguio over those obtained by Aron in Manila may be accounted for, to some extent, by the difference in the method of measurement.

Aron records data obtained by exposing 9 subjects: 3 Americans, 5 Filipinos, and 1 mestizo, to the sun's rays. His statement:[7] "In the sun, the white skin is always slightly hotter than the brown * * *" is entirely borne out neither by the data he records in Table VIII nor by my experimental work in Baguio, but on the whole, except in a few instances, his measurements showed higher temperatures for the white skin than the brown. In the first part of his table on page 124, data obtained on January 9, 1911, two cases are shown where the temperature of the forehead and arm are higher for the brown skin than for the white, and in the second part, data obtained on January 17, 1911, the temperatures of the brown skin on the arm are recorded as equal to or higher than those of the white. These records were obtained from 2 subjects, Gz. a Spanish mestizo with white skin and dark brown hair, and Cs. a Filipino with dark skin and black hair.

In the continuation of the same table, on page 125, the comparative measurements recorded for B. American, brown hair, and Or. Filipino, dense black hair, show considerably lower temperatures for the American on the arm, cheek, and forehead up to about twenty-five minutes' exposure to the sun; the final measurements recorded after thirty-five minutes show higher temperatures for the American. The final higher temperature, I believe, can be explained on perfectly rational grounds to be brought out later.

Aron's statements on page 127: "The results obtained so far indicate that the temperature of the human skin increases in the sun, but does not reach the normal body temperature," and on page 129: "An increase, even to the normal body temperature is prevented by evaporation of sweat" are not in accord with the results I obtained in Baguio.

I continually observed skin temperatures 1° to 1°.5 higher than Aron's maxima and 2° higher than blood temperature. The

[7] *Loc. cit.*, 125.

highest, except the thigh temperature of the Igorot recorded in Table III, were registered by the black skin of a Negro and were in several measurements 2°.4 above blood temperature. The thigh of the Igorot showed the remarkable temperature of 52°.7. The Igorots never wear clothing upon their legs, which are consequently always exposed to the weather. Comparing the Negro, the Filipino, and the Canadian, the temperatures are highest in the order named, and in the case of the two Igorots and the American the final temperatures were very close together, with one Igorot higher and one lower than the American. These comparisons, recorded in Tables III and IV, are the most accurate. They were made after a number of other series had been completed and the technique and conditions were as nearly perfect as possible, due to the skill of those who assisted me in almost all of the measurements and the handling of the subjects; namely, Dr. D. G. Willets, Mr. F. T. Eddingfield, Professor M. V. del Rosario, and my Filipino assistant, all of the Bureau of Science or University of the Philippines. A comparison of these results with Aron's measurements upon four subjects recorded in Table VIII, page 123, of his article shows some noteworthy differences. My measurements, made on April 29, give distinctly higher temperatures for the dark skin than for the light-colored one.

The variations between my results in Baguio and Aron's in Manila may be accounted for, in part, by the fact that almost all of Aron's measurements were made upon parts of the skin which are constantly exposed, while mine in the cases above cited were on the back, which is always covered. Even the Igorots employed in my experiments, always wore coats of light material.

The preliminary measurements upon portions of the skin constantly exposed to the weather; namely, the cheek, forehead, nose, neck, and arm, using various subjects, in the sun and shade, are not strictly comparable for the reason that they were made on different days and at different times of the same day. The sunlight and other conditions vary so frequently that accurate comparisons can be made only when the results are obtained almost simultaneously. Moreover, the figures recorded in Tables I and II, were secured in the early stages of the work before the best technique was adopted.

TABLE I.—*Temperature of the skin of various individuals in sun and shade.*

Subject.	Date.	Time.	Sunny side.				Shady side.				Remarks.
			Cheek bone.	Fore-head.	Nose.	Neck.	Cheek bone.	Fore-head.	Nose.	Neck.	
Gil. Filipino	Apr. 29	9.37	33.24	32.6	34.22	.....	31.2	.....	34.0	33.48	Sitting in chair.
			34.85	34.89	34.39	.....	34.37	.....	34.05	34.34	
			35.23	34.88	34.80	.....	33.97	.....	.....	.....	Not perspiring visibly.
			33.8	34.0	34.0	34.11	33.48	32.27	33.38	33.06	Same as above.
			34.3	34.5	34.1	33.7	33.28	32.8	32.2	32.77	
F. American	do	10.07	33.6	34.1	33.7	34.4	33.22	.....	.....	.....	
			33.83	.....	.....	.....	33.14	.....	.....	.....	Perspiring freely.
			34.46	.....	.....	.....	.....	.....	.....	.....	
Gil	do	10.11	35.1	35.3	34.68	35.7	34.2	34.6	34.68	34.7	Same as above. Not visibly perspiring.
F	do	11.50	31.04	32.18	32.98	33.00	33.2	33.3	.....	33.34	After walking exercise in white cotton shirt. Perspiring freely.
Ros. Filipino	May 3	10.15	34.15	33.9	34.14	33.64	33.46	33.03	34.01	33.24	Sitting in chair in sun. Perspires very easily.
Gil	May 4	.....	34.95	35.85	36.55	34.35	35.1	36.3	.....	34.95	
W. American	do	.....	35.40	36.25	.....	36.0	34.57	35.77	.....	35.17	Sitting on chair in sun.
			35.17	36.07	.....	35.17	.....	.....	.....	.....	
E. American	do	11	33.8	33.8	35.5	34.3	34.4	.....	.....	34.4	After running exercise in woolen khaki shirt. Almost no visible perspiration.
Ros. Filipino	do	11	33.85	33.65	31.7	33.2	34.1	.....	.....	33.98	After running in cotton shirt about one-half as much as above subject. Wet and perspiring very freely.

TABLE II.—*Comparative temperatures of skin of arms of Filipino and American exposed to the sun.*[a]

Gil. Filipino	34.78	34.93	34.30	34.95	34.60	34.60	35.62	35.91	35.2
M. American	35.35	33.60	34.40	34.90	35.20	35.15	35.77	[b]34.88	35.3
E. American	Arm in sun after running exercise.							35.9	
Ros. Filipino	Same as above except perspiring very freely.							34.9	

[a] The measurements were commenced at 10.30 in the morning, May 4, 1911, and were made alternately, first Filipino then American, at intervals of a few seconds.

[b] Some unwarranted fluctuations were found, due to gentle breezes which could not entirely be prevented and also to perspiration.

TABLE III.—*Comparisons of the skin temperatures of 2 Igorots and 1 American in sun and shade, May 17, 1911.*

Subject.	Time.	Over level of third dorsal vertebra.	Over level of fifth dorsal vertebra.	Scapula upper right angle.	Remarks.
Alipit Igorot. In shade at 9.30; in the sun thereafter.	9.30	32.1	32.7	32.4	
	9.34	33.8	33.65	33.8	
	9.49	34.50	34.05	34.65	At 9.55 slight visible perspiration.
	9.59	37.4	36.8	36.5	Light breeze.
	10.06	37.5	37.35	36.9	No wind.
	10.10	38.05	38.35	37.9	Slight breeze.
	10.14	37.7	37.55	38.1	
Magamba Igorot.[a] In shade at 9.38; in the sun thereafter.	9.38	33.7	33.48	33.4	
	9.40	32.8	34.3	33.5	
	9.54	36.8	34.8	36.3	
	10.04	36.7	37.0	36.5	Some breeze.
	10.13	37.4	37.9	36.8	
American. In shade at 9.45; and in the sun thereafter.	9.45	29.8	30.3	30.1	Breeze.
	9.48	32.8	31.9	33.45	Breeze.
	9.51	33.45	33.3	33.95	Very little wind.
	9.58	36.65	36.35	37.05	Very little wind.
	10.00	36.8	36.3	35.7	Breeze.
	10.05	36.7	36.3	35.2	Wind stronger.
	10.08	36.3	35.7	36.45	Almost no breeze.
	10.12	37.3	36.8	36.8	Very slight breeze.
	10.15	37.65	37.15	37.35	

NOTE.—All 3 subjects were showing visible perspiration at 10.15 a. m.

[a] Temperature of skin of thigh which was constantly exposed to sun, 52°.7.

These 3 subjects were first measured in the shade and then placed in the sun, side by side, with their backs exposed to the rays of the sun. The 2 Igorots had very dark brown skins, were accustomed to much outdoor work, and possessed athletic figures. The American's skin was remarkably white. He was accustomed to much outdoor exercise and was quite athletic, had been in the Tropics two years, had stood the climate well, and seldom showed

visible perspiration. One week after the thirty minutes' exposure to the sun the entire epidermis of his back peeled off.

Wind screens were used to protect the subjects from the cooling effects of the breezes. A light wind was blowing during the above observations and occasionally eddies reached the men. In the column under remarks, breeze and light wind refer only to the gentlest of zephyrs, for the men were so protected that only eddies reached them.

In this table it is of interest to observe that in spite of the fact that the American's temperature in the shade was, on the average, 2°.9 lower in the beginning, than the Igorot's (Igorot A. 32°.4, M. 32°.52, American 30°.06), on moving into the sun the three subjects reached, on the average, about an equal temperature, near the maximum, in thirteen minutes for the American and about thirty minutes for the Igorots. The white skin warmed much faster than the darker-colored skins. While this fact is contrary to what would be expected from a consideration of the rates at which different colored objects absorb heat, it may be accounted for by the irritation which is undoubtedly produced by the rays. This irritation of either the sensory nerve-endings, nerve-endings in the vessel walls, or of the vessel walls produces a flushing of the skin due to a greater quantity of blood and a more rapid flow. The pigmentation of the darker skins is undoubtedly a protection against this irritation of the sun's rays.

TABLE IV.—*Comparison of skin temperatures of a Canadian, a Filipino, and a Negro in sun and in shade, May 20, 1911.*

Subject.	Time.	Temperature— Over third dorsal vertebra.	Over fifth dorsal vertebra.	Over upper right angle of scapula.	Remarks.
	a. m.				
Ray. Tagalog.	9.20	33.20	33.80	33.95	Temperature in shade.
	9.23	34.20	35.85	36.80	In sun.
	9.28	38.75	38.20	39.20	
	9.36	38.30	37.60	38.30	Visible perspiration at 9.35.
	9.42	38.75	38.80	38.78	Axillary temperature at end of experiment, 35°.48.
R. Canadian.	9.22	33.65	34.35	33.90	Temperature in shade.
	9.25	36.30	36.90	36.95	In sun.
	9.29	37.95	37.55	38.25	
	9.34	36.53	37.00	37.55	Very slight breeze; slight perspiration visible.
	9.38	37.90	37.30	38.10	
	9.40	38.30	37.55	38.10	
	9.44	38.55	37.40	38.85	Axillary temperature at end of experiment, 35°.78.
C. Negro.	9.24	34.80	34.80	34.95	Temperature in shade.
	9.26	37.25	37.35	39.42	In sun.
	9.30	38.70	38.75	39.45	Perspiration visible at 9.35.
	9.37	38.90	38.75	38.90	
	9.43	39.32	38.85	39.15	Axillary temperature at end of experiment, 33°.38.

These three subjects represent the extremes and a mean of skin pigmentation. The Negro is quite black, the Tagalog brown, and the Caucasian white. There was no greatly marked difference in the temperatures of the Caucasian and the Tagalog. The Negro showed distinctly higher temperatures throughout the investigation, but it is to be noted that the white skin rises more rapidly than the brown. After this initial rise, on placing in the sun, the brown skin maintains a slightly higher temperature than the white.

In the investigation, the subjects were kept in the shade until stripped to the waist and the shade measurements taken. So soon as the initial measurements were made, the subjects were seated in the sun side by side with their backs directly exposed. The Tagalog was in the habit of wearing clothes to the same degree as the others.

The temperature, humidity, and amount of sunshine recorded at Mirador Observatory, Baguio, on the five days during which the above experiments were conducted are given in Table V.

TABLE V.—*Temperatures and amounts of sunshine recorded at Mirador Observatory, Baguio, for days of experiments.*

Date.	Time.	Maximum temperatures by mercury thermometers.			Relative humidity (mean).	Amount of sunshine during the day.
		Under shelter.	Black bulb.	Clear bulb.		
						h. m.
April 29	1.00	23.7	52.9	27.5	89.3	7 50
May 3	12.05	23.0	52.1	26.2	90.4	6 13
May 4	11.10	24.6	50.9	27.4	74.9	6 36
May 17	11.55	24.0	52.4	28.4	83.2	6 19
May 20	9.55	24.4	50.7	27.4	77.2	7 58

The sunshine record, made by the Friez Quadruple Register, can not be regarded as being of much value. Light clouds which would interfere seriously with my work are often not recorded by this instrument. In fact at this season at Baguio, I had difficulty in finding a sufficient number of hours of good uninterrupted sunshine to carry on the measurements given in this article.

My Baguio observations on the temperature under the hair of the head resulted as did those of Aron, obtained in Manila. This question is so closely governed by the idiosyncracies of each individual case that I believe the results are of no value for comparative purposes. In the full sun, I see no reason for doubting that the variations will be slight for the same individual in different localities, provided the air temperatures do not vary

within too wide limits. My measurements were made with the thermocouple employed by Aron; which, however, is a different one from that used in the skin measurements. The results are recorded in the following table:

TABLE VI.—*Temperatures in hair.*

Subject.	Date.	Time.	Temperature.		Remarks.
			Sunny side.	Shady side.	
Gil. Filipino. Sitting in chair in sun. Thick, coarse, black hair.	Apr. 29, 1911	9.37	44.5	35.4	
F. American. Fine, thin, silvery-white hair. Sitting in chair in sun.	do	9.41	[a]50.1	36.7	
G. American. Thick, brown hair. Sitting totally in shade.	do	10.40		33.45	In shade under hat.
F. American. Totally in shade	do	10.45		34.05	In shade under hat.
Ros. Filipino. Thin, black hair. Sitting in chair in sun.	May 3, 1911	10.00	39.2	34.1	Subject perspiring freely where hair is quite thin.
Rey. Filipino. Thick, coarse, black hair. Sitting in chair in sun.	May 4, 1911	10.30	45.5	36.1	Bright sun.
M. American. Sitting in chair in sun. Thin, light brown hair.	do	10.35	46.4		
Gil. (See above)	do	10.40	41.5		
E. American. Hair, dark brown	do	11.00	37.6	32.2	After running exercise, almost no visible perspiration.
Ros. (See above)	do	11.10	40.0		After running exercise perspiring freely.
Alipet. Igorot. Thick, coarse, black hair.	May 17, 1911	9	35.3	34.1	
Magamba. Igorot. Coarse, black hair, thinner than last.	do	9.10	42.3	32.8	

[a] This value is remarkably high, due to the fact that the subject has silvery-white hair which is rather thin and affords insufficient protection. The thermocouple, even though it was so buried in the hair as to be invisible, absorbed a considerable amount of heat by direct radiation.

In the consideration of the skin temperatures of human beings it must be remembered that the number of sweat glands, the thickness of the subcutaneous fat layer and especially the sensitiveness of the vasco-motor apparatus, certain subjects flushing under much weaker stimulus than others, are factors which must be excluded by experiments upon a large number of subjects before the influence of pigmentation can be determined. My experiments are not sufficiently extensive to warrant the drawing of general conclusions.

EXPERIMENTS WITH THREE MONKEYS IN THE SUN AND IN THE SHADE, AT BAGUIO.

The animals were small, tame, accustomed to captivity, and thickly covered with dark gray, almost black, hair. To facilitate the observations and prevent undue movement, they were tied to small boards which could be moved easily. So far as could be observed all were in perfect health.

TABLE VII.—*Temperatures of monkeys in sun and in shade. First series. May 7, 1911.*

Position.	Time.	Temperature of—	
		Monkey No. 1 in sun.	Monkey No. 2 in shade.
	a. m.		
Put in sun	9.15		
Temperature in hair	9.40	45.2	34.2
Temperature under skin[a]	9.45	40.6	
Do	9.50	40.6	
Do	9.53	42.7	
Do	9.54	43.6	
Do	9.56	45.5	
Do	9.59	47.6	
Do	10.01	48.8	
Do	10.04	50.9	
Do	10.07	52.8	
Do	10.09	54.0	
Do	10.10	(Dead)	

[a] The thermocouple was placed under the skin and not moved until after the death of the monkey.

Monkey No. 2 was in the shade cast by a piece of heavy cardboard, the two animals being not over 0.5 meter apart. He was perfectly comfortable during the entire period of the experiment and showed no noteworthy variations from a perfectly normal animal.

Monkey No. 1 suffered a little and several times attemped to turn his hot side, the back, away from the sun. The respirations after a short time became more rapid and death ensued in about fifty minutes. Some urine was passed and at the last there was frothing at the mouth.

Necropsy was performed about twenty-five hours after death and only the brain removed. The superficial vessels were congested and here and there extravasations beneath the pia-arachnoid were present. No evidence of hæmorrhage into the substance of the brain upon section was noted. The brain was preserved in 10 per cent formalin.

TABLE VIII.—*Temperatures of monkeys in sun and in shade. Second series. May 10, 1911.*

Position.	Time.	Sunshine observations and condition of subject No. 2.	Monkey No. 2 in sun.		Monkey No. 3 in shade.	
			Respiration.	Temperature.	Respiration.	Temperature.
	a. m.					
Rectum temperature	9.40			37.2		36.6
Under skin	9.45	Sun behind cloud	(a)	36.6		
Do	9.49	Sun shining				37.2
Do	9.50	Bright sun		37.2		
Do	9.53					36.6
Do	9.54	Bright sun		38.1		
Do	9.57					36.8
Do	9.58	Bright sun		38.9		
Do	10.04					36.95
Do	10.05	Cirrus clouds before sun		38.9		
Do	10.12		58	38.9	41	
Do	10.14					36.1
Do	10.23	Light clouds and light wind	66	41.6	50	36.2
Do	10.41	Moderately bright sun		42.7		
Do	10.44					35.5
Do	10.50		60	44.1	44	35.3
Do	10.57			44.7		
Do	10.58			45.3		
Do	10.58½			46.2		
Do	10.59			47.1		
Do	11.00			47.2		
Do	11.02	Stertorous breathing and slobbering.		47.9		
Do	11.03	Labored breathing		48.2		
Do	11.04	Tremors of posterior part of body.	72	47.9		
Do	11.06	Hard jerking of head and upper left extremity.		48.2		
Do	11.08			48.2		
Do	11.09			48.0		
Do	11.10	Sun going behind a cloud		48.3		
Do	11.11			48.1		
Do	11.12	Sun out again		47.5		
Do	11.15	Dead				36.7

[a] Put in sun.

During these experiments the animals were protected from the wind as much as possible by screens. The air temperatures to which they were subjected were the same for each. Monkey No. 2 remained perfectly healthy and lively during the three days elapsing between the first and second experiments.

The necropsy was performed within one-half hour after death.

Dura mater, acutely congested. *Brain*, superficial vessels acutely con-

gested, and here and there extravasations beneath the pia-arachnoid; this is rather less marked on the under than on the upper surface. No evidence of hæmorrhage into the substance of the brain upon section. *Heart*, apparently nothing unusual; coronary arteries apparently not congested. No hæmorrhagic areas in the wall or upon the internal surface of the left ventricle. *Lungs*, acutely congested.

Abdominal organs. *Liver*, *omentum*, and *mesentery* apparently acutely congested. *Spleen* and *kidneys* slightly, if at all, congested. *Intestine*, not opened.

EXPERIMENTS WITH SIX RABBITS IN THE SUN AND IN THE SHADE, AT BAGUIO.

Since the black or dark-gray-haired monkeys succumbed so easily to the sunlight, it was determined to employ rabbits having the widest possible range of fur pigmentation. For this purpose 6 rabbits, 2 pure white, 2 gray, and 2 black were shipped to me from Manila.

TABLE IX.—*Subcutaneous temperatures of differently-colored rabbits exposed to the direct rays of the sun. Baguio, May 26, 1911.*

Time.	White rabbit (1).	Gray rabbit (2).	Black rabbit (3).	Remarks.
9.18	38.6	38.6	43.9	Temperature in fur.[a]
9.21	------	------	41.8	Under skin.
9.22	38.9	------	------	Do.
9.22½	------	39.5	------	
9.23	------	------	43.9	
9.24	38.6	------	------	Sun under cloud 1 minute, 9.24 to 9.25.
9.25½	------	42.4	------	
9.26½	------	------	44.2	
9.27	39.3	------	------	
9.28	------	42.8	------	
9.30	------	------	45.8	
9.31	41.0	------	------	Sun behind cloud for 3 minutes, 9.31 to 9.34.
9.34	40.4	------	------	
9.35	------	------	42.2	
9.36	39.8	------	------	
9.37	------	41.9	------	Good sun.
9.38	40.7	------	42.8	
9.39	------	42.8	------	Sun behind cloud for 2 minutes, 9.39 to 9.41.
9.42	40.7	41.9	42.8	
9.44	41.0	42.8	43.9	Good sun.
9.46	------	------	44.2	At 9.46 the sun went behind a large cloud and the observations were discontinued.

[a] The first readings in this table were taken in the fur, while all of the subsequent readings were taken under the skin.

The experiments were conducted in such a way that all of the subjects handled at one time received equal treatment. When exposed to the sun, they were placed side by side with only a few centimeters of space between any two animals. The subcutaneous temperatures were taken through a small orifice in the skin of the lower dorsal region. Three rabbits, one of each color, were employed in each series in order to bring out any differences due to color. It was found that the thermocouple came to rest in a few seconds and could be transferred from rabbit to rabbit so quickly that all three could be measured quite accurately in from thirty to forty seconds.

The subjects were put in the sun at 9.10 in the morning, and remained exposed until 9.46, at which time they were returned to their cages for the reason that the clouds were becoming so heavy that the work could not be continued with profit. The white and gray rabbits soon recovered from the exposure, were lively, and ate with relish. The black rabbit recovered a little, but soon relapsed, and died at 12.30 in the afternoon.

Before the second series of experiments was begun, it appeared that the results would be unsatisfactory for the reason that the physical condition of the three rabbits employed was so different. The black and gray were large, strong, and healthy specimens, while the white rabbit was small and thin, and had every appearance of being a weakling.

TABLE X.—*Summary of the physical characteristics of the three rabbits.*

Color.	Fur.	Skin.
Black	Moderately thick	Moderately thick.
Gray	Very thick	Very thick.
White	Thin	Thin.

The gray had every appearance of being stronger than the black, although the difference between the two was not so marked as that between the black and the white. Under the circumstances it would not have been at all surprising had the white died first. In view of the fact that the black died in thirty-three minutes, the gray in one hour and thirty-two minutes, while the white recovered and is alive at this writing, several days later, the experiment is as convincing as it is possible for any one piece of work to be.

TABLE XI.—*Subcutaneous temperatures of rabbits described in Table X, exposed to direct rays of the sun, Baguio, May 22, 1911.*

Time.	White rabbit (4).	Gray rabbit (5).	Black rabbit (6).	Position of animal.	Remarks.
8.55–8.59	38.0	37.85	37.7	In shade	
9.02		39.2	38.9	In sun[a]	
9.02½				do	
9.03	40.1	39.2	40.1	do	
9.04	39.5		40.7	do	
9.05		40.1		do	
9.06	40.4			do	
9.07		40.4	40.7	do	
9.08	41.3		42.2	do	
9.09	41.0	40.7		do	
9.11½		41.6	41.6	do	
9.13	41.4			do	
9.14		42.3		do	
9.15	41.7		43.2	do	
9.17	42.0	42.9	43.5	do	
9.19	42.0	42.9	43.5	do	
9.21	42.3	42.9	43.8	do	
9.24	43.2	43.2	43.5	do	
9.25		43.8	44.7	do	
9.26	42.0	44.1	46.2	do	
9.27	43.5		44.7	do	
9.28	43.5	44.1	46.5	do	
9.30	43.65	44.1	47.1	do	
9.31	44.1	44.4		do	
9.32			45.3	do	Black rabbit slobbering.
9.33	44.4	44.4	47.8	do	Black rabbit died.
9.34	43.8	44.7		do	
9.36	44.8	45.1		do	
9.38	43.6	43.6		do	
9.40	43.1	43.7		do	Sun behind a cloud for 4 minutes then appeared 1 minute and then hidden for 8 minutes.
9.53	40.7	41.9		do	
10.13				do	Sun at 9.55 for 2 minutes then shade until 10.12 then sun for a minute then shade till 10.18. Good sun at 10.20.
10.23	41.0	42.5		do	
10.24	41.9	43.1		do	
10.25	42.2	43.4		do	
10.26	43.1	44.0		do	
10.27	43.4	44.6		do	
10.28	43.4	44.6		do	
10.28½	43.7	44.9		do	Sun behind cloud for 2 minutes.
10.32				do	Gray rabbit dead.

[a] These animals were put in the sun at 9.00 a. m.

So soon as the gray rabbit died, the white one was put in the shade, a little water sprinkled on the fur and he was fanned

gently. Although very much exhausted, the rabbit slowly recovered. In ten or fifteen minutes it stood up and in half-an-hour begun licking its paws. Doubtless it could not have stood the exposure a few minutes longer.

In the table it is to be noted that the temperatures of the three rabbits are often given for the same minute. This is not strictly correct, but is meant to signify that the temperatures were taken quickly one after the other and that less than one minute intervened between the first and the last readings. All the rabbits passed fæces; first, the black, then the gray, and then the white. The black rabbit died very suddenly with quivering and two sharp squeals. The gray did not die so suddenly as the black, but showed the same twitching of the muscles and jerking of the head, and gave a squeal at death.

The necropsies showed the following results:

BLACK RABBIT.—NECROPSY, 11.25 A. M., MAY 22, 1911.

Brain, superficial vessels somewhat injected. No extravasation of blood beneath pia-arachnoid. *Lung*, hyperaemic and rather dark. *Heart*, apparently normal. *Liver*, hyperaemic. *Spleen* and *kidney*, apparently normal.

GRAY RABBIT. NECROPSY 11.40 A. M., MAY 22, 1911.

Brain, superficial vessels somewhat injected. No extravasation of blood beneath pia-arachnoid. *Heart*, inner surface of the wall of the left ventricle hyperæmic. *Lungs*, hyperæmic; rather dark in color. *Liver*, hyperæmic; soft, probably fatty. *Spleen*, surrounded by masses of fat. Apparently normal.

The necropsies were performed by Dr. David G. Willets.

A DISCUSSION OF THE PROPER CLOTHING FOR A TROPICAL CLIMATE.

Clothing for the Tropics must be adapted not only to the climate and the physical characteristics of the wearer, but also to the work being performed and the amount of protection required against dust-laden winds, rains, and the bites of insects. The only questions here considered are protection against the heat and light of the sun.

There can be no doubt that the skin temperature will rapidly rise to heights above that of the blood if exposed to the sun under some kind of clothing, and in some cases, in the absence of clothing. If work is performed during the exposure, this rise will be accelerated. The measurements of skin temperatures have been discussed previously and in the following table a few observations of temperatures under clothing are recorded.

TABLE XII.—*Temperature under different kinds of clothing. Measurements made at Baguio by means of thermocouple.*

Subject.	Date.	Time.	Temperature.		Remarks.
			On shoulder next to skin, in the sun.	In axilla.	
	1911.				
F. American. Woolen coat, cotton shirt	Apr. 29	10.27	37.4	37.3	Perspiring.
Same with woolen coat off			37.2	37.2	
Gil. Filipino. All cotton clothing			33.5	33.9	
Rey. Filipino. Flannel shirt			34.35	31.05	Perspiring freely.
G. American. Cotton shirt			32.75	33.45	Sitting in shade all the time.
F. In shade. Woolen coat, cotton shirt		10.40	32.85	35.45	
Do		11.50	34.7	35.8	
Ros. Cotton shirt	May 3	10.15	33.7	35.8	
E. Woolen khaki shirt	May 4	10.00	38.9		After running exercise.
Ros. Filipino. Cotton shirt	do	10.00	37.1		Do.
Alipit. Igorot. Khaki coat only	May 17	9.00	37.4	35.9	
Magamba. Igorot. Clothing consists of 2 white cotton shirts under a mixed black and gray cotton coat.			38.0	36.8	

It is evident that the rise of temperature will be most rapid under clothing which has a maximum capacity for heat absorption and a minimum capacity for circulation of air to allow for the evaporation of moisture. Clothing which, in the sun, will cast a shade upon the body without hindering the air circulation and heat radiation will be the most desirable, and if a color is used which will give a minimum of heat absorption, the efficiency is increased. This ideal condition is fulfilled by the umbrella, and it is evident that a large, white umbrella lined with a material of a color agreeable to the eyes, for example a shade of green, will be the most efficient. The more nearly this condition of clothing is approached, the more comfortable will the subject be in the sun and the better prepared to withstand its evil effects. In the case of the foreigner, it is manifestly impossible to meet these requirements, but in the case of the native it is astonishing how closely he has instinctively, or otherwise, adopted this form of protection. The native hat woven from a variety of materials and called the *salacot* is a common sight in the country and it is often seen in the cities. It is arranged so that the crown is supported some distance above the head and is so large, often nearly a meter in diameter, that the wearer is thrown completely

in the shade when the sun is near the zenith and is almost completely shaded throughout the heat of the day. In many localities this article with the exception of short trousers constitutes the entire costume of the wearer, during work in the fields, in others, a loin cloth is worn. Workers in the rice fields and gardens most frequently use this attire. (Plates I and II.)

The large-brimmed helmet which will cast a shadow over the back, shoulders, and chest is the best substitute for the umbrella or the hats of crude native workmanship and design. It should be white in color, light in weight to avoid fatigue, and should be fixed up and away from the head to allow a circulation of air. The heavy helmets commonly seen in the Tropics appear to me to be without justification. They are very fatiguing to the head and neck of the wearer and answer no purpose which will not be fulfilled by the lighter variety. The idea that there are injurious rays emitted from the sun, which find their way through the earth's atmosphere and which can not be stopped by ordinary opaque material, is also without justification.

Custom prescribes that the white man shall cover his body, and, moreover, his insufficient skin pigmentation probably demands it. The most favorable covering should be as thin a material, pervious to air currents, as is consistent with decency. White will generally absorb the smallest amount of radiated energy.[8]

Rubner[9] gives the comparative absorption of different colored clothing materials as follows:

White	1.00
Light yellow	1.02
Light green	1.40
Dark yellow	1.40
Dark green	1.61
Red	1.68
Light brown	1.98
Black	2.08

Thus black is seen to absorb more than twice the quantity of heat taken up by white, and the experiments with rabbits are strikingly conclusive upon the superiority in this respect of the protective value of white over dark colors. The white rabbits, it is to be remembered live much longer in the sunlight than those of the darker hues.

[8] R. W. Wood has shown that ultra-violet light is not reflected from all white surfaces. For example zinc oxide, or Chinese white, completely absorbs the ultra-violet and when photographed by this light appears absolutely black. *Johns Hopkins University Circular* (1910), 2, 9; and *Century Magazine* (1910), February.

[9] Schilling, Tropenhygiene. Leipzig (1909), 159.

Schilling[10] states that, for protection for the body against the heat of *contact*[11] of the air, the clothing need not be considered, since all clothing materials are better conductors of the heat than the air. This is undoubtedly true in the Philippines and other parts of the Tropics which have come under my observation. However, I have heard of conditions in deserts where there are currents of highly heated air, in which case clothing would be a protection in so much that the movement of hot air would be retarded and its temperature somewhat reduced before reaching the skin. The protection from hot air carrying dust and sand particles would undoubtedly be necessary, but this is another consideration.

The natural tendency and custom in the Tropics are to keep out of the direct rays of the sun and seek shade, during the middle of the day. Within the shade created either by natural or artificial means, the thinner the clothing and the fewer the garments worn, the better. The experimental evidence upon this point with monkeys and rabbits is conclusive and shows that in the shade the skin temperature remains practically constant below that of the blood, while in the sun, temperatures above that of the blood are not uncommon in men and ensue in the animals with fatal results.[12]

The ill effect of light upon the eyes I believe is to be accounted for not so much by the ultra-violet as by the general glare of the reflected light. The direct rays of the sun are, of course, very disagreeable and injurious in all latitudes, but are so instinctively avoided that they seldom strike the retina and, therefore, need only this passing mention. The glare in the lowlands outside of cities in the Philippines, is not so much due to the light reflected from the surface of the earth, which is usually more or less covered with vegetation and which reflects the longer waves of the spectrum to a far greater extent than the shorter wave lengths, as it is to reflections from the sky.[13] In the lowlands, the sky reflection is very different from that encountered in the mountains. In Baguio, for example, I have observed that the clear, blue sky, so notable during a considerable portion of the year, is seldom disagreeable to the eyes, even though the intensity of the sunlight is greater than in lower altitudes. Here, the reflected sky-light is less throughout the visible portion of the

[10] *Ibid.*, 159.

[11] The italics are mine.

[12] The experiments with clothing in Baguio are incomplete because, when they were begun, it was impossible to secure clear days.

[13] In extreme northern and southern latitudes the evil effects of the glare from snow fields, even when the direct sunlight is near its minimum, horizontal intensity due to the low altitude of the sun in winter, are well known.

spectrum, except possibly the ultra-violet, than it is in the lowlands. This may be accounted for by the larger proportion of cirrus clouds and haze and the dust-laden atmosphere of the lower altitudes.[14]

The absence of clear, blue skies over the tropical seas and islands is not fully realized until experimentally demonstrated. For about eighteen months I watched each day, in Manila, for clear, blue skies for the purpose of taking photographs with the rays of the spectrum lying between 690 $\mu\mu$ and 740 $\mu\mu$,[15] which give the effect of silvery foliage against a black sky, and it was on rare occasions only, due to the haze or cirrus clouds in good weather, that successful photographs could be taken. In Baguio the conditions required for this work occur quite frequently. The large umbrella or the sun helmet again demonstrates its usefulness as a protection to the eyes from the glare of the lowlands.

In a later article I hope to consider the question of the protection of colored glasses from the standpoint of their absorption spectra.

SUMMARY.

In this paper the measurements of the skin temperatures in the tropical sun, of a number of different races, the temperatures under the hair and under various kinds of clothing, and the subcutaneous temperatures of monkeys and rabbits together with some observations of the physiological effects of sunlight are described.

In the shade, the skin temperatures of human beings remain constantly below blood temperature. In the sun the temperatures of the lighter-colored skins sometimes rise more rapidly than those of the darker colors, but, after the initial rise, the darker colors maintain higher maxima than the lighter, provided the exposure of the lighter-colored skins is not too long. Usually temperatures of the darker-colored skins rise more rapidly. In the case of too long exposure an irritation of the sensory nerve-endings, nerve-endings in the vessel walls, or of the vessel walls themselves, produces a flushing of the skin due to a greater quantity of blood and a more rapid flow. This effect is absent in the darker skins the pigmentation of which is undoubtedly a protection in this regard.

[14] Blue color of the sky. Lord Rayleigh, *Phil. Mag.* (1871), 41, 107, 274, 447 and (1899) 47, 375; Bauer and Moulin, *Radium*, 7, 372 through *Chem. Abstracts* (1911), 5, 3642.

[15] Wood, *loc. cit.*

While the darker skins absorb heat more rapidly, the radiation is more rapid than from those of lighter colors and, since, in full sun, the proportion of the body exposed is less than the proportion in the shade, the darker-skinned races may for this reason be somewhat better prepared to withstand the sun.

In the sun, hair temperatures above 40° and a maximum of 50°.1 are recorded.

Gray-haired monkeys showed normal subcutaneous temperatures in the shade and were quite comfortable, while in the sun the temperatures rose above 48° and death ensued in less than one hour and in one case in thirty minutes.

White, gray, and black rabbits all die on exposure to the sun; the black first, the gray next, and the white withstand the effect longest. The subcutaneous temperatures do not rise as high as in the case of the monkeys before death ensues.

All measurements of temperature were made by means of thermocouples and the subjects, men, monkeys and rabbits, were protected from air currents.

Clothing for human beings for protection from the sunlight, should afford the greatest shade without obstructing air currents carrying off evaporated moisture. The superiority of white over colored materials as a reflector of the sun's rays is demonstrated by the experiments with rabbits and a few measurements under clothing. The ideal condition is attained by the shade of a white umbrella lined with green cloth and supplemented by as little clothing as possible. A broad brimmed, light weight, white helmet, the band of which is so arranged that the frame of the hat does not touch the head and allows the free passage of air currents, is the best substitute for an umbrella. I can find no justification for the heavy helmets.

ILLUSTRATIONS.

(Photographs by Cortes.)

PLATE I.

Hat from Mavitac, Laguna Province, made of the leaf sheath of the betel-nut palm (*Areca catechu* Linn.), held in place by strips of bamboo. The diameter, 75 centimeters, is not unusually large, and greater sizes are frequently seen. The hat almost completely shades the body and forms an almost ideal protection for the worker in the fields.

PLATE II.

FIG. 1. Figure on the left: Hat the same as figured on Plate I. Shows a large portion of the body shaded at 10 a. m. when the sun is comparatively low.

Figure on the right: *Salacot* from Calasiao, Pampanga. Interior frame of coarse *buntal;* that is, the fibro-vascular bundles from the leaf-stalk of the buri palm (*Corypha elata* Roxb.), exterior covering of *nito* (*Lygodium circinnatum* Sw.).

2. Figure on the left: Hat which shades only the head, made from a gourd (*Lageraria vulgaris* Seringe), lined with split bamboo.

Figure on the right: *Salacot* from Tagbilaran, Bohol. This is in many respects an ideal hat for every day wear and might be adopted by Caucasians with profit. It is light in weight and is set away from the head by a soft network of rattan which is easy on the head and affords a maximum air circulation. The hat is well made and the appearance is pleasing.

The materials of construction are: network of under and upper surface *nito* (*Lygodium* sp.); foundation, leaves of *anahao* (*Livistona* sp.); ornamentation at top partly coconut fiber and framework of rattan.

PLATE I. PALM HAT FROM MAVITAC, LAGUNA PROVINCE, LUZON.

Fig. 1. Hats from Mavitac and Calasiao.

Fig. 2. Two kinds of Philippine hats.

PLATE II.

TYPHOID FEVER IN THE PHILIPPINE ISLANDS FROM THE SANITARY STANDPOINT.[1]

By Victor G. Heiser.[2]

(*From the Bureau of Health, Manila, P. I.*)

I desire, at the outset, to express my appreciation of the opportunity which your Association has so kindly afforded me to bring this subject to your notice. The question is one of great importance to the Philippine Islands, from both a medical and economical standpoint; and is, therefore, one that may well merit our attention.

Typhoid fever has been written about in Europe and America more extensively than any other disease, and its presence or absence is regarded by many as the chief index of the sanitation of a place. In many wars its ravages have been greater than the mortality and disability from the wounds of battle. In civil camps and temporary settlements it has been the chief factor in causing disease and death. It has been responsible for the deaths of hundreds of thousands of persons annually, and the losses due to its prevalence amount to millions of dollars. However, the hopeful feature in connection with this disease is that it is preventable, owing to the fact that the organism causing it has been identified and is found only in the intestinal and urinary discharges of infected persons. If these discharges are disinfected or destroyed, the disease will not spread.

In a recent article, Chamberlain,[3] president of the United States Army Board for the Study of Tropical Diseases as They

[1] Address before the Primera Asamblea Regional de Medicos y Farmaceuticos, February 8, 1912.

[2] Passed assistant surgeon, United States Public Health and Marine-Hospital Service; director of health for the Philippine Islands; and professor of hygiene, College of Physicians and Surgeons, University of the Philippines.

[3] *This Journal, Sec. B* (1911), 6, 302.

Exist in the Philippine Islands, states that the average yearly deaths in Manila amount to 82.4 which would indicate a yearly incidence of 412 cases. There is considerable question as to the correctness of the figures as regards Manila. For instance, in the Annual Report of the Director of Health for 1906 it is stated that

"In the last annual report mention was made of the fact that it was believed that typhoid fever was not so prevalent as the statistical tables seemed to indicate. At that time a number of cases had already been investigated by laboratory methods of diagnosis and a considerable number of them were found not to be typhoid fever. These investigations were continued during the present year and the results have fully confirmed the presumption that mistakes are frequently made in the diagnosis of this disease.

"During the year 45 deaths from typhoid were reported in the city of Manila. Of these only 4 were found positive to the Widal reaction. Among those who recovered from diseases diagnosed as typhoid, 9 cases were found positive, or a total of 13 found positive during the year."

Be that as it may, there can be but little question that the disease does prevail to a considerable extent in many portions of these Islands, and the first step necessary in order that we may be in a position to attack the problems of the prevalence and distribution of the disease and of the local factors favoring its spread is the collecting and recording of reports of all cases and their history.

DIAGNOSIS.

It is not the purpose of this paper to discuss at length the diagnostic features of typhoid, but it will not be out of place to refer to a few points. The literature of the disease shows that errors in diagnosis are most common. In order that this factor may be reduced to a minimum, it is desirable to have a Widal blood-test made in all cases. To this end the Bureau of Health will have made, free of charge, a Widal reaction for any practitioner who may desire it. It will only be necessary to place a drop of blood on a sheet of paper, write upon the paper the name of the patient, the sex, the town and province, and send it to the Bureau of Health. The result of the examination will be communicated to the doctor who sent the specimen as soon as it is known. Preferably, the blood should not be taken until the tenth day of the fever, and if the first result is negative and the fever persists, another specimen should be sent.

Attention is also invited to the fact that although diarrhœa is a common symptom in typhoid, it is not unusual to have epidemics in which constipation is a marked feature.

PREVENTIVE MEASURES.

Whenever typhoid fever does make its appearance in a community, steps should immediately be taken to prevent its spread, and in this connection it should be borne in mind that, although a Widal test should be carried out in all cases, precautionary measures to prevent the spread of the disease should be taken as soon as any case of illness presents symptoms suggestive of typhoid fever. The disease is conveyed in much the same way as cholera, and therefore the measures applicable in the case of that disease may be employed also in combating typhoid. It must be remembered, however, that the organism is not so easily killed as the cholera vibrio and that in some instances it is present for months, and even years, in the stools of persons who have had the disease. The urine and fæces of typhoid patients must be thoroughly disinfected by being placed in a 5 per cent solution of carbolic acid, or in a 1 per cent kreso solution; or, when that is not possible, they should be burned or boiled. A simple method of disinfecting by heat is to put the discharges and body washings into a kerosene tin covered by a wet bag, and place the tin on a fire. The hands of all persons who come in contact with the patient and particularly of those who come in contact with his discharges, either indirectly, through the means of his bed clothes, etc., or directly, by handling the vessels in which the discharges are placed, must be disinfected thoroughly after each contact of this kind and always before touching food with the hands. A soapy cresol preparation, such as liquor cresolis compositus, U. S. P., is most suitable for this purpose.

It has frequently happened that the milk supply of a town has become infected on account of the milk, in its preparation, being handled by someone who comes in contact with the discharged matter of a person who excretes typhoid bacilli. The possibility of milk infection should always be considered, and inquiries made as to the source of the milk supply used by the patient, and proper action should be taken when it is found or suspected to be at fault, as the occurrence of several cases having the same milk supply will at once lead to an investigation of the sanitary conditions under which the milk is produced, stored, or sold.

Drinking water may become infected by discharges finding their way into the water supply. This has been reported to have happened on a large scale where a case occurred upon a watershed, the water from which is collected into a reservoir

and then distributed by means of pipes. The disease may also be spread by infected sewage or infected water coming in contact with oysters and other shellfish, or with vegetables, especially when these are eaten raw. The practice of using liquified human excrement as a manure or as an insecticide in vegetable gardens, and especially in growing salad vegetables, is suspected of being a fruitful source of typhoid fever.

The linen or other textiles which come into contact with a typhoid patient have been reported as having spread that disease; therefore, this should always be rendered sterile as soon as it leaves the patient. This is best done by steam under pressure, but where that is not available, the textiles may be immersed in a 1 to 1,000 bichloride solution contained in wooden vessels, a 6 per cent carbolic solution, or a 1 per cent kreso solution.

The common house fly is also involved in the spread of typhoid fever, and the itinerary of this insect pest from the manure heap or closet to the pantry has only to be remembered to understand how its evil work in this regard is done.

SUMMARY.

Probably one of the greatest services we can render the people of the Philippine Islands is to set ourselves assiduously to the task of preventing the further spread of typhoid fever and of eradicating that which is already here. In order that we may know, then, just to what extent our communities are infected, a blood specimen should be sent to the Bureau of Health in every suspected case. This will insure accurate diagnosis and enable a systematic study of the disease to be carried out, as well as intelligent application of measures for its eradication.

In closing, I desire to thank you for your attention, and earnestly ask that you lend your hearty coöperation, in order that the useless sacrifice of lives may be avoided and our highest ambitions as physicians realized.

SOME COMMON SIPHONAPTERA OF THE PHILIPPINE ISLANDS.

By Carroll Fox.[1]

(*From the Bureau of Health, Manila, P. I.*)

Xenopsylla cheopis Rothschild.

Schultze and Herzog, in connection with the latter's study of plague, described [2] a rat flea which at the time was believed to be a new species and was named *Pulex philippinensis*. Forty-two specimens of this flea from the genera *Epimys* and *Mus* were studied. Since this publication Rothschild has pronounced the flea identical with his *Xenopsylla cheopis*, which was first described from the vicinity of the River Nile. It is the common rat flea of India, and is rapidly becoming cosmopolitan, having been reported from the United States, England, Italy, France, Australia, Japan, and other places.

A short anti-rat campaign in Manila during June and July, 1911, enabled the writer to secure 449 specimens of rat fleas.

A careful study of these, together with a comparison with the type specimens of *Pulex philippinensis* in the Bureau of Science, proves without a doubt, that *P. philippinensis* Herzog and Schultze and *X. cheopis* Rothschild are identical.

The four commonest species of the genera *Epimys* and *Mus* [3] were trapped in Manila, namely *Epimys norvegicus Exerl.*, *E. rattus* Linn., *E. quercti* Hollister, and *Mus commissarius* Mearns the first named of the genus greatly predominating while the specimens of *E. rattus* were scarce. Some fleas were collected from each of these species, but, needless to say, the greatest number were taken from the commonest host, *E. norvegicus*.

The greatest number of fleas taken from one rat was 32. Many females contained eggs.

[1] Passed assistant surgeon, U. S. Public Health and Marine-Hospital Service; assistant director of Health for the Philippine Islands; associate professor of Hygiene, College of Medicine and Surgery, University of the Philippines.

[2] *Bu. Govt. Labs.*, Manila (1904), No. 23, 78.

[3] Vide *This Journal, Sec. D* (1912), 7, 5, for a change in synonymy of the rats.

It is interesting to note that not one example of *Ceratophyllus fasciatus* Bosc. or of *Ctenopsylla musculi* Dugés was observed. This series, taken with Herzog's, would indicate that *Xenopsylla cheopis* is practically the only rat flea present in the Philippine Islands or at least in Manila. It is not improbable that conditions of temperature and humidity in the Tropics are inimical to the multiplication of *Ceratophyllus fasciatus* or *Ctenopsylla musculi* which seem to be fleas of the temperate zone. On the other hand *Xenopsylla cheopis,* which is primarily a flea of the Tropics, finds little difficulty in adapting itself to the conditions of a cooler climate.

The following brief description of the rat flea in Manila will suffice to identify it as *Xenopsylla cheopis.*

Head.—Noncombed-eyed. Two bristles on the gena, 1 in front of eye, 1 on lower genal edge. Occiput contains a subapical row of 6 bristles on each side with 2 behind the antennal groove. The rostrum reaches to the apex of the fore coxae.

Thorax.—The mesosternum bears 5 bristles. The episternum of the metathorax is separated from the sternum and bears 1 bristle, the epimerum 2 rows of bristles, about 7 in the first row and about the same number in the second row.

Abdomen.—Each tergite has a single row of bristles, as have also the sternites. There is one subapical (antepygidial) bristle on each side of the seventh segment which is much longer than the second hind tarsal segment.

Legs.—There is a comb of about 6 teeth on the inner side of the hind coxa. On the inside of the hind femur there is a row of 5 to 9 bristles, and on the outside 2 subapical bristles. The second mid tarsal segment is twice as long as the third. The longest apical bristle of the second hind tarsal segment reaches to the middle of the fifth segment.

Modified segments.— ♂ The clasper has 2 free processes, one slender, finger-like, the other much broader and well rounded and bearing long bristles on its upper margin and apex.

♀ Along the apical edge of the eighth tergite there are about 12 bristles with an inside row of about 8, and an irregular row on the lateral surface of about 9 bristles.

A full description of *Xenopsylla cheopis* may be found in articles by Jordan and Rothschild[4] and by others.[5]

[4] Parasitology (1908), 2.

[5] The Rat and its Relation to the Public Health. U. S. Public Health and Marine-Hospital Service, Washington (1910).

Ctenocephalus felis Bouché.

Some years ago the writer had an opportunity to study a collection of fleas taken off a dog, in Cebu, Philippine Islands, and was surprised to find that all the specimens conformed to the type *C. felis*. There is a statement appearing somewhere, although the reference is forgotten, that an observer in India doubted the correctness of Rothschild's separation of *Ctenocephalus canis* and *Ctenocephalus felis*, believing them to be identical. He, however, upon being given an opportunity to see a specimen of *C. canis*, realized that the separation was quite proper and that his reasons for doubt lay in the fact that in India *C. canis* did not exist and that he had, therefore, never seen any but *C. felis*.

Further studies, in the Philippine Islands, of specimens of *Ctenocephalus* from the dog, cat, rat, domestic rabbit, man, and of some taken from the floor of a house, indicate that *Ctenocephalus canis* does not exist in the Philippines. The specimens from man were collected in Baguio having an altitude of about 1,400 meters and with a temperature nearly approximating that of the temperate zone. The rest were secured in Manila.

The identification as *C. felis* was based upon the following characteristics as pointed out by Rothschild.[6]

The head, of the female especially, is compressed and elongated, in a few, however, less so than in others, and therefore more nearly approaching *C. canis* in this respect.

Bristles on epimerum of metathorax never more than 8 in first row nor more than 7 in second row.

Bristles on metathoracic episternum never more than 3, and in the majority of instances 2 only.

Bristles on inner side of hind femur never more than 10. There is only a single bristle, and a small hair, situated between the fifth pair and apical group of bristles on the posterior border of the hind tibia. In this series of *C. felis* studied, there was also a constant absence of the third pair of bristles, this pair being represented by a single bristle and a small hair, or more frequently 1 or sometimes 2 small hairs only. In this respect specimens of *C. felis* in the Philippine Islands seem to differ from those of *C. felis* found in the United States and Europe, which have a pair of bristles in this location.

The movable finger has its dorsal edge quite rounded and

[6] *Ent. Rec. and Journ. of Variation* (1901), 13; and *Novit. Zool.* (1905), 12.

hairy, while the ventral edge is decidedly curved. The manubrium is only slightly enlarged at its anterior end.

Pulex irritans Linnæus.

The specimens of this flea from man were collected in Baguio. They do not differ from those of *P. irritans* found in other parts of the world.

TABLE I.—*Specimens of Xenopsylla cheopis Rothschild examined.*

Host.	Males.	Females.	Total.	Locality.	Date.
Epimys norvegicus Epimys rattus Epimys querceti Mus commissarius	187	259	446	Manila, P. I.	June 15, 1911, to July 31, 1911.
Pachyura murina[a]	2	2	4		

[a] These shrews were caught with rats in the same trap. The identifications were made at the United States National Museum. Hollister, *This Journal, Sec. D* (1912), 7, 5, gives only two species of this genus from the Philippine Islands viz., *P. edwardsiana* Trouvesart and *P. luzonensis* Peters.

TABLE II.—*Specimens of Ctenocephalus felis Bouché examined.*

Host.	Males.	Females.	Total.	Locality.	Date.
Homo sapiens	9	24	33	Baguio, Benguet, P. I.	May, 1911.
Homo sapiens	2	1	3	Manila, P. I.	
Epimys norvegicus	1	2	3	do	
Canis familiaris	3	15	18	do	
Felis domestica	3	10	13	do	
Lepus cuniculus	2	1	3	do	
Floor of house	3	5	8	do	

TABLE III.—*Specimens of Pulex irritans Linn. examined.*

Host.	Males.	Females.	Total.	Locality.	Date.
Homo sapiens	3	8	11	Baguio, Benguet, P. I.	May, 1911.
Floor of house	10	14	24	Manila, P. I.	July, 1912.

REVIEWS.

Honan's Handbook to Medical Europe. By James Henry Honan, M. D. Pp. 261. Price $1.50. Philadelphia: P. Blakiston's Son & Co. 1912.

The object of this little book is to serve "as a guide to English-speaking physicians who go abroad for post-graduate work and as a book of reference for all who are interested in medical work in other lands." It is thoroughly practical and is of value both in helping to decide where to go for the particular work desired and in enabling one on his arrival quickly to familiarize himself with conditions there.

The author devotes 117 pages to German universities including Vienna and only 11 pages to those of France; this uneven treatment of this subject is in part justified by the fact that post-graduate courses for foreigners are much more thoroughly organized in Germany, but one feels that it is also largely due to the author's lack of an intimate knowledge of French medical institutions. The book is well worth having if one is planning to go for the first time to Berlin, Vienna, or one of the British universities for post-graduate work.

O. T.

Medical-Service in Campaign. A Handbook for Medical Officers in the Field. By Major Paul Frederick Straub. Medical Corps (General Staff) United States Army. Second edition. Illustrated. Pp. x+186. Price $1.50. Philadelphia: P. Blakiston's Son & Co. 1912.

In reviewing so excellent and satisfactory a book as this, one is tempted to indulge in superlatives, but in view of the fact that, despite the narrow field covered, it has already gone through its first edition and is so well known and appreciated by those engaged in that field, an effort will be made to restrain such a tendency.

Prior to the appearance of the first edition relatively few American (to speak of no other) medical officers were sufficiently familiar with the collateral military subjects or had had so much practical experience in the organization and administration of military medical units that they did not find the solution of even simple problems in military tactics a matter of

inconvenience, if not of embarrassment. The necessary data were scattered and, at times, inaccessible. That state of affairs was ended with the appearance of the first edition of this book, which therefore supplied a want and did it in a way considered eminently satisfactory.

The second edition contains the same chapters under the same titles, and most of the text is unchanged. Additions have been made, however, to increase the number of pages from 164 to 186, these being "new matter suggested by further experience in connection with the instruction in sanitary tactics at the Army War College, and with sanitary units of the troops recently mobilized in Texas." The new matter includes both text and illustrations and is all worthy of place.

Among the more important changes noted are those made in the model field order on page 21 and in the Chief Surgeon's field order on page 25, both showing improvement, the latter particularly so. The chapter on map reading is amplified and improved. The new matter on pages 60 and 61 is interesting and helpful, as is that at the end of the book dealing with Red Cross organizations and functions. The book is altogether worthy of praise and of even more extended use than it has yet had.

Paper, print, binding, and size are all satisfactory.

P. M. A.

A Text-book of Medical Chemistry and Toxicology. By James W. Holland, A. M., M. D. Third edition, thoroughly revised. Cloth, 8vo. Pp. 655. Illustrated. Price $3. Philadelphia and London: W. B. Saunders Company, 1911.

The advance of medical education in the past decade has been such that it would appear as if general compilations of this kind for use of medical students were not of so much importance as previously. The medical student should have, during his undergraduate college career, a thorough course in inorganic and organic general chemistry with the resulting knowledge of analytical methods. Therefore when he has finished his medical college course and secured a knowledge of biochemistry, the books which he should make use of are of a broader character.

The present third edition is well printed and an effort has been made to introduce modern facts, yet the basis of these facts is of necessity so briefly sketched that the reader obtains empiric knowledge rather than a general foundation. So, for

instance, the chapter on osmosis, while containing a number of facts, does not give the experimental basis for these facts. The method of determining osmotic pressure by means of vegetable cells and known solutions isotonic with the contents of these cells should be more interesting to the medical student than the discussion of the apparatus of Pfeffer. In other words, the attempt to compile what the modern medical man needs to know about chemistry in one volume of about 630 pages results of necessity in leaving out many important things and cutting many others short. However, the volume would still be useful to practitioners who have not access to more extended works on chemistry.

P. C. F.

Microbiology for Agricultural and Domestic Science Students. Edited by Charles E. Marshall, professor of Bacteriology and Hygiene, Michigan Agricultural College. Cloth, 8vo. Pp. 724 and 128 illustrations. Price $2.50. Philadelphia: P. Blakiston's Son & Co. 1911.

As the title indicates, this book is intended primarially as a text for students. Unlike most textbooks the work follows the plan usually adopted by larger reference books and is the product of a number of different contributors. These, some nineteen in all, are from various educational institutions and experiment stations of the United States and Canada.

The subject matter is treated under three chief divisions: Morphology and Culture of Microörganisms, Physiology of Microorganisms, and Applied Microbiology. The last named division comprehends by far the greater part of the book and treats of the microbiology of air, water and sewage, soil, milk and of special industries. There is, besides a division on the microbial diseases of plants and one on those of man and animals.

As a briefer book of reference this book will be of much service to students especially as it touches such subjects as Invisible Microörganisms (treated by M. Dorset) and descriptions of certain special industries, subjects not commonly treated except in rather extensive books of reference.

In discussing the merits of a book of this sort as an elementary text for students one might quote the Editor in his preface: "In presenting this textbook, *the product of several hands*, there is the most serious difficulty in obtaining unity of thought and expression without repetition; besides, that very conspicuous weakness of emphasizing some feature unduly while other features of importance are scarcely mentioned, confronts us."

It may be questioned whether these difficulties are fully overcome in this book. The author of the chapter on Molds, for instance, must condense his matter into fifteen pages with the result that the brief summary of so large a field must be difficult of comprehension for a beginner. Other topics, as the discussion of certain special industries offer less difficulties to the author in making the subject comprehensible to elementary students. The success or failure of a text of this sort must depend more on the teacher than in the case of a book written by one author, the more so since laboratory features in this work have been largely eliminated.

M. A. B.

Ophthalmic Surgery. A treatise on surgical operations pertaining to the eye and its appendages, with chapters on para-operative technic and management of instruments. By Charles H. Beard, M. D. * * * With 9 plates, showing 100 instruments, and 300 other illustrations. Cloth. Pp. 674. Philadelphia: P. Blakiston's Son & Co. 1012 Walnut Street. 1910.

Ophthalmic Surgery by Charles H. Beard is a treatise on surgical operations pertaining to the eye and its appendages, with chapters on para-operative technic and management of instruments. The author is well known and looks back to an experience at the operating table of more than twenty-five years. The book serves as an excellent guide for the young specialist starting on his career and gives food for reflection to the one who has critical knowledge to compare his own ideas and approved methods with those of the author.

The first chapter deals with the preparation of surgeon, assistant, patient, instruments, dressings, sterilization, and anæsthesia. The second chapter gives a critical review of the ordinary instruments used in ophthalmic surgery. The commendable and objectionable features are enlarged upon with reasons and explanations; last, but not least, how to take care of the delicate instruments is carefully gone into.

Operations upon the lacrimal apparatus, both secretory and drainage, technic of the leading measures for correction of tendons and cheek ligaments, ectropion, entropion, ptosis, blepharoplasty, pterygium, and the surgical treatment of trachoma are the main subjects dealt with in Chapters III to IX.

Chapter X and XI relate to operations upon the globe. Foreign bodies in the cornea, corneal cautery, paracentesis, keratic plasty, staphyloma, and tattooage. The scleral surgery includes sclerotomy, exenteration, enucleation, and the substitution of

prothesis in the globe or in Tenon's capsule. The different operations on the iris, extraction of cataract is exhaustively gone into. Chapter XII takes up operations upon the orbita for foreign bodies and retroöcular tumors. Chapter XIII deals with removal of foreign bodies from the interior of the eye, magnet operations and their technic. The book contains many original illustrations and is printed in clear type on good paper.

R. REMBE.

Manual of the Diseases of the Eye for Students and General Practitioners. By Charles H. May, M. D. * * * Seventh edition, revised. With 362 original illustrations including 22 plates, with 62 colored figures. Cloth. Pp. 407. New York: William Wood and Company. 1911.

May's Manual of the Diseases of the Eye is a compact textbook for the student and one of ready reference for the general practitioner.

The book contains twenty-six small chapters covering all the principal points in regard to the diseases of the eye, ophthalmoscopy, and errors of refraction. The book has many illustrations and is well gotten up. It serves excellently its purpose as a textbook for the student.

R. REMBE.

A Textbook of Physiology for Medical Students and Physicians. By William H. Howell, Ph. D., M. D., Sc. D., Ll. D., professor of physiology in the Johns Hopkins University, Baltimore. Fourth edition, thoroughly revised. Cloth. Pp. 1018. Price $4. Philadelphia and London: W. B. Saunders Company. 1911.

On looking over this book, one feels that there is here presented a judicious selection of the facts of physiology most important for the student of medicine, in clear, smooth, elegant English. The facts are presented with sufficient clearness to be easily comprehended by the student possessing an elementary knowledge of anatomy, physics, and chemistry, and also with sufficient fulness of expression to leave a serviceable impression in the student's mind. The author has not been content with the bare presentation of only those "conclusions about which there is no difference of opinion" and which too often "represent the uncertain compromises of past generations," but has essayed to open to view "the live issues of the present day which are of so much importance to physiology and to all branches of medicine." The older facts are presented with their historical setting and the newer with "the trend of contemporary discussion" in such

a way as to tend to arouse the interest of the student in the development of the subject and to induce in him the open-minded attitude of the true scientist, as well as to foster a scientific curiosity and to create impulses toward original investigation. In preparing this new edition, the author has "made diligent search through the literature of the subject to find what new facts have been discovered, what new views have been advanced and what old views have been discarded." The new references to the literature which cover the years 1910 and 1911 and number forty-three are especially numerous on the subjects of blood and circulation, internal secretions, and nutrition.

Further and material evidence of the success of this text is found in the fact that the six years of its existence have been marked by eleven reprints and three thorough revisions. The general plan of the book remains the same and its size has been increased from 998 to 1018 pages.

A. O. SHAKLEE.

Clinical Diagnosis. A Manual of Laboratory Methods. By J. C. Todd. Second edition. Revised and enlarged. Pp. 469. 164 text illustrations, 13 colored plates. Cloth. Price $2.25. Philadelphia and London: W. B. Saunders Company. 1912.

This book contains all of the important clinical laboratory methods that are in use, including certain tests of very recent origin such as: the antiformin method for tubercle bacilli, Tsuchiya's modification of Esbach's test, the formalin test for ammonia, Benedict's method for sugar in urine, volume index of red corpuscles, Harlow's blood stain, Wassermann's reaction, Frothingham's impression method in the diagnosis of rabies, and many other tests that are the products of the recent advances in medical science.

The descriptions of the technique of the different laboratory methods are precise and clear, and make the book a real guide to students and beginners, as well as a help to those who are more advanced in laboratory work.

A. G. S.

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

THE SUBANUNS OF SINDANGAN BAY.

By EMERSON B. CHRISTIE.

121 pages, 1 map, 29 plates.

Order No. 410. Paper, $1.25 United States currency, postpaid.

Sindangan Bay is situated on the northern coast of Zamboanga Peninsula. The Subanuns of this region were studied by Mr. Christie during two periods of five and six weeks, respectively.

The following is an abstract from the contents of Mr. Christie's report on the Subanuns: Habitat and history; relations with the Moros; material culture; houses; industries; trade; agriculture; family life; social customs; administration of justice; religion; the medicine man; ceremonies; tales; word-lists; physical measurements.

The 29 plates illustrate the Subanuns at work and at play; their industries, houses, altars, and implements; and the people themselves.

THE HISTORY OF SULU.

By NAJEEB M. SALEEBY.

275 pages, 4 maps, 2 diagrams.

Order No. 406. Paper, $0.75 United States currency, postpaid.

In the preparation of his manuscript for The History of Sulu Doctor Saleeby spent much time and effort in gaining access to documents in the possession of the Sultan of Sulu. It is fortunate that these records have now been translated and preserved in permanent form. This book is a history of the Moros in the Philippines from the earliest times to the American occupation.

[T]AES IN MORO HISTORY, LAW, AND RELIGION.

By NAJEEB M. SALEEBY.

107 pages, 16 plates, 5 diagrams.

Order No. 405. Paper, $0.25; half morocco, $0.75 United States currency postpaid.

This volume deals with the earliest written records of the Moros in Mindanao. Doctor Saleeby was fortunately able to obtain exact copies of carefully preserved early records written in the Maginda[illegible] dialect with Arabic characters. The author presents translations of these as well as 16 half-tone illustrations of certain pages from the originals. The names of the rulers of Magindanao are recorded in five folding diagrams.

NEGRITOS OF ZAMBALES.

By WILLIAM ALLAN REED.

83 pages, [illegible]

Order No. 402. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

The introductory chapter deals with the general distribution of Negritos and with the distribution of the Philippine branch of the race. The succeeding chapters deal with the various industries, amusements, and social relations of these little men.

Plates from photographs, the greater part of which was taken for this publication, show ornaments, houses, men making fire with bamboo, bows and arrows, dances, and various types of the people themselves.

CONTENTS.

The "Philippine Journal of Science" is issued as follows:	U. S. currency.
Section A. Chemical and Geological Sciences and the Industries	$2.00
Section B. The Philippine Journal of Tropical Medicine	3.00
Section C. Botany	2.00
Section D. General Biology, Ethnology and Anthropology (Section D began with Volume V)	2.00
Entire Journal, Volume II, III, IV, or V	5.00
Entire Journal, beginning with Volume VI	7.00
Single numbers	.50
Volume I, 1906 (not divided into sections)	10.00
Supplement to Volume I (botany)	3.50
Volume I (without supplement)	6.50

Each section is separately paged and indexed.

Publications sent in exchange for the Philippine Journal of Science should be addressed: Library, Bureau of Science, Manila, P. I.

Subscriptions may be sent to the BUSINESS MANAGER, Philippine Journal of Science, Bureau of Science, Manila, P. I., or to any of the agents listed below:

AGENTS.

The Macmillan Company, 64–66 Fifth Avenue, New York City, U. S. A.
Wm. Wesley & Son, 28 Essex Street, Strand, London, W. C., England.
Martinus Nijhoff, Nobelstraat 18, The Hague, Holland.
Mayer & Müller, Prinz Louis Ferdinandstrasse 2, Berlin, N.W., Germany.
Kelley & Walsh, Limited, 32 Raffles Place, Singapore, Straits Settlements.
A. M. & J. Ferguson, 19 Baillie Street, Colombo, Ceylon.
Thacker, Spink & Co., P. O. Box 54, Calcutta, India.

Entered at the post-office at Manila, P. I., as second-class matter.

VOL. VII, SEC. B, NO. 3 JUNE, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

SECTION B

THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

RICHARD P. STRONG, PH. B., M. D.
EDITOR

MANILA
BUREAU OF PRINTING
1912

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

REPORT OF THE INTERNATIONAL PLAGUE CONFERENCE.

Held at Mukden, April, 1911, under the auspices of the Chinese Government.

Edited by ERICH MARTINI, G. F. PETRIE, ARTHUR STANLEY, AND RICHARD P. STRONG.

483 pages, 18 plates (2 colored, 4 half-tones, 12 charts and maps).

Order No. 416. Cloth, $3.50; paper, $2.50 United States currency, postpaid.

The proceedings of this International Conference and information gained therefrom, together with the results of certain bacteriological investigations, constitute the present report.

Nothing hitherto has been published which gives such a complete and comprehensive account of the entire subject of pneumonic plague.

Delegates from America (United States of), Austria-Hungary, France, Germany, Great Britain, Italy, Japan, Mexico, the Netherlands, Russia, and China attended the Conference.

The Bureau of Science of the Government of the Philippine Islands has been appointed sole agent for the distribution of the printed proceedings of the International Plague Conference.

THE SUGAR INDUSTRY IN THE ISLAND OF NEGROS.

By HERBERT S. WALKER.

145 pages, 10 plates, 1 map.

Order No. 412. Paper, $1.25 United States currency, postpaid.

Considered from the viewpoint of practical utility, Mr. Walker's Sugar Industry in the Island of Negros is one of the most important papers published by the Bureau of Science. This volume is a real contribution to the subject; it is not a mere compilation, for the author was in the field and understands the conditions of which he writes. The following is a brief synopsis of the contents:

Tables of soil analyses, both chemical and physical; analyses of the cane, juice and bagasse; estimates based on actual information as to the costs of production and of cultivation; and estimates of the cost and location of possible central factories. The island is considered by sugar-producing districts; the area of cultivation and the production per hectare are given, and the possibility for future expansion discussed.

The plates illustrate various phases of sugar industry from the cultivation of the field to the transportation of sugar in native sailboats.

A MANUAL OF PHILIPPINE SILK CULTURE.

By CHARLES S. BANKS.

53 pages, 20 plates.

Order No. 413. Paper, $0.75 United States currency, postpaid.

The silk industry is particularly adapted to be undertaken by persons with small capital, and like the making of hats in the Philippine Islands it should thrive with a little encouragement.

In A Manual of Philippine Silk Culture we have presented the results of several years' actual work with silk-producing larvæ together with a description of the new Philippine race. Half-tone plates illustrate in natural size silkworms in different stages of development, pupæ, adult moths, samples of cloth made from eri silk, hand reel, and silk house. Other plates illustrate the various appliances used in raising silkworms and in spinning silk; hand and power reels are illustrated; working drawings are given for a silk house and for a hand reel.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

VOL. VII JUNE, 1912 No. 3

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

CONTENTS.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

I. INTRODUCTION. THE EXPEDITION TO MANCHURIA AND THE CONDITIONS UNDER WHICH THE WORK WAS PERFORMED THERE.

By Richard P. Strong.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

During the winter of 1910 to 1911, Manchuria was ravaged by an epidemic of pneumonic plague which in modern times knows no parallel. Upon the receipt of cable advices from the War Department, Washington, and the American National Red Cross Society, sufficient laboratory apparatus for emergency work in plague was hastily packed and Doctor Teague and the writer proceeded with this equipment by the quickest possible transportation to Mukden, Manchuria, arriving in this city on March first.[1] Here our services were at once placed at the disposal of the representatives of the Chinese Government.

The story of the Manchurian epidemic of pneumonic plague has been told at some length in the Report of the International Plague Conference, recently published in Manila under the supervision of the writer. In the present report it is merely the intention to recount our more important personal experiences and studies regarding pneumonic plague, either carried out by us in Manchuria or in this laboratory by ourselves or other members of the staff of the laboratory since our return. The epidemic had reached its height at Mukden a few days before our arrival there, and our investigations were immediately commenced at the plague hospital where we found about 50 cases of this disease on the occasion of our first visit. As is frequently

[1] The expenses of this expedition to China, where Doctor Teague and the writer acted as representatives of the American National Red Cross Society and as American representatives to the International Plague Conference, were largely paid for by the American National Red Cross Society and by the Chinese Government.

the case in other countries, when large epidemics of disease suddenly arise, China was unprepared to cope with this outbreak of plague. In Mukden there was no suitable building that could be used for a pneumonic-plague hospital. However, an old temple, situated about a mile from the city, had been converted for this purpose. (See Plate I.) About the various court yards of the temple numerous wards had been hastily constructed of light timber and boards, and the crevices between the boards covered with paper. Three small rooms, situated in the center of the hospital, were turned over to us for laboratory purposes. (See Plate II.) Tables, basins, etc., were supplied, and our laboratory apparatus having been installed, we began regular clinical and laboratory studies, which were continued until the end of the epidemic. In addition to the laboratory supplies brought with us, we ordered by cablegram from Messrs. Lautenschläger, Berlin, the emergency plague laboratory adopted by Professor Koch for the Institut für Infektionskrankheiten, Berlin, to be shipped to us by express. This laboratory apparatus is very compactly packed in five aluminum cases and cost, delivered in Mukden, exclusive of express, 6,925 marks. While with this additional equipment we were able to carry on satisfactory laboratory work, nevertheless, in our improvised laboratory building there was no running water, and even in the day time it was difficult to heat the rooms properly. At night, the temperature in the building was frequently below freezing point, so that incubators could not be kept at satisfactory temperatures. Obviously there was no gas in Mukden, and for bacteriological work alcohol blast lamps were employed and for sterilization purposes, primus burners. In addition, we found it difficult or impossible to replenish our chemicals and other supplies. These and other unfavorable conditions served as obstacles to the performance of ideal work, and many of our researches were, therefore, only completed in this laboratory after our return. We had previously purchased in Shanghai at the Municipal Laboratory, through the kindness of its director, Dr. Arthur Stanley, all the guinea pigs that that institution could spare. This proved a fortunate purchase, for we were unable to obtain any more of these animals during the entire time we were engaged in plague work in Mukden. Mice, however, were obtainable in limited numbers, and two species of marmots were kindly supplied us by the Chinese.

In the plague-hospital-wards, wooden platforms, about 70 centimeters high and 2 meters broad, and extending along one

wall the full length of the room, served as beds. (See Plate III.) On our first arrival at the hospital, we found that, owing to the great fear of contracting the disease that existed among the hospital attendants, the patients secured practically no medical attention. They were merely brought to the hospital to die, and the dead were removed each morning to the dead house. The patients lay on these platforms, or couches, side by side in their ordinary street clothes, and were not separated one from another in any way. We sometimes found patients with other diseases and with forms of lung trouble other than plague pneumonia on these couches, and in some instances we were able to save them from plague infection by the early diagnosis of the disease and by their speedy removal. The floors and walls of the wards were frequently spotted copiously with bloody sputum which had been expectorated upon them. We at once instituted a system by means of which an early diagnosis was made and an immediate bacteriological examination of the sputum of each case entering the hospital was performed. Later some beds were secured and many of the patients were placed on these. Also, hot tea and rice were supplied to them when they were able to receive such food. The wards were very inadequately heated by small iron stoves, and the temperature in them was at least during the night below the freezing point. The sputum in the sputum cups was frequently found in the morning to be frozen solid. No other European or American physicians attended the hospital, but there was a staff of Chinese doctors and medical students under the direction of Dr. Y. S. Wang, and towards the end of the epidemic an English male nurse was employed by the Chinese. In the early part of the epidemic a number of the native staff of the hospital became infected and died of plague.

We observed the strictest personal precautions against contracting the disease and never entered the wards unless fully protected by a proper mask, by goggles, usually rubber gloves, and by a cotton uniform. (See Plate IV.) Although we worked in the wards each day until the end of the epidemic and were often with patients for several hours continually, giving intravenous injections, leaning over coughing patients, exposing agar plates before them, making physical examinations, etc., we remained entirely healthy.

The type of mask which we used consisted of a cotton-wool pad, 12 centimeters wide, broadly folded in plain gauze, the two ends of which were each cut into three parts as a three-tailed bandage.

The tails of the bandage were tied one below the ear behind the neck, one above the ear, and the third above the head as a jaw bandage. The spaces on each side of the nostrils between the mask and the cheeks were plugged with cotton-wool. The whole mask was then covered with another piece of gauze in which openings for the eyes were made and the ends cut into four tails and tied behind the head and neck. (See Plate V.) This gauze served to keep the mask in place and to hold it securely against the face. While this form of mask appeared during the epidemic to be efficacious in preventing the wearer from contracting plague infection from a pneumonic-plague patient, two preliminary experiments performed in this laboratory by Teague, Barber, and the writer [2] have shown that this type of mask is not perfectly bacteria-proof. Since, however, as it has already been pointed out, we were frequently for hours at a time in close contact with coughing pneumonic-plague patients and remained entirely healthy, it appears that, during an epidemic, this form of mask is, at least, usually safe for practical purposes, and that while the gauze and cotton comprising the mask may not intercept bacteria, which are suspended and sprayed in a fine vapor in salt solution or even in saliva, they nevertheless usually intercept the fine droplets of sputum emitted, for example, by the cough of pneumonic-plague patients.[3] However, the very careful and complete experiments of Barber and Teague, for which they deserve entire credit,[4] throw considerable doubt upon the question of the degree of protection that would be afforded by this mask during a pneumonic-plague epidemic. These authors also demonstrate that the Broquet type of mask is more efficient.

[2] Report of the International Plague Conference held at Mukden, April, 1911. Manila (1912), 394.

[3] The droplets of mucus emitted from coughing pneumonic-plague patients are evidently much larger and heavier than the majority of those which are disseminated from an artificial spray of any kind and particularly is this true in the case of those where a force-pump is employed. Where the bacteria are suspended in saline solution and sprayed with a fine spray, the particles are always very much finer than those emitted from coughing individuals and have a much greater power of permeability. See Kirstein, *Ztschr. f. Hyg. u. Infectionskrankh.* (1900), **35**, 123; Hutchinson, *ibid.* (1901), **36**, 223. Laschtschenko states, *ibid.* (1899), **30**, 132, the mucus droplets are also not so easily transportable as the particles from a spray. According to Heymann, *ibid.* (1899), **30**, 139; (1901), **38**, 21, the smallest droplets emitted by coughing tuberculous patients have a diameter of not less than 30 $\mu\mu$.

[4] See XII, p. 255 of this report.

Should an epidemic of pneumonic plague occur again, it is believed that it will be possible to employ in the wards female nurses for the care of the sick, with but moderate danger to themselves from contracting infection if they are properly protected with a suitable mask and uniform.

On our arrival in Mukden, in discussing the preliminary plans of our work, we were informed by some European missionary doctors that, owing to the sensitiveness of the Chinese people and to the reverence with which they regard the bodies of the dead, it would be quite impossible for us to perform necropsies in Manchuria, that necropsies had never been permitted, and if we should attempt to perform them, there would be riots among the people, and that we would surely be mobbed. Nothing of this kind was experienced, but frequently we found it difficult to secure necropsies. When we were first presented to the Viceroy of Manchuria, he asked for our assistance and advice in combating the plague. We replied that all assistance and advice possible would be given, but that at first it would be necessary to study the plague cases in the hospital, to have liberty to treat the plague patients, and to examine their bodies after death to see the effects of the treatment, etc. The Viceroy did not state definitely that permission would be granted us to perform necropsies, but spoke only of the danger from infection in performing them. However, he did not refuse to let us carry them on, and this was considered by us at the time as a satisfactory arrangement. In spite of the obstacles in obtaining pathological material from time to time, nevertheless we finally secured 25 perfectly fresh, complete necropsies.[5] We were told that these were the first post-mortem examinations that had ever been permitted in Mukden. (See Plate II, Necropsy room.) The examinations were sometimes performed under difficulties, owing to the extreme cold. The water in the buckets would sometimes freeze while the necropsy was being performed, and the blood formed icicles as it flowed upon and over the edges of the table.

The study of the pathological anatomy of the disease was considered important, owing to the fact that previously no such study had been pursued during an extensive epidemic of pneu-

[5] During the epidemic, Koulecha performed 28 necropsies in Harbin, the majority of which were upon bodies which were frozen and subsequently thawed, and Fujinami examined 26 bodies in Changchun and Dalny. See Report of the International Plague Conference, pp. 151 and 144.

monic plague. Tissues from each human necropsy, as well as many of the gross organs and pathological material from inoculated animals, cultures, microscopical specimens, etc., were brought by us to Manila and have been used in completing the work. It is believed that the study of this disease during the Manchurian epidemic and the further experiments relating to the subject, performed in this laboratory and outlined in the following pages of this report, have materially increased our knowledge of pneumonic plague.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

II. THE METHOD OF TRANSMISSION OF THE INFECTION IN PNEUMONIC PLAGUE AND MANNER OF SPREAD OF THE DISEASE DURING THE EPIDEMIC.

By Richard P. Strong and Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

Immediately after establishing our laboratory in Mukden, experiments were undertaken with the idea of elucidating the method of transmission of the infection in pneumonic plague and the manner of spread of the disease during the epidemic.

The sputum of pneumonic-plague patients in the advanced stages of the disease always contains enormous numbers of plague bacilli. The temperature of the hospital wards at Mukden was sufficiently low so that the expired air became immediately condensed to a vapor which was clearly visible to the eye as it issued from the mouth, and frequently could be seen for a distance of 30 centimeters or more from the face. In many of the patients advanced pulmonary œdema was present and the respirations were sometimes very forcible and sometimes even stertorous. Therefore, experiments were carried on to show, first, whether in cases of pneumonic plague the specific organism of this disease became disseminated into the air by the expired air or vapor arising from the breath in ordinary or dyspnœic respiration, and, secondly, whether this organism was disseminated by moderate attacks of coughing in pneumonic-plague cases in which the cough did not result in the expulsion of particles of sputum visible to the naked eye. These questions were studied extensively by means of exposing Petri dishes containing agar before undoubted plague cases and of then identifying the organisms which developed on the media by the usual bacteriological methods and particularly by animal inoculations.

In the course of the experiments, on a number of occasions during coughing, small droplets or larger particles of sputum, visible to the eye, were expelled, and touched the surface of the media in the Petri dishes which were exposed before the plague patient. The study of these cultures obviously is not included in this investigation. The Petri dishes containing agar were invariably exposed before cases of pneumonic plague with bloody sputum, in which enormous numbers of plague bacilli had been shown to be present. All of the cases before which the plates were exposed died of plague infection within twenty-four to forty-eight hours from the time of the exposure. Twelve series of experiments have been performed in which 82 plates containing agar were exposed and in 78 the microörganisms which have developed upon them studied as far as was practicable.

The experiments were performed in the following manner: The plates were sterilized in the hot-air sterilizer within a metal plate-holder. They were then removed, the agar-cultures melted and poured in the usual way, and, as soon as the medium was sufficiently hard, were replaced within the plate-holder and taken to the bedside of the patient in whose sputum plague bacilli had previously been found. All of the attendants were asked to retire from the ward in order that as little dust as possible might be present in the air. The condition of the patient before whom the plates were exposed was noted, and during the exposure of the plate the character of the respirations was particularly observed and notes made of whether coughing or talking occurred. The time of the exposure of the plate and the distance from the patient were also recorded in each instance. After the exposure, the plate was returned to the holder and placed in the incubator. Twenty-four hours later the plates containing the culture-media were examined for the appearance of colonies and the number of colonies counted, but the plates were not usually opened until after forty-eight or seventy-two hours. The colonies were then again counted and carefully studied. Any of the colonies which in any way resembled colonies of the plague bacillus were transplanted to slants of agar. The morphology and staining properties of the organisms on the plate- and agar-slant-cultures were then studied. In every instance in which the morphology was at all similar to that of the plague bacillus or the organism decolorized by Gram's stain, it was inoculated either into mice or guinea pigs. In a number of cases the colonies were so thick on the plate, or surface growths from contamination

with bacteria from the air were so extensive, that the separate organisms could not be isolated and studied. In a few of these instances a suspension of the whole growth upon the plate-culture was made, and a portion of the suspension either rubbed over the freshly-scarified abdomen of a guinea pig or inoculated subcutaneously into a mouse. On several occasions in which it seemed hopeless to determine whether the plague bacillus was present or not on the medium in the plate, owing to the extensive contamination of the culture with bacteria other than the plague bacillus, the guinea pig so inoculated died of plague. In some instances the plate-cultures were discarded because of very extensive contamination probably from air organisms which covered the whole surface of the medium with a very thick layer of growth. The ideal method would have been to inoculate guinea pigs by the cutaneous method with light scarification of the abdomen, with suspensions of the bacteriological growth on all those plate-cultures in which the separate colonies could not be isolated, and in this manner, perhaps, in others of these plate-cultures the presence of the plague bacillus might have been demonstrated. There is no more delicate a test for the presence of the plague bacillus than this procedure, and its efficacy is very great even when the few plague bacilli present are extensively overgrown by other microörganisms. Unfortunately, our supply of guinea pigs was limited to those we brought with us and none could be obtained in Mukden during the winter. Since we had numerous other experiments to perform, which also required the use of guinea pigs, we could only allow, while in Mukden, a very limited number for the present study. In the case of all of the organisms which suggested in any way the plague bacillus and the colonies of which had been transplanted to agar slants from the plates, inoculations of guinea pigs were made after our return to Manila.

During the colder weather in Mukden, the plates containing agar, exposed before plague patients during ordinary respiration, were frequently entirely sterile. The plates were usually exposed vertically before the mouth and nose of the patient, the time of exposure varying generally between two and five minutes; usually the shorter period was employed. In the experiments performed in the earlier part of the investigation, the plates were held at a distance of from 5 to 7 centimeters to 90 centimeters or 1 meter from the mouth of the patient. Later in the experiments, when it became evident that in cases without cough during exposure no plague bacilli were encountered at

the greater distances, they were exposed before cases which did not cough, usually at a distance of from 5 to 18 centimeters in front of the mouth and nose. Before coughing patients the distances varied from 5 centimeters to 2 meters. A summary of the details of the experiments follows.

EXPERIMENTS.

SERIES I.

On March 4, six plates containing agar were exposed in a ward containing 6 patients. Dimensions of ward about 3.5 by 4.5 meters. All plates exposed before pneumonic-plague cases, none of which coughed during the time of exposure.

Plates A and B exposed for three minutes at a distance of 30 centimeters from the mouth of the patient. Result after forty-eight hours: Both plates negative for colonies.

Plates C and D exposed for one and one-half minutes at a distance of 70 centimeters. Result after forty-eight hours: Both negative for colonies.

Plate E exposed for two minutes at a distance of 5 centimeters. Result after forty-eight hours: Three colonies developed on the plate. Two of these colonies are composed of a coarse bacillus which does not decolorize by Gram. The third is composed of a coccus.

Plate F exposed horizontally for eight minutes in the ward, 1 meter from the nearest patient. After forty-eight hours 8 colonies developed. On microscopical examination, none of the organisms composing these colonies resembled the plague bacillus, either in cultural characteristics, morphology, or in staining reactions.

SERIES II.

Case 1.—Pneumonic-plague patient; sputum not markedly blood-tinged, but patient very ill. Plate containing agar exposed at a distance of 5 centimeters from the mouth for one minute. Respirations quiet. Result after forty-eight hours: Two colonies have developed on the plate, one a large white colony of a coarse bacillus which does not decolorize by Gram's stain, the other a small and delicate colony planted on an agar slant. This organism partially decolorizes by Gram's stain. Mice Nos. 4 and 6 inoculated subcutaneously with 0.5 *œse* of this organism. Neither of these animals developed plague.

Case 2.—Sputum slightly bloody; respirations quiet. Plate exposed at a distance of 5 centimeters for one minute. Result after forty-eight hours: Negative for colonies.

Case 3.—Patient asleep. No coughing during exposure. Plate exposed for two minutes at a distance of 5 centimeters from the mouth. Result after forty-eight hours: Plate negative for colonies.

Case 4.—Patient very ill. Advanced case of plague pneumonia, with much bloody sputum. Vapor arising from breath. Marked dyspnœa. Groaned slightly while breathing.

Plate A exposed at a distance of 5 centimeters for one minute. Result after forty-eight hours: One colony, a pleomorphic bacillus, with square ends. Evidently not plague.

Plate B exposed at a distance of 5 centimeters for one minute. Result after forty-eight hours: Three colonies. All examined and proved to be a very large bacillus which does not decolorize by Gram.

Plate C exposed for two minutes at a distance of 5 centimeters. Result after forty-eight hours: Negative for colonies.

Case 5.—Patient delirious. Plate exposed for two minutes at a distance of 11 centimeters. Patient coughed slightly while plate was exposed. Result after forty-eight hours: Negative for colonies.

Case 6.—Advanced case with bloody sputum. Temperature 39° C.

Plate A exposed for forty seconds at a distance of 11 centimeters. Patient coughed slightly twice during exposure. No visible sputum on agar in plate. Result after forty-eight hours: A single large colony, resembling a colony of the colon bacillus. Microscopically, a very small bacillus which decolorizes by Gram. Planted on an agar slant. This organism was later inoculated in a dose of 0.5 *œse* subcutaneously into guinea pig No. 5475. The animal remained healthy.

Plate B exposed for two minutes at a distance of 11 centimeters. No coughing during exposure. Result after forty-eight hours: Three colonies; 2 large white colonies which consist of a coccus, the third of a bacillus that morphologically might be the plague bacillus. The colony is small and delicate. This organism decolorizes by Gram's stain. It was planted on an agar slant and later inoculated in a dose of 0.5 *œse* subcutaneously into guinea pig No. 5487, which remained healthy.

Case 7.—Plate exposed for a few seconds at a distance of 11 centimeters. Patient coughed three times during the interval. Apparently no sputum touched the medium in the plate. One colony after twenty-four hours. After forty-eight hours no further organisms developed. The single colony consists of a large coccus.

Case 8.—Plate exposed for one minute at a distance of 11 centimeters. Patient talked slightly while plate was exposed. Result after forty-eight hours: Negative for colonies.

Case 9.—With much bloody sputum. Plate A exposed for one minute at a distance of 11 centimeters. No coughing during exposure. Result after forty-eight hours: Fifteen colonies; rather heavy and white in appearance. None of these suggest plague. Microscopical examination of a number of them reveals a coarse bacillus which does not decolorize by Gram.

Plate B exposed for two minutes at a distance of 15 centimeters. No coughing. Result after forty-eight hours: A single colony=a large coccus.

Case 10.—Plate exposed for fifteen minutes in ward horizontally about 1 meter from a very sick patient, with much bloody sputum. No coughing during time of exposure. Result after forty-eight hours: Four colonies of moulds and 3 large colonies with yellow centers; evidently not those of the plague bacillus. Microscopically=a coccus.

Case 11.—Very sick case. Much bloody sputum. Plate exposed for one minute at a distance of 5 centimeters. Patient coughed slightly during exposure. Result after forty-eight hours: Negative for colonies.

SERIES III.

Case 1.—Plate exposed for one minute at a distance of 11 centimeters from the mouth. No coughing. Result after forty-eight hours: About 50 colonies have developed on the medium. Some of these look macroscopically

as though they might be those of the plague bacillus, but microscopically a number of them consist of a large bacillus which does not decolorize by Gram's stain.

Case 2.—Plate exposed for two minutes at a distance of 11 centimeters. No coughing. Result after forty-eight hours: One large colony of a coarse bacillus which does not decolorize. A group of several hundred pin-point-sized colonies; evidently not plague colonies. Microscopical examination shows a large bacillus in long chains.

Case 3.—Plate exposed at a distance of 90 centimeters from the mouth for fifteen minutes. No coughing. Result after forty-eight hours: About 20 scattered colonies and a patch of several thousand (?) colonies that do not look at all like colonies of the plague bacillus. A number of these colonies examined consist of a fine bacillus which does not decolorize by Gram's stain.

Case 4.—Plate exposed for one minute at a distance of 11 centimeters. No coughing. Result after forty-eight hours: Negative.

SERIES IV.

Case 1.—Advanced case with bloody sputum. Much vapor arising from the mouth.

Plate A exposed for two minutes at a distance of 11 centimeters. No coughing. Result after forty-eight hours: One large spreading colony, evidently not plague. Two large white colonies, evidently not plague. Two pin-head-sized colonies might possibly be plague colonies. On March 17, only 3 colonies are present on the plate that could possibly be plague. These were transplanted and studied. They all consist of a very short bacillus which partially decolorizes by Gram's stain. This organism was later inoculated by the cutaneous method into guinea pigs Nos. 5462 and 5477, which remained healthy.

Plate B exposed in similar manner to Plate A. No coughing. Result after forty-eight hours: One-half of the plate is overgrown by a surface growth; the other portion is free from colonies. Discarded.

Case 2.—With much bloody sputum. Vapor arising from the mouth during respiration.

Plate A exposed for two minutes at a distance of 11 centimeters. Patient coughed four times during exposure. Result after twenty-four hours: Almost the whole surface of the plate covered with a thick growth, which may be that of the Hay bacillus. In addition, there are 14 pin-head-sized colonies which may be seen beneath this growth. Plate discarded.

Plate B exposed for two minutes at a distance of 11 centimeters. Patient coughed three times during exposure. No visible sputum on plate. Result after forty-eight hours: Entire plate overgrown, except near the edge. Here are situated 5 small white colonies. Two of these are pin-point in size; the others are larger. The large colonies=a bacillus which does not entirely decolorize. The small colonies entirely decolorize by Gram's stain. One of these planted on an agar slant and later inoculated cutaneously into guinea pig No. 5486, which died of typical plague infection with early inguinal buboes, four days after inoculation. The whole plate-culture was suspended in a little saline solution, and several *œsen* of this suspension rubbed over the shaved and scarified abdomen of guinea pig No. 11. This animal died four days later. At necropsy there were typical inguinal buboes and a typical plague spleen.

Case 3.—Much bloody sputum. Patient asleep during exposure and groaning slightly. Plate exposed for two minutes at a distance of 5 centimeters. Result after forty-eight hours: Two large yellow colonies, evidently not plague. On March 17, one red colony had also developed on this plate, but no other colonies.

Case 4.—Advanced case with bloody sputum. Patient coughed several times during exposure. Plate exposed for two minutes at a distance of 11 centimeters. Result after forty-eight hours: The whole surface of plate covered with a thick layer of growth which has the odor of the Hay bacillus. Plate discarded.

Case 5.—Advanced case with bloody sputum. Patient snoring during exposure. Plate exposed for two minutes at a distance of 11 centimeters from the mouth. Result after forty-eight hours: 11 colonies; 3 resembling colonies of the colon bacillus, the others are more delicate and might be colonies of the plague bacillus. March 17, the majority of these colonies are of bacilli which do not decolorize by Gram's stain. Three colonies are found of a bacillus which does decolorize. These organisms were planted on agar slants and later inoculated into guinea pigs Nos. 12, 5471, and 5472. All of these guinea pigs remained healthy.

No. 6.—Plate exposed in plague ward for nine minutes about 1 meter from the nearest patient. Result after forty-eight hours: The whole surface covered with a whitish growth, beneath which are about 40 large white colonies which do not resemble plague colonies. Plate discarded.

No. 7.—Plate exposed in the ward, same as No. 6. Result after forty-eight hours: Growth over entire surface of the plate. Impossible to study individual colonies. Plate, therefore, discarded.

SERIES V.

Case 1.—Very sick, with much bloody sputum. In last stages of the disease. Much dyspnœa and pulmonary œdema and much vapor arising from the mouth.

Plate A. Patient coughed once during exposure of plate which lasted for one minute at a distance of 11 centimeters from the mouth. Result after forty-eight hours: About 60 colonies are scattered over one-half of the plate. Some of these look as though they might be plague colonies. Three of these, the organisms comprising which decolorized by Gram's stain and were bipolar when stained, were planted on agar slants and later inoculated by the cutaneous method into guinea pigs Nos. 13, 5474, and 5304, all of which died of typical plague infection.

Plate B exposed for two minutes at a distance of 11 centimeters from the mouth. Patient coughed slightly during the time of exposure. Result after seventy-two hours: Thirteen colonies on the plate. Six, which were large white colonies, could not be those of the plague bacillus. Seven of them might be colonies of the plague bacillus. A number of these colonies planted on agar slants as follows: 1 B 1=a short bacillus or coccus; Gram-positive. 1 B 2=a very fine coccus; Gram-positive. 1 B 3, no growth. 1 B 4=a very small coccus. 1 B 5 and 1 B 6=a bacillus which decolorizes by Gram's stain; inoculated cutaneously into guinea pigs Nos. 14 and 5309; both of these animals died of typical plague infection.

Case 2.—Much bloody sputum, pulmonary œdema, and marked dyspnœa. Much visible vapor arising from the mouth.

Plate A exposed for two minutes at a distance of 11 centimeters.

No cough. Result after twenty-four hours: No colonies. After forty-eight hours: Sixteen colonies made up of moulds and yellow colonies. Two small white colonies which possibly might be colonies of the plague bacillus planted on agar slants. One of these=a coccus, the other=a bacillus which decolorizes by Gram. Growth on agar develops a deep yellow pigment; evidently not plague.

Plate B exposed for two minutes at a distance of 5 centimeters. No coughing. Result after seventy-two hours: Four colonies; 1 very large yellow, 1 small yellow, and 2 small white colonies. The white colonies are planted on agar. They are composed of a bacillus which partially decolorizes by Gram's stain. These cultures were later inoculated into guinea pigs Nos. 5320, 5470, and 5473 by the cutaneous method, all of which remained healthy.

Case 3.—Much sputum; temperature 40° C. Plate exposed for two minutes at a distance of 11 centimeters from the mouth. No coughing. Result after forty-eight hours: Twenty-two colonies, none of which resemble colonies of the plague bacillus. In growth on agar slants, morphology, and staining reaction, the organisms comprising a number of these colonies all differ essentially from the plague bacillus.

Case 4.—Advanced case with marked dyspnœa and pulmonary œdema. Coughed slightly during exposure of plate. Plate exposed for two minutes at a distance of 15 centimeters from the mouth. Result after twenty-four hours: Eleven colonies have developed, 3 or 4 of which might possibly be colonies of the plague bacillus. After seventy-two hours about 40 colonies have developed. Only about 6 of these could possibly be colonies of the plague bacillus. These were planted on agar slants. Four of these organisms proved to be cocci and 2 bacilli, which partially decolorized by Gram's stain. Cultures of the 2 bacilli were later inoculated by the cutaneous method into guinea pigs Nos. 5312 and 5465, both of which remained healthy.

Case 5.—Advanced case with much bloody sputum.

Plate A exposed for two minutes at a distance of 11 centimeters. Patient talked slightly during time of exposure. Result after forty-eight hours: One large and 12 pin-point-sized colonies. Microscopical examination shows these to be composed of a bacillus that does not decolorize by Gram's stain. Growth on agar too delicate for plague.

No. 6.—Plate 1 exposed horizontally in a plague ward containing 3 cases of plague for ten minutes. Patient coughing about 1 meter away from the plate. Result after twenty-four hours: Six colonies and 1 small group of colonies. After forty-eight hours, the whole surface of plate overgrown with a heavy growth. Impossible to identify colonies. Plate, therefore, discarded.

No. 7.—Plate 1 exposed in same ward containing 3 persons with pneumonic plague. Plate exposed for twelve minutes at a distance of about 2 meters from advanced case of plague. Patient coughed a number of times during exposure. Head turned in direction of plate. Result after forty-eight hours: Fifteen colonies and a thick surface growth covering almost the entire surface of the plate. The whole of this plate was suspended in a little saline solution and several *œsen* of this suspension rubbed over the shaved and scarified abdomen of guinea pig No. 6. This animal died five days later of plague infection with typical inguinal buboes and plague spleen.

SERIES VI.

Case 19.—Advanced case, breathing heavily. Temperature 40° C., pulse 130. Much bloody sputum, containing large numbers of plague bacilli.

Plates A and B each exposed for two minutes at a distance of 11 centimeters. Patient breathing heavily during the exposure. Surface of media in plates wet by the breath. No coughing during time of exposure. Result after forty-eight hours: Plate A, 16 colonies; 1 very large colony with irregular borders about 1 centimeter in diameter; 6 heavy white colonies from 3 to 4 millimeters in diameter which do not resemble colonies of the plague bacillus in any way; 2 groups composed respectively of 4 and 5 pin-point-sized colonies were examined microscopically and transferred to agar slants.

Results of cultures from Plate A: 19 A 1=a bacillus mostly staining as rods, a few taking the bipolar stain; this organism decolorizes by Gram. 19 A 2=a similar bacillus to 19 A 1. 19 A 3=a large diplococcus. 19 A 4 and 5=a large coccus. 19 A 6 to 9=a bacillus similar to 19 A 1. Culture 19 A 1 inoculated into mouse No. 13; dose 0.5 *œse* subcutaneously; animal remained healthy. Cultures 19 A 2, 6, and 9 inoculated by the cutaneous method respectively into guinea pigs Nos. 5463, 5480, and 5481. All of these animals remained healthy.

Result of Plate B after forty-eight hours: A single small pin-head-sized colony. Evidently the same bacillus as 19 A 1. This organism grows very delicately upon agar.

Case 20.—Advanced case with bloody sputum. Temperature 40°C., pulse 134. Enormous numbers of pest bacilli in sputum. Three plates exposed before this patient, each for two minutes at a distance of 15 centimeters as follows:

Plate A. Patient coughed slightly three times during exposure. Result after forty-eight hours: Seven colonies had developed; 1 large colony with uneven edges; 1 very large surface colony and another similar but slightly smaller one. None of these could be colonies of the plague bacillus. The remaining colonies are pin-head in size and were planted on agar-slant-cultures as follows: Cultures 20 A 1 and 4=a short bacillus which partially decolorizes by Gram's stain. These cultures were later inoculated by the cutaneous method into guinea pigs Nos. 5464 and 5484. Both of these animals remained healthy. Culture 20 A 2=a thick bacillus which does not decolorize by Gram's stain. Culture 20 A 3=a short bacillus which also does not decolorize.

Plate B. Patient coughed slightly once during exposure. Result after forty-eight hours: Four colonies developed as follows: Culture 20 B 1=a spore-bearing bacillus; culture could not be plague. Cultures 20 B 2 and 3 are very large, heavy, white colonies;=a large spore-bearing bacillus which does not decolorize by Gram. Culture 20 B 4=a plump bacillus which also does not decolorize.

Plate C. No coughing during exposure. Result after forty-eight hours: Four colonies, 3 large pin-head-sized and 1 pin-point-sized. All transferred to agar-slant-cultures. Results as follows: 20 C 1=a very small bacillus; does not decolorize by Gram. 20 C 2=a bipolar staining organism, but does not decolorize at all by Gram. 20 C 3=a coccus. Colony on agar, yellow. 20 C 4=a bacillus; colony white, rather heavy for plague; morphology does not resemble that of the plague bacillus. This organism was

inoculated later into guinea pig No. 5461 by the cutaneous method. The animal remained healthy. Culture 20 C 5 shows very heavy white colonies of a coarse bacillus; evidently not plague.

Case 21.—Advanced case with bloody sputum, containing enormous numbers of plague bacilli. Temperature 40° C., pulse 130. Marked dyspnœa, much vapor arising from the mouth.

Plate A exposed for two minutes at a distance of 11 centimeters. No coughing during exposure. Surface of plate wet by the vapor from the breath. Result after forty-eight hours: Fifty-eight colonies. Most of these do not resemble colonies of the plague bacillus. Nine of the colonies that might possibly be plague were inoculated on agar slants and studied further as follows: 21 A 1 and 2=cultures of bacilli that do not decolorize by Gram; morphology not right for plague. 21 A 3=a coccus or coccobacillus which decolorizes by Gram; 0.5 *œse* of this culture was inoculated subcutaneously into mouse No. 12 and 1 *œse* cutaneously into guinea pig No. 5482; both of these animals remained healthy. Culture 21 A 4=a bacillus which does not resemble the plague bacillus morphologically and which only partially decolorizes by Gram's stain; 1 *œse* of this culture was inoculated by the cutaneous method into guinea pig No. 5483; the animal remained healthy. Cultures 21 A 5 and 6=large bacilli, Gram-positive. 21 A 7=the same culture as 21 A 4. 21 A 8=the same bacillus as 21 A 3; inoculated into guinea pig No. 5322 by the cutaneous method; this animal remained healthy. 21 A 9=a bacillus whose morphology does not resemble the plague bacillus; only partially decolorizes by Gram's stain; 1 *œse* of this culture was inoculated by the cutaneous method into guinea pig No. 5485; this animal remained healthy.

Plate B exposed for two minutes at a distance of 11 centimeters. No coughing during exposure. Result after forty-eight hours: A large surface growth covers two-thirds of the plate, in which are situated 3 rather large white colonies which do not resemble plague. Three small isolated colonies, situated near the edge of the plate, might possibly be plague. Microscopically, these colonies are made up of a small bacillus which only partially decolorizes by Gram's stain. One of these colonies was transplanted to an agar slant and later inoculated into guinea pig No. 5479 by the cutaneous method; this animal remained healthy.

SERIES VII.

Case 25.—Advanced case with much bloody sputum, containing enormous numbers of plague bacilli. Patient died two hours after exposure was made. Plates exposed for two minutes at a distance of 15 centimeters from the mouth.

Plate A. Patient coughed four times during exposure. Result after twenty-four hours: Twelve colonies. After forty-eight hours, 33 colonies. All of the colonies, which looked at all suspicious of plague, planted on agar slants Nos. I to IX. A suspension was then made with 0.5 centimeter of peptone solution of all the colonies on the plate and 4 *œsen* of this suspension rubbed over the scarified abdomen of guinea pigs Nos. 8 and 15 respectively. Guinea pig No. 8 was found dead less than twenty-four hours after inoculation. There were no evidences of plague infection. Guinea pig No. 15 was found dead four days after inoculation. At the necropsy there were inguinal hæmorrhagic buboes and a typical plague spleen. Innumerable plague bacilli were present in the buboes and spleen.

The cultures formerly made from the colonies on the plate resulted as follows; 25 A 1=a coarse bacillus with square ends; decolorizes by Gram's stain; this culture was later inoculated into guinea pig No. 5307 by the cutaneous method; the animal remained healthy. Culture 25 A 2=a bacillus which decolorizes by Gram; growth on agar appears somewhat heavy for the plague bacillus; inoculated later into guinea pig No. 5459; this animal died of typical plague infection after five days. 25 A 3, 8, and 9=cultures of a spore-bearing bacillus; heavy white growth on agar. 25 A 4=a bacillus which partially decolorizes by Gram, but whose morphology is not right for plague and whose growth on agar is much heavier than that of the plague bacillus. 25 A 5 and 6=heavy white colonies; the same bacillus as 25 A 4. 25 A 7 decolorizes by Gram; morphology looks right; this culture was later inoculated into guinea pig No. 5460 which died six days later of typical plague infection.

Plate B. Patient talked a little during the time of the exposure and coughed once. Result after forty-eight hours: Sixteen colonies and a large surface growth. Only 3 of the colonies could possibly be colonies of the plague bacillus. These were planted on agar slants as follows: 25 B 1, colonies too heavy for plague;=a large spore-bearing bacillus. 25 B 2, a large bacillus; morphology not right, ends square, partially decolorizes; growth on agar not right for plague. 25 B 3=a bacillus which partially decolorizes; 1 *œse* of this culture was later inoculated into guinea pig No. 5308 by the cutaneous method; this animal remained healthy.

Plate C. No cough while exposed. Patient talked most of the time. Result after twenty-four hours: Eleven colonies. Result after forty-eight hours: Sixteen colonies. Only 4 of these colonies could possibly be those of the plague bacillus. These were planted on agar slants as follows: Culture 25 C 1, the colonies might be those of the plague bacillus, but are a little heavy. The organism is a bacillus which decolorizes by Gram; 0.5 *œse* inoculated subcutaneously into mice Nos. 18 and 26; both of these animals remained healthy; 1 *œse* of this same culture was later inoculated into guinea pig No. 5467 by the cutaneous method; the animal remained healthy. 25 C 2 and 3, the colonies have a yellowish-gray tinge; evidently not plague. 25 C 4, colonies have a deep yellowish-orange color; evidently could not be plague.

SERIES VIII.

Case 28.—With much bloody sputum, containing large numbers of plague bacilli. Temperature 38°C., pulse 132. Patient died twelve hours after exposure of plates. Physical signs in the lungs very slight.

Plate A exposed for two minutes at a distance of from 11 to 15 centimeters. Patient snored during the time of exposure. Result after forty-eight hours: The whole plate covered with a very heavy buff-colored surface growth. Plate, therefore, discarded.

Plate B exposed for two minutes at a distance of from 11 to 15 centimeters. Patient coughed slightly once during the time of exposure. Result after forty-eight hours: Sterile; no colonies have developed.

Plate C exposed for two minutes at a distance of from 11 to 15 centimeters. Patient coughed severely once. Result after forty-eight hours: About two hundred small colonies scattered over all parts of the plate, from pin-point to pin-head in size; one large light, buff-colored colony with irregular margins. A number of the small colonies planted upon

agar-slant-cultures. One-fourth of an *œse* made up of several of the small colonies on the plate was inoculated into mouse No. 16 and 0.25 *œse* of several of the other colonies into mouse No. 17, both subcutaneously; both of these animals died after forty-eight hours with marked swelling of the inguinal glands which contained innumerable plague bacilli; in each the spleen was swollen and contained innumerable plague bacilli; in each, cultures from the heart showed *Bacillus pestis.* Results of colonies transplanted previously from the plate to agar slants are as follows: Culture 28 C 1, a very short bacillus which resembles the pest bacillus morphologically and takes a bipolar stain; does not decolorize by Gram; 0.5 *œse* inoculated into mouse No. 21; the animal did not develop plague infection. Culture 28 C 2, short bacillus which does not decolorize by Gram's stain. 28 C 3, evidently the same organism as 28 C 1. 28 C 4, a coccus or very short bacillus which does not decolorize by Gram; evidently the same as 28 C 1. 28 C 5, colonies suggest those of *Bacillus pestis;* morphologically, a short bipolar staining organism; later inoculated into guinea pig No. 5457 by the cutaneous method; this animal died of typical plague infection six days after inoculation. 28 C 6, a coarse bacillus, evidently not plague. 28 C 7, evidently the same organism as 28 C 1, not plague. 28 C 8, 9, and 10, a bipolar organism which decolorizes by Gram's stain; 0.5 *œse* of 28 C 10 was later rubbed over the shaved abdomen of guinea pig No. 5458, which died of typical pest infection five days after inoculation.

Plate D. Patient coughed several times during exposure. Plate exposed at a distance of about 70 centimeters and only during the time of coughing. Result after forty-eight hours: A large surface growth covers about three-fourths of the plate. In this are situated about 50 colonies which might be plague colonies. Outside of this growth are situated 3 colonies which were planted on agar slants. Examined microscopically, the organism from these cultures is a very large bacillus which does not decolorize by Gram, but the culture does not look pure and in it there appear to be a few smaller bacilli which decolorize. For this reason, 1 *œse* of 28 D 1 and 1 *œse* of 28 D 2 were inoculated into guinea pigs Nos. 5454 and 5323 by the cutaneous method; both of these animals remained healthy; evidently the culture did not contain the plague bacillus.

Plate E exposed for one-half a minute at a distance of about 70 centimeters from the mouth of the patient. Patient coughed several times during exposure. Result after forty-eight hours: About 100 colonies are scattered through a large surface growth which covers the entire plate. Since it is impossible to isolate the colonies, the whole plate was suspended in a few drops of saline solution and several *œsen* rubbed over the scarified abdomen of guinea pig No. 9; this animal was found dead four days later. There were marked inguinal buboes on both sides and the spleen showed miliary abscesses; innumerable plague bacilli were present in smears from the spleen and buboes, and *Bacillus pestis* was isolated from the heart.

Plate F exposed for two minutes at a distance of about 5 centimeters. No coughing during exposure. Result after forty-eight hours: Eight colonies. Only 5 of these could possibly be plague. These were planted on agar slants. Only 3 of them looked at all like plague colonies. 28 F 1, 2, and 4 might be plague colonies; however, a microscopical examination

shows a very large bacillus which does not decolorize. Cultures 28 F 3 and 5 reveal a coarse bacillus which only partially decolorizes; these cultures were later inoculated into guinea pigs Nos. 5468 and 5469 by the cutaneous method; both of these animals remained healthy.

Plate G exposed at a distance of about 70 centimeters. Patient requested to cough, which he did 8 times. Plate exposed for a few seconds during the period of coughing. Result after forty-eight hours: About 100 colonies are scattered over the surface of the plate from pin-point to pin-head in size and up to a little larger in diameter. Thirteen of these colonies which resembled more or less colonies of the plague bacillus were planted on agar slants. One-fourth *œse* of several suspicious-looking colonies on the plate were inoculated subcutaneously into mouse No. 14, and another 0.25 *œse* of these colonies into mouse No. 15; one animal died forty-eight hours later and the other five days later of plague infection; in the first, the inguinal glands were swollen and contained innumerable plague bacilli, while in the second there was a typical left inguinal bubo; innumerable plague bacilli were present in the spleen of each animal. All the colonies on the plate (28 G) exposed before this patient were suspended in a few drops of saline solution and several *œsen* rubbed over the shaved and scarified abdomen of guinea pig No. 19; the animal died three days later with typical buboes and plague spleen; smears from the bubo and spleen showed innumerable bipolar organisms. The results of the agar-slant-cultures made previously from the colonies on the plate are as follows: Culture 28 G 1=a bacillus which does not decolorize. 28 G 2=a bipolar staining bacillus which decolorizes. Inoculated later into guinea pig No. 5455 by the cutaneous method; the animal died six days later of typical plague infection. 28 G 3 did not develop on agar. 28 G 4=a bipolar organism which decolorizes by Gram's stain. 28 G 5, a similar organism to 28 G 4; inoculated later into guinea pig No. 5456 by the cutaneous method; the animal died six days later of typical plague infection. 28 G 6=a bacillus which does not decolorize by Gram's stain 28 G 7, 8, and 9=a bipolar organism which decolorizes by Gram's stain; 28 G 9 inoculated later by the cutaneous method into guinea pig No. 5324, which died of typical plague infection five days after inoculation. 28 G 10, a very short bacillus which does not decolorize. 28 G 11, 12, and 13, a bipolar organism which decolorizes by Gram's stain; probably the plague bacillus.

28 H, ward plate, exposed in the center of the ward at about 2 meters from the nearest coughing patient. Time of exposure, four minutes. After forty-eight hours, only 2 isolated, large white colonies and a surface growth over about one-half of the plate had occurred. Plate discarded.

Plate 28 I, ward plate, exposed in the same manner, 2 meters from coughing patient, as Plate H for ten minutes. Light surface growth covers the entire plate. There are a few colonies situated beneath this. Plate discarded.

SERIES IX.

Case 29.—Three plates exposed for a few seconds each about a quarter of an hour before death of the patient, at a distance of about 11 centimeters from the mouth. Much vapor arising from the breath. No cough during time of exposure. Result after forty-eight hours: On all 3 plates, no colonies have developed; after seventy-two hours, plates still sterile.

SERIES X.

Case 32.—Advanced case, temperature 39°.2 C., pulse 110. Pulmonary œdema of both lungs; much bloody sputum, containing innumerable plague bacilli.

Plate A exposed for two minutes at a distance of 11 centimeters. No coughing during exposure. Talked slightly. Result after forty-eight hours: A surface growth covers the entire plate. It was, therefore, impossible to study any isolated colonies beneath this. The whole plate was, therefore, suspended in a few drops of peptone solution and mouse No. 23 inoculated with several *œsen* subcutaneously. This animal remained healthy.

Plate B exposed for two minutes at a distance of 11 centimeters. No coughing during time of exposure. Patient breathing quickly. Result after twenty-four hours: Plate sterile. After forty-eight hours, a heavy growth covers most of the plate, around the edge of which are a few delicate colonies measuring from 1 to 2 millimeters in diameter. Microscopical examination of these colonies shows a short bacillus which only partially decolorizes by Gram's stain; 2 *œsen* of a suspension of these colonies were inoculated subcutaneously into mouse No. 24, which did not develop plague infection.

Plate C. Patient coughed slightly about ten times during exposure. Result after forty-eight hours: Surface growth over four-fifths of the plate. A few small colonies in this growth. Four or 5 pin-point colonies outside the growth. Twenty-four hours later the whole plate covered by growth. Plate discarded.

Plate D. Exposed at a distance of about 70 centimeters. Patient gave one good cough during time of exposure which was for about one-fourth of a minute. Result after forty-eight hours: Surface growth over four-fifths of the plate. Three colonies outside of this which might be plague. Transplanted to agar slants. Results as follows: 32 D 1=a bacillus which decolorizes by Gram; morphologically, it looks rather thick for the plague bacillus, though from the colony, the organism might be the plague bacillus; inoculated later into guinea pig No. 5318 by the cutaneous method; the animal died seven days after inoculation with typical plague infection. 32 D 2=a bacillus which does not decolorize for the most part; however, there are a few organisms which are smaller and decolorize by Gram's stain; culture does not appear to be pure; 1 *œse* of this impure culture was later inoculated into guinea pig No. 5446 by the cutaneous method; the animal died of typical plague infection four days after inoculation; there were typical inguinal buboes and beginning miliary abscesses of the spleen.

Plate E exposed at a distance of about 30 centimeters for three-quarters of a minute. Patient gave one good cough during exposure. Result after forty-eight hours: Two irregular-shaped colonies that could not be plague; otherwise plate sterile. After seventy-two hours about 32 colonies, pin-point and pin-head in size scattered over the plate. Six of these colonies were planted on agar slants; microscopical examination of all revealed a bacillus which took a bipolar stain and decolorized completely by Gram's stain. Two of these agar-cultures were inoculated later by the cutaneous method into guinea pigs Nos. 5311 and 5447; the former died nine days after inoculation and the latter ten days after inoculation, both of typical plague infection with miliary abscesses in the spleen.

Plate F exposed for two minutes at a distance of about 70 centimeters,

while many attempts at coughing were made. Result after forty-eight hours: Large surface growth covering the entire center of the plate, in which are situated about one dozen smaller colonies. Impossible to isolate. Plate discarded.

Plate G exposed at a distance of 70 centimeters for a few seconds, while patient gave one good cough and made several attempts at coughing. Result after forty-eight hours: A number of suspicious-looking colonies present which take the bipolar stain and decolorize by Gram's stain. The organism is evidently the plague bacillus. Surface of plate became wet and plate, therefore, being dangerous to handle was disinfected.

Plate H exposed at a distance of 70 centimeters. One very good cough during time of exposure. Plate only exposed for a few seconds. Sputum was raised after the cough, but not during the cough. Result after forty-eight hours: Several hundred colonies which look suspicious for plague colonies. The colonies are not isolated, however, but in groups of very fine pin-point colonies and larger heavier colonies, about pin-head in size. A subsequent study of these cultures proves that 2 organisms are present on the plate; 1 a very small short bacillus which only partially decolorizes by Gram and whose colony is very delicate on agar and the other a bipolar-staining organism which entirely decolorizes by Gram. The latter organism was inoculated by the cutaneous method into guinea pigs Nos. 5310 and 5448, both of which died of typical plague infection, the former eight days after infection, the latter three days after infection. Two of the cultures of the organism which formed very delicate colonies on agar and which only partially decolorized by Gram's stain, were inoculated into guinea pigs Nos. 5313 and 5317, both of which remained healthy.

Plate I exposed at a distance of about 85 centimeters from the mouth for one and one-half minutes. Two good coughs during time of exposure. No visible sputum on plate. Result after forty-eight hours: Several hundred colonies that look suspicious of the plague bacillus. Colonies in small groups. Four of these groups planted on agar. Culture 32 I 1 did not develop; cultures 32 I 2, 3, and 4 all revealed a bipolar organism which decolorized by Gram's stain; three of these cultures were later inoculated into guinea pigs Nos. 5303, 5449, and 5450, all of which died of typical plague infection four days, six days, and eight days, respectively, after inoculation.

Plate J. Patient coughed during exposure. Small amount of sputum touched the plate. Plate, therefore, discarded.

SERIES XI.

Case 33.—Much bloody sputum which contained innumerable plague bacilli. Temperature 39°.8 C. Physical examination shows tubular modification of breath sound and signs of early œdema of the lungs.

Plate A exposed at a distance of about 85 centimeters. Patient gave five coughs during time of exposure. Plate then closed. Result after forty-eight hours: About 100 colonies scattered over the surface of the plate. Many look like plague. A number of these transferred to agar-slant-cultures. Subsequent study of these cultures shows that the majority consists of a bacillus which takes a bipolar stain and is completely decolorized by Gram's stain. Three of these cultures were later inoculated into guinea pigs Nos. 5302, 5451, and 5452 by the cutaneous method; all of these

animals died of typical plague infection; the first, four days after infection; the second, seven days after infection; and the third, eight days after infection. In addition to this organism on the plate, there was also present a small bacillus which has a very delicate colony and which usually does not decolorize by Gram's stain. This organism was encountered previously on other plates and is not the plague bacillus, as has been shown also by animal inoculation.

Plate B exposed at a distance of 85 centimeters, while the patient gave six good coughs. Result after forty-eight hours: A heavy surface growth in which several hundred colonies are situated; only 1 colony outside the edge of the surface growth. On microscopical examination, this proves to be a very short bacillus or coccus which does not decolorize by Gram's stain.

Plate C exposed at a distance of 85 centimeters for fifteen seconds, while the patient gave 4 coughs. Result after forty-eight hours: About 100 colonies scattered over the surface of the plate; many look like plague colonies. Five of the most suspicious were planted on agar slants; microscopical examination of all of these cultures shows a bipolar-staining bacillus which decolorizes by Gram's stain. Two of these cultures were later inoculated into guinea pigs Nos. 5301 and 5453 by the cutaneous method; both of these animals died of typical plague infection; one seven days after inoculation and the other nine days after inoculation.

Case 34.—Advanced case, partially delirious. Physical examination shows tubular respiration and signs of advanced œdema at the bases of the lung posteriorly.

Plate A exposed for two minutes at a distance of 11 centimeters from the mouth. No cough during time of exposure. Result after forty-eight hours: Many surface colonies. All colonies at all suspicious of plague were planted upon agar slants. A suspension was then made of all the colonies on the plate in a few drops of saline solution, and 3 *œsen* of this heavy suspension rubbed over the scarified abdomen of guinea pig No. 27; this animal remained entirely healthy. The result of the colonies previously transplanted on agar slants is as follows: 34 A 1 and 2=a bacillus, short and very thick which, however, decolorized completely by Gram's stain; this organism was later inoculated into guinea pig No. 5306, which remained healthy and did not develop plague infection. 34 A 3= a very large and thick bacillus which does not decolorize by Gram. 34 A 4=a coccus. 34 A 5=a bacillus which partially decolorizes by Gram's stain; this organism was later inoculated into guinea pig No. 5475, which remained healthy.

SERIES XII.

Case 35.—Advanced case of plague pneumonia. Patient with marked dyspnœa. Died about two hours afterward.

Plate A exposed for two minutes at a distance of 7 centimeters. No cough during exposure of plate. Result after forty-eight hours: About 28 colonies on the plate. Seven of these are large, irregular colonies which could not be plague. A number of smaller ones, from pin-point- to pin-head-size in diameter were planted upon agar slants. All the remaining colonies on the plate were then suspended in a few drops of peptone solution and 3 *œsen* of this suspension inoculated subcutaneously into mouse No. 25. This animal did not develop plague infection. The result of the colonies previously planted upon agar slants is as follows: 35 A 1

and 5=a bacillus with very delicate colonies which partially decolorizes by Gram's stain; these two cultures were later inoculated into guinea pig No. 5305, 1 *œse* of each culture being rubbed in different places over the shaved and scarified abdomen; the animal remained healthy. 35 A 2, 3, and 4 are cultures of a small bacillus which does not decolorize by Gram's stain; this culture was inoculated into guinea pig No. 5319, which remained healthy. 35 A 6=a bacillus which partially decolorizes by Gram's stain; this organism was later inoculated into guinea pig No. 5321, which remained healthy.

Plate B exposed at a distance of about 7 centimeters for two minutes. Patient breathing heavily; no cough during time of exposure. Result after forty-eight hours: Irregular surface growth, covering practically the whole surface of the agar in which many isolated, round colonies, from 2 to 4 millimeters in diameter, are situated. The growth on the plate was suspended in a few drops of peptone solution, and several *œsen* rubbed over the shaved and scarified abdomen of guinea pig No. 28 with a scalpel; the animal died six and one-half days after of typical plague infection; there was a hæmorrhagic local lesion about the point of inoculation; hæmorrhagic inguinal buboes; and the spleen showed early miliary abscesses; there was no pneumonia; smears from the spleen and bubo showed innumerable plague bacilli, and a culture of *Bacillus pestis* was obtained from the heart.

Plate C was exposed for two minutes at a distance of about 7 centimeters; no coughing during time of exposure. Result after forty-eight hours: Irregular surface growth covering almost entire surface of the plate, in which are scattered numerous colonies, 2 to 3 millimeters in diameter. Just outside the edge are 3 small white colonies, which are planted on agar slants. The growth on the surface of the plate was then suspended in a few drops of saline solution and 3 *œsen* inoculated subcutaneously into mouse No. 26, which did not develop plague infection. Results of the cultures on agar slants are as follows: 35 C 1=a bacillus which decolorizes by Gram's stain; the growth is rather heavy for plague; the culture was inoculated later into guinea pig No. 5478, which remained healthy. 35 C 2 and 3 are cultures of a large bacillus which partially decolorizes by Gram's stain; these 2 cultures were inoculated later into guinea pigs Nos. 5316 and 5315, which did not develop plague infection and remained healthy.

Case 36.—Advanced case of pneumonic plague. Plate exposed at a distance of about 85 centimeters for one and three-quarters minutes. Patient coughed five times during exposure. Only 3 colonies developed on the plate. These were transplanted to agar. Two of these colonies failed to develop; the third proved to be a coccus or very short bacillus which partially decolorized by Gram's stain. This organism was later inoculated into guinea pig No. 5314 by the cutaneous method. The animal remained healthy.

From these experiments it may be seen that of the 82 plates containing agar, 8 were exposed in the wards in the neighborhood of pneumonic-plague patients, 4 were exposed before patients who talked during the time of the exposure, and 35 before patients who coughed during the time of the exposure. In 39 instances the plates were exposed before patients who did not

cough during the time of exposure, and, notwithstanding the fact that many of the patients suffered with marked dyspnœa and advanced œdema of the lungs, in only a single instance was the plague bacillus encountered in one of these plate-cultures, although in a number of the experiments the surface of the medium was visibly wet by the vapor arising from the breath.

In this one case, the conditions of the experiment were as follows:

Three plates containing agar (Series XII) were all exposed at a distance of about 7 centimeters and for two minutes before a patient with marked dyspnœa and who died two hours afterward. A suspension of the bacterial growth upon one of these plates, which covered almost the entire surface of the plate, was made and a portion rubbed with the side of a scalpel over the abdomen of a shaved guinea pig and the skin then freshly scarified. The animal died of plague infection six and one-half days later; there were inguinal buboes and miliary nodules in the spleen. The animals inoculated with the colonies from the other 2 plates exposed in exactly the same manner did not develop plague infection. The results obtained from the examination of this one plate are different from those obtained from the remaining 38 plates exposed before patients who did not cough. Two possible explanations of the result suggest themselves, first, that the plague bacilli reached the medium on the plate exposed before the patient in the plague ward in some other way than by the expired air from the patient; and, secondly, that the plate was infected with plague bacilli by the droplet method through the forced expirations of the patient during the time this one plate was exposed.

The remaining number of plates (35)[1] were exposed before patients who coughed during the time of exposure, and in 15 instances colonies of plague bacilli developed on the media in the exposed plates. In some cases more than 100 colonies of this organism were obtained upon the media after a single cough, sometimes in almost pure culture.

Guinea pigs, the abdomens of which had been shaved and extensively scarified just before the time of the experiment, were exposed before 3 cases of pneumonic plague for a period of two minutes and at a distance of 5 centimeters from the mouth, the abdomen being placed toward the mouth. The breathing of the patients in all of these experiments was so

[1] In 4 other instances the patients talked during the time of the exposure, but no plague bacilli were demonstrated on these plates.

labored that the hair of the guinea pigs waved back and forth in the breeze made by the expired air, but no cough occurred during the time of the exposure. The animals remained alive, and did not develop plague infection.

The results of our experiments are in accord with the well-known bacteriological facts that bacteria are not detached from moist surfaces by ordinary currents of air, but that when sudden and forcible currents of air are forced from a distance through narrow apertures as, for example, from the trachea through the vocal cords, the tongue being against the gums and teeth, or through the lips, as occurs in talking or coughing, that small droplets of mucus, frequently invisible, may be emitted. The question of whether the expired air of patients afflicted with pulmonary tuberculosis was infectious was investigated particularly by Nägeli and Buchner [2] who demonstrated that such air was sterile. Flügge and his pupils, however, demonstrated that by coughing, tubercle bacilli were emitted in droplets from about 40 per cent of the tuberculous cases examined. Cornet and Meyer [3] after considering all of the experimental evidence concluded that droplet infection did not play an important rôle in the dissemination of tuberculosis.

In pneumonic plague the conditions are very different, owing to the enormous numbers of plague bacilli which are present in the lungs and bronchi. In our experiments, performed with cases of marked pulmonary œdema, the conditions were also different. The opportunities for infection by means of the droplet method must be very great in a pneumonic-plague ward. The distance from the patient that the air may be infected by droplets containing plague bacilli would apparently vary up to certain limits, particularly with the strength of the cough, the amount of mucus in the throat and larynx at the time, the size of the droplets emitted, the currents of the air in circulation, and the temperature [4] in the ward at the time.

CONCLUSIONS.

1. During normal and dyspnœic respiration of primary pneumonic-plague cases, plague bacilli are not usually expelled by means of the expired air.

2. During coughing of such cases, even when sputum visible

[2] Die niedern Pilze, München (1877), 53, 108. *Centralbl. f. d. med. Wiss.* (1882), 20, 513.

[3] Kolle und Wassermann, Handbuch der pathogenen Mikroorganismen (1903), 1, 146.

[4] See III, p. 157 of this report.

to the naked eye is not expelled, plague bacilli in large numbers may become disseminated into the air surrounding the patient.

The idea that infection of doctors, nurses, attendants, etc., in plague hospitals is caused entirely by particles of sputum expectorated by the patient and visible to the naked eye is erroneous. It follows from these experiments that the wearing of masks and the proper covering of any surface of the skin where fresh abrasions are present are important, personal, prophylactic measures against plague infection. It also follows that the eyes should be protected against this manner of conjunctival infection by proper glasses.

Articles of clothing worn in the wards should be sterilized immediately after removal, since plague bacilli may be present even though no particles of sputum may be visible upon them.

From these experiments, also, it is evident how dangerous an infective agent a pneumonic-plague patient is. In no other disease is the individual so dangerous and in no other disease does the danger from droplet infection approach that which exists in pneumonic plague. The number of plague bacilli expelled in droplets from pneumonic-plague cases is probably far greater than the number of bacilli ever expelled by patients afflicted with tuberculosis, croupous pneumonia, diphtheria, or influenza.

MANNER OF SPREAD OF THE DISEASE DURING THE EPIDEMIC.

During the epidemic the disease was evidently spread directly from man to man by droplet infection and by the more or less intimate contact of healthy individuals with an infected person. Whatever may have been the primary source of the epidemic, its dissemination occurred entirely independently of tarbagans, rats, donkeys, or any other animals.[5]

The disease was introduced into uninfected villages and towns by the importation of individuals infected with pneumonic plague or by those in the incubation period of this disease. No definite bacteriological evidence, that healthy carriers of the disease with plague bacilli in their sputa existed during the epidemic, has been produced. We had opportunity to examine two healthy individuals who were supposed to have given rise to the disease in other persons but who themselves remained healthy. We were unable to demonstrate any plague bacilli in their sputum, and it was not infective for guinea pigs.

[5] For evidence regarding dissemination by donkeys, see VIII, p. 225 of this report.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

III. INFLUENCE OF ATMOSPHERIC TEMPERATURE UPON THE SPREAD OF PNEUMONIC PLAGUE.

By Oscar Teague and M. A. Barber.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

In Manchuria, during the winter of 1910 to 1911, pneumonic plague spread with such rapidity that within three months 50,000 people died of the disease. Except toward the close of the epidemic, sanitary conditions were bad, the weather was bitterly cold, and quarantine measures were inadequately enforced. In India, where sanitary conditions are, perhaps, equally as bad, although there have been numerous isolated cases of pneumonic plague during the past fifteen years (from 2 to 5 per cent of all plague cases), this type of the disease has not assumed epidemic proportions.

Why was there a rapid spread of the pneumonic type of the disease in the one instance and a failure to spread in the other? The most obvious difference in the two instances is one of temperature, in the one case as low as 30° C. below zero as compared to 30° C. above zero in the other. Can the failure of pneumonic plague to spread in India be due to the high temperature that prevails in that country? If we consider only the direct action of the high temperature upon the plague bacilli, this question must be answered in the negative; for the optimum temperature for the cultivation of the plague bacilli upon artificial media is 30° C., which is approximately the temperature to which they would be subjected in India. We believe, however, that indirectly the temperature of the atmosphere is a factor of vast importance in the spread or failure to spread of pneumonic plague.

It is quite generally accepted that infection in pneumonic plague is due to the inhalation of plague bacilli and, as plague bacilli are readily killed by drying, it is fair to assume that infection is due to the inhalation of moist bacilli—the so-called "droplet infection." In plague pneumonia, the mucous membranes of the bronchi, trachea, larynx, and mouth are covered with enormous numbers of plague bacilli. It follows that such

a patient in coughing throws out droplets of sputum which must contain plague bacilli. Strong and Teague [1] demonstrated that this does in fact occur. Petri dishes, containing solidified agar-culture-medium, were held before the mouths of coughing plague patients, and, even when no visible particles of sputum appeared, colonies of plague bacilli developed on the plates. Granted that infection is due to the inhalation of droplets of sputum containing plague bacilli, it follows that the longer these droplets remain suspended in the air, the greater the danger of infection.

These droplets may disappear from the air in the immediate neighborhood of the patient in three ways; namely, (1) by evaporation, (2) by settling, and (3) by being borne away by currents of air.

The rate of evaporation depends chiefly upon the water deficit of the atmosphere. Under ordinary conditions this is far greater in warm weather than in cold and hence, ordinarily, evaporation of droplets of moisture in the air will take place far more rapidly in warm weather than in cold. At 4° C., with a maximum of moisture in the air, the water vapor has a pressure of only 6.0 millimeters of mercury; hence, even if the atmosphere were absolutely dry at this temperature, the water deficit would be small and evaporation would take place very slowly.

At 30° C., with a maximum of moisture in the air, the pressure of the water vapor amounts to 31.5 millimeters. With 70 per cent of moisture in the air, there would still be a greater water deficit (9.4 millimeters of mercury) than in a perfectly dry atmosphere at 4° C. In a cold climate, with snow on the ground and a rise of several degrees in temperature during the middle of the day, the water deficit of the air would be approximately zero during the greater part of the twenty-four hours. These were the conditions in Manchuria during the recent epidemic of pneumonic plague; hence there must have existed a very low water deficit in the air and little tendency for the droplets of sputum to disappear by evaporation. In India, on the contrary, with a temperature ranging around 30° C., there is usually a large water deficit in the air and hence the droplets of sputum would tend to disappear quickly by evaporation, thus leading to the death of the contained plague bacilli by drying.

According to curves given in the Report of the International Plague Conference, the temperature at Harbin during the course of the epidemic ranged between —9° C. and —32° C. and the humidity between 61 and 92. At —10° C., the vapor tension

[1] See II, p. 137 of this report.

of water is 2.09 millimeters of mercury and at −20° C., it is 0.92 millimeters. Hence, with an average humidity of about 80, the water deficit of the air at Harbin during the epidemic would be represented by from 0.4 to 0.2 millimeters of mercury. Under these circumstances, evaporation could take place only with extreme slowness.

In India, with a temperature of +30° and a humidity of 70, the water deficit of the air would be represented by 9.46 millimeters of mercury. In other words, evaporation would take place from twenty-five to fifty times more rapidly in India than in Harbin.

During the plague epidemics of both India and Manchuria, the fact that the poor people were much overcrowded in their living quarters undoubtedly hastened the spread of the disease. In Manchuria, on account of the bitterly cold weather, the doors and windows of the overcrowded houses were kept tightly closed. Under these circumstances, another factor is introduced of perhaps no small importance in its bearing upon the rate of disappearance by evaporation of droplets of sputum in the air; namely, the moisture in the expired air. In the cold, the moisture from the breath of the inmates of an overcrowded room would quickly saturate the air and reduce evaporation to a minimum, whereas the air of a similar warm room could take up large quantities of moisture without becoming saturated.

The following hypothetical case will illustrate the point in question. Let us assume that there are 10 men in a room 4 meters by 4 meters with the ceiling 4 meters high and that the room is without ventilation. If the air of the room had a humidity of 50 and a temperature of 30° C., it would become saturated after about four hours, for the room contains 64,000 liters of air. The expired air, which has a temperature of 37° and is saturated with moisture, totals about 4,800 liters per hour. The vapor pressure of air saturated at 37° is 46.7 millimeters of mercury, and of half-saturated air at 30° it is 15.7. Therefore, the men would have to breathe $\frac{15.7}{46.7}$ or approximately one-third of the air of the room in order to cause saturation of all of it. This would require $\frac{1}{3}$ of $\frac{64000}{4800}$ or about four hours.

If the air of the room had a humidity of 50 and a temperature of 8° C., the men would have to breathe $\frac{4.0}{46.7}$ or approximately one-twelfth of it in order to produce saturation, and this would require $\frac{1}{12}$ of $\frac{64000}{4800}$ or approximately one hour. Hence the air of the room at the lower temperature would become saturated in about one-fourth of the time required at the higher temperature.

Furthermore, the overcrowded rooms in a warm climate would in reality be thrown open and the moisture of the expired air would be consequently more or less rapidly dissipated, whereas in the cold climate conditions would approximate the hypothetical case at 8° C. just cited; hence the difference in the rate of evaporation of droplets in the air due to overcrowding in cold and in warm climates respectively would be, in fact, greater than is indicated by the figures in the hypothetical case just described.

The surface tension of water at 4° C. is 74.9, and at 30° C. it is 71.03. The surface tension being greater at the lower temperature, with the same amount of water deficit, evaporation would take place more slowly there than at the higher temperature. This is, therefore, an additional factor which would tend to cause droplets of pneumonic sputum to persist longer in the air in a cold climate than in a warm one. However, it is a factor of far less influence than the water deficit of the air and hence deserves no further discussion.

It seems highly probable that plague bacilli in suspended droplets of sputum would survive much longer at a low temperature than at a high one, even were the water deficit of the air the same in both cases; or, in other words, that with the same rate of drying, the bacilli would remain alive longer at low temperatures than at higher ones. This would, then, be also an important factor in causing pneumonic plague to spread more rapidly in cold climates than in warm ones.

It is noteworthy that the only large epidemic of pneumonic plague in India of which we have a record occurred during cold weather in Kashmir in the winter of 1903 to 1904. The epidemic is described by A. Mitra,[2] who stated that it lasted from November, 1903, to August, 1904, "but the virulence was only from December to March." "In the districts there were altogether 1,443 cases with 20 recoveries. The recoveries being bubonic cases, which were seen at the end of the epidemic." We judge from these statements that the epidemic of pneumonic plague lasted from December till March. Mitra says:

> The conditions of life in these villages during the month of January and February were extremely unfavorable. Everything round was frozen.

The Indian Weather Review shows that Srinagar, which was the center of the Kashmir epidemic, had, during the month of December, 1903, a mean daily temperature of 36°.1 F. and a

[2] *Indian Med. Gaz.* (1907), 42, 133.

mean humidity of 81°.0; during January, 1904, a mean daily temperature of 29°.1 F. and a mean humidity of 88°.0; during February, 1904, a mean daily temperature of 36°.0 F. and a mean humidity of 85°.0.[3]

Therefore the conditions were such that droplets of sputum suspended in the air would have had a tendency to evaporate to dryness only with extreme slowness.

Gill [4] appears to have been the only investigator who has devoted especial attention to the epidemiology of pneumonic plague in India. He says:

Pneumonic plague presents well-marked features as regards its time of occurrence, which cannot be considered altogether accidental and without significance.

In the four epidemics of which I have notes the time of its first appearance was as follows:

1905–1906	Epidemic	(Sept.–Sept.)	Jan. 24th, 1906.
1906–1907	"	"	Feb. 1st, 1907.
1907–1908	"	"	Dec. 13th, 1907.
1908–1909	"	"	Oct. 10th, 1908.

The last outbreak in the 1907–1908 epidemic was on March 16th, and in the two former epidemics this was noted as about the time of the last outbreak and its occurrence after April 1st has not been noted.

The characteristic of pneumonic plague is therefore its occurrence at the early part of the plague season, during the months of January, February, and March, that is, while the epidemic is on the increase but before it has reached its maximum intensity.

Thus, while in the Punjab, the time of maximum intensity is April and the beginning of May pneumonic plague is chiefly prevalent in February.

But not only is this the case, but it exhibits the same features in regard to its time of occurrence in the individual epidemics in villages.

For as was exemplified in regard to the typical case of Mokal it was at the commencement of the epidemic that it appeared and it lasted a comparatively short time, being succeeded or replaced by a more prolonged bubonic outbreak.

It is not easy to understand the reason for this, but it suggests that the organism of plague has acquired at this time an unusual or perhaps "exalted" degree of virulence which, however, it is not long able to maintain.

I am unable to give any figures showing the actual prevalence of the disease or even to roughly estimate the proportion it bears to the general epidemic.

Judging from reports one reads it is probable that it varies in different parts of India, and it is my impression that it is commoner in the comparatively cool climate of the Punjab than in the warmer and moister parts of India.

[3] These data are taken from observations made at 10 a. m. and 4 p. m. The 8 a. m. temperatures and humidity for the same months are: Dec., 1903, 28°.9 and 92°.0, respectively; Jan., 1904, 28°.4 and 93°.0; Feb., 1904, 33°.1 and 90°.0.

[4] *Indian Med. Gaz.* (1909), 44, 135.

That plague bacilli may be unable "to long maintain their unusual or perhaps exalted degree of virulence" by passage from lung to lung, as is suggested by Gill, appears to us to be highly improbable, since the experimental data at hand indicate that passage from lung to lung in susceptible animals is the method of choice and, perhaps, the only method of exalting the virulence of plague bacilli and maintaining the high virulence thus attained.

The epidemiological observations of Gill possess, however, great interest with regard to the influence of atmospheric temperature upon the spread of pneumonic plague. He found that pneumonic plague occurred during cold weather and ceased when the warm weather began, in spite of the fact that the number of bubonic cases was still on the increase. Unfortunately, he did not publish his notes in sufficient detail for us to determine the atmospheric temperature and humidity which existed during his several epidemics, but as far as his observations go, they indicate that the atmospheric temperature was probably a factor of importance in the spread of pneumonic plague and the suppression of the epidemic.

The only other epidemic of pneumonic plague of recent years of which we find a reliable record is the small one which occurred in Osaka, Japan, also in the cold season of the year. The first patient was taken sick on December 19, 1899. This case was quickly followed by twelve others, the last dying on January 13, 1900.

The above discussion has been confined entirely to pneumonic plague, but obviously the same ideas apply also to other pneumonias. In other pneumonias, however, it is not unlikely that the dosage and virulence of the inhaled bacilli and the susceptibility of the host at the time of exposure are factors of far greater importance than in plague pneumonia; hence, the influence of atmospheric temperature on their spread would be more or less obscured by these other factors.

We have endeavored to obtain experimental data confirmatory of the ideas advanced in the foregoing discussion. It was, of course, impracticable to perform actual experiments with plague bacilli sprayed into the air on account of the danger of contracting pneumonic plague. We, therefore, sprayed harmless bacteria and determined how they behave in the air under different conditions, believing that the results obtained would justify us in drawing conclusions as to how plague bacilli would act under similar conditions. We selected for most of the experiments *B. prodigiosus* and a yellow sarcina obtained from the

air. Those organisms possess the following advantages for these experiments: (1) They are harmless, (2) their colonies on agar are readily recognized on account of the characteristic pigment production, and (3) they differ considerably in their resistance to death by drying, the prodigiosus being killed more readily than the sarcina. In a few experiments the cholera vibrio was used; this organism is much more readily killed by drying than is *B. prodigiosus*. The following experiment demonstrates the relative resistance to death by drying of the three varieties of bacteria just mentioned and of the plague bacillus.

EXPERIMENT NO. 1.

Suspensions in 0.5 per cent sodium chloride solution were made from fresh cultures of sarcina, *B. prodigiosus*, plague, and cholera. The suspensions were passed through filter paper with the exception of that of the sarcina, which was filtered through cotton. Carefully cleaned slides were sterilized in the hot-air sterilizer and allowed to cool to room temperature. Pledgets of cotton were soaked in the suspensions, squeezed out thoroughly, and quickly rubbed over the surfaces of a series of the sterile slides. The slides were placed at intervals face down upon solidified agar in Petri dishes and brought into close contact with the agar by gentle pressure. After the first few minutes had elapsed, the remaining slides of the series were placed face down upon a sterile wire-netting frame in a box which was covered with a sheet of blotting paper. This was done to reduce the number of contaminating air-organisms upon the slides which were exposed for long intervals.

Each slide was left upon the agar for an hour or longer and then moved back and forth a few times over the surface and finally transferred to a second Petri dish. It remained in the second Petri dish overnight and was then removed. The number of colonies that developed on the first plate gave an indication of the number of bacteria that were alive on the slide, but the second plate merely furnished information as to whether or not living bacteria were present.

The result of one such experiment will be recorded in full.

Cholera suspension on slide.

(1,200,000,000 per cubic centimeter.)

Time exposed.	Plate No. 1.	Plate No. 2.
	Colonies.	
At once.	1,000	Positive.
Min.		
½	5	Positive.
1	0	Negative.
2	0	Negative.
3	0	Contaminated.
4	0	Negative.
6	0	Negative.
8	0	Negative.
10	0	Negative.

Plague suspension on slides.

(100,000,000 per cubic centimeter.)

Time exposed.	Plate No. 1.	Plate No. 2.
	Colonies.	
At once.	8,000	Positive.
Min.		
1	1,000	Positive.
2	100	Positive.
5	0	Negative.
10	0	Negative.
15	0	Negative.
21	0	Negative.
30	0	Negative.

Prodigiosus suspension on slides.

(273,000,000 per cubic centimeter.)

Time exposed.	Plate No. 1.	Plate No. 2.
	Colonies.	
At once.	1,000	Positive.
Hrs. min.		
0 15	6	Positive.
0 30	0	Positive.
0 45	0	0
1 00	1	0
1 30	0	0
2 00	0	0
2 30	0	0
3 00	0	0
3 30	0	0
4 00	0	0
4 30	0	0

Sarcina suspension on slides.

(3,000,000 per cubic centimeter.)

Time exposed.	Plate No. 1.	Plate No. 2.
	Colonies.	
At once.	1,000	Positive.
Hours.		
1	800	Positive.
2	400	Positive.
3	175	Positive.
4	17	Positive.
5	33	Positive.
6	0	1 colony.
20	0	Negative.

This experiment was done in a large room with the doors and windows closed. The bacteria upon the slides were exposed to diffuse daylight during the first few minutes and were then placed in a covered box. The temperature of the room ranged between 32°.5 and 33°.6 Centigrade and the dry-bulb thermometer registered about five degrees lower than the wet-bulb one.

This experiment indicates, as do several other similar ones that we have done, that the plague bacillus occupies an intermediate position between cholera and prodigiosus with regard to its resistance to death from drying. Sarcina is much more resistant than the other organisms.

Having determined the relative resistance to death by drying of sarcina, *B. prodigiosus*, and *cholera vibrio* when spread in a thin layer upon glass slides, we next planned an experiment to find the result with these same organisms when contained in fine droplets of saline solution suspended in the air.

EXPERIMENT NO. 2.

Fresh cultures of the bacteria were suspended in 0.5 per cent sodium chloride solution, the cholera suspension being made thicker than the prodigiosus and the latter thicker than the sarcina.[5] The spraying was done by means of an ordinary throat atomizer connected by rubber tubing with a double cylinder force-pump such as is used for filling automobile tires. The spray was directed during a period of half a minute toward all parts of a chemical hood, measuring 175 centimeters long, 80 centimeters deep, and about 2 meters high. Paper had been previously pasted over all cracks in the hood, and arrangements had been made for sliding a Petri dish into the hood over moist blotting paper by opening a small orifice for only two or three seconds.

The cholera suspension was sprayed first and plates were exposed in the hood at intervals until we judged (from preliminary experiments) that all the living cholera vibrios had disappeared from the air. The hood was then thrown open and about fifteen minutes later a similar experiment was performed with the prodigiosus suspension. Then the hood was again left open for a while and finally the experiment with sarcina was done. Each Petri dish containing solidified agar-culture-medium was left in the hood for a period of two minutes.

[5] The prodigiosus suspension was shown by plating out in agar to contain 120,000,000 organisms per cubic centimeter, the sarcina suspension, 33,000,000; the number per cubic centimeter in the cholera suspension was not determined.

Through the glass door of the hood, readings were made from the wet-bulb thermometer as follows:

Time.	Dry-bulb thermometer.	Wet-bulb thermometer.	Difference.
a. m.			°C.
9.37½ to 9.38. Cholera suspension sprayed.			
9.40	29°.9 C.	28°.2 C.	1.7
9.45	30°.2	28°.6	1.6
9.54	30°.6	28°.7	1.9
10.10½ to 10.11. Prodigiosus suspension sprayed.			
10.15	30°.0 C.	28°.2 C.	1.8
10.20	30°.4	28°.4	2.0
10.33	30°.65	28°.65	2.0
11.02	30°.8	28°.95	1.85
11.43½ to 11.44. Sarcina suspension sprayed.			
11.48	30°.3 C.	28°.6 C.	1.7
11.57	30°.85	28°.8	2.05
12.09	31°.05	29°.0	2.05
2.55	31°.8	30°.3	1.5

The results of this experiment are recorded in Table I.

TABLE I.—*Results of spraying suspensions.*

Time after spraying.	Cholera suspension.	Prodigiosus suspension.	Sarcina suspension.
Hrs. min.	*Colonies.*	*Colonies.*	*Colonies.*
0 ½	37,000	260,000	78,000
0 3	75	67,000	65.000
0 6	7	47,000	40,000
0 9	0	4,900	35,000
0 12	0	2,700	36.000
0 15	0	160	37,000
0 18	----	25	28,000
0 21	----	7	27.000
0 24	----	7	25,000
0 30	----	1	16,000
0 36	----	1	----
0 42	----	0	----
0 45	----	----	13,000
0 50	----	0	----
1 0	----	0	10,000
1 15	----	0	5,800
1 30	----	----	4,800
1 45	----	----	3,600
2 0	----	----	2,600
2 30	----	----	1,400
3 0	----	----	850

It is seen from the table that, when sprayed into the air under similar conditions, living cholera vibrios disappear from the air in about six minutes and living prodigiosus bacilli in about twenty minutes, whereas sarcina remains alive for more than three hours. There is a striking similarity shown by these organisms in their relative resistance to drying on glass slides and their persistance in the air when contained within fine droplets of saline solution. It would seem, therefore, that had plague bacilli been sprayed under similar conditions, the living ones would have disappeared from the air between six and twenty minutes after spraying.

This similarity in the behavior of the organisms on the slides and in droplets strongly suggests that also in the latter instance the disappearance of the living bacilli from the air is due to death from drying. If this were true, then if we were able to retard the evaporation of the water of the fine droplets, the living bacteria should remain in the air for a longer time. The most obvious method of retarding the evaporation of the fine droplets is to spray them into an atmosphere saturated with moisture. The following experiment was therefore carried out.

EXPERIMENT NO. 3.

The chemical hood used in the previous experiment was also employed for this one, but sheets of dry blotting paper were tacked against the walls and strips of cloth were tacked to the ceiling and allowed to hang down to within about 60 centimeters of the floor of the hood. A suspension of cholera vibrios in 0.5 per cent sodium chloride solution was sprayed into the dry hood, and Petri dishes were exposed for periods of two minutes each at intervals of three minutes until we could assume (from previous experiments) that living cholera vibrios were no longer present in the air. The entire interior of the hood was then thoroughly sprinkled with water and the cloths and sheets of blotting paper were also made soaking wet. After the wet hood had been kept tightly closed for some time, the same cholera suspension was sprayed into it for the same length of time as before; this time, however, the pump was placed in a tin vessel which was covered with towels soaked in hot water, so that the air going into the hood with the spray would contain more moisture. Plates were exposed as before for one hour. Then water was again sprinkled over the interior of the hood and a suspension of sarcina in 0.5 per cent sodium chloride solution was sprayed and followed a minute later by the same suspension of cholera that was used for the previous sprayings. Plates were exposed for three and one-half hours.

Temperature readings were made through the glass doors of the hood as follows:

Time.	Dry-bulb thermometer.	Wet-bulb thermometer.	Difference.
10. 51½ to 10.52. Cholera suspension sprayed.			
10. 58 a. m.	30°. 6 C.	28°. 3 C.	2°. 3 C.
12. 02½ to 12.03. Cholera suspension sprayed.			
12. 38 p. m.	31°. 0 C.	30°. 9 C.	0°. 1
1. 43 to 1.43½. Sarcina suspension sprayed.			
1. 44½ to 1.45. Cholera suspension sprayed.			
1. 50 p. m.	31°.95 C.	31°. 3 C.	0. 05
2. 00 p. m.	31°.31	31°. 26	0. 05

The results of this experiment are shown in Table II.

TABLE II.—*Results of spraying experiments.*

Time after spraying.	Cholera suspension in the dry hood.	Cholera suspension in the wet hood.	Wet hood.	
			Cholera.	Sarcina.
Hrs. min.	*Colonies.*	*Colonies.*	*Colonies.*	*Colonies.*
0 ½	21,000	130,000	Innumerable.	104,000
0 3	170	33,000	34,000	31,000
0 6	0	24,000	4,700	15,000
0 9	0	2,600	1,800	13,000
0 12	0	470	195	7,000
0 15	0	220	300	6,000
0 18	0	38	20	3,000
0 21	----------	18	52	2,400
0 24	----------	8	18	2,800
0 27	----------	2	8	1,600
0 30	----------	0	4	1,700
0 36	----------	0	0	1,000
0 40	----------	0	0	900
0 50	----------	0	0	600
1 0	----------	0	0	360
1 30	----------	----------	0	135
2 0	----------	----------	0	86
2 30	----------	----------	0	31
3 0	----------	----------	0	16
3 30	----------	----------	0	1

In the dry hood the living cholera vibrios had all disappeared from the air six minutes after the spraying was discontinued, whereas in the wet hood living cholera vibrios were present after twenty-seven minutes. The wet- and dry-bulb thermom-

eters showed that the air of the wet hood was nearly saturated with moisture, and hence evaporation of suspended droplets of water must have been reduced almost to the minimum. Therefore, we are justified in concluding that the extremely rapid disappearance of the living cholera vibrios in the dry hood is due to the rapid evaporation of the suspended droplets of saline solution which leads to the death of the contained cholera vibrios from drying.

The last part of the experiment shows conclusively that the rapid disappearance of living cholera vibrios is not due to settling or removal through air currents, for droplets containing cholera vibrios and those containing sarcina were subjected to identical conditions and yet living sarcinæ were present in the air long after the cholera vibrios had disappeared. The sarcina being a larger organism and having a greater tendency to remain in clumps would settle out more rapidly than the cholera vibrio. It remained alive in the air longer than the cholera vibrios because of its greater resistance to drying. A similar experiment was performed with *B. prodigiosus*.

EXPERIMENT NO. 4.

A fresh culture was suspended in 0.5 saline solution and passed through filter paper. When plated out this suspension was found to have contained about 100,000,000 organisms per cubic centimeter.

The same suspension was sprayed for the same length of time into the dry hood, the wet hood, and into a cold storage room the temperature of which was about 18° C.

The temperature of air in the hood was read as usual through the glass door.

Time.	Dry-bulb thermometer.	Wet-bulb thermometer.	Difference.
a. m.			
9.47½ to 9.48. Prodigiosus suspension sprayed.			----------
9.55	30°.5 C.	29°.2 C.	1.3
10.12	31°.1	29°.0	2.1
11.02	31°.2	29°.25	1.95
p. m.			
12.05½ to 12.06. Prodigiosus suspension sprayed.			----------
12.20	31°.3 C.	31°.2 C.	0.1
12.50	31°.3	31°.25	0.05
1.50	31°.52	31°.42	0.1
2.30	31°.7	31°.6	0.1
3.40	31°.8	31°.7	0.1

In the cold storage room the spraying continued from 10.55½ to 10.56 a. m. The temperature of the room was as follows: At 11.02, 20°C.; at 11.30 a. m., 19°; at 12.35, 18°. Then it remained at 18° until the end of the experiment.

TABLE III.—*Showing growth of colonies.*

Time after spraying.	*B. prodigiosus* in dry hood.	*B. prodigiosus* in wet hood.	*B. prodigiosus* in cold room.
Hrs. min.	*Colonies.*	*Colonies.*	*Colonies.*
0 1	78,000	Innumerable.	44,000
0 5	52,000	Innumerable.	37,000
0 10	19,000	130,000	19,000
0 20	170	57,000	9,500
0 30	1	22,000	6,000
0 40	0	15,000	4,500
0 50	2	8,500	3,500
1 0	0	7,000	3,000
1 10	0	4,000	2,000
1 20	----------	1,500	2,000
1 30	----------	330	1,400
1 40	----------	170	1,300
1 50	----------	50	900
2 0	----------	15	750
2 15	----------	8	450
2 30	----------	----------	300
2 45	----------	0	350
3 0	----------	0	200
3 15	----------	----------	150
3 30	----------	0	150
3 45	----------	----------	125
4 0	----------	----------	90

As with the cholera vibrios so also in the case of *B. prodigiosus* there is a striking difference in the length of time that the bacilli remain alive in a dry and in a moist atmosphere. In the cold room the bacilli remain alive in the air even longer than in the wet hood. Unfortunately, the humidity of the cold room during this experiment was not determined.

It was, therefore, necessary to perform the following experiment. The same suspension of *B. prodigiosus* was sprayed for one-half a minute into a moist hood and into a cold storage room, and Petri dishes containing solidified agar were exposed in both places for periods of two minutes each at intervals of four hours. In the cold room the dry-bulb thermometer registered 12° C. and the wet-bulb one about 10°.5 C. throughout the experiment. In the hood the dry-bulb thermometer varied between 31.1 and 31.5 and the wet-bulb one registered about 0°.2 below the dry one. It is clear that the water deficit of the atmosphere was greater in the cold room than in the hood. The result of this experiment is recorded in Table IV.

TABLE IV.—*Showing growth of colonies.*

Time after spraying.		*B. prodigiosus* in moist hood.	*B. prodigiosus* in cold room.
Hrs.	*min.*	*Colonies.*	*Colonies.*
0	1	Innumerable.	78,000
0	5	260,000	42,000
0	10	52,000	30,000
0	20	29,000	17,000
0	30	13,000	11,000
0	40	5,000	6,300
0	50	3,500	5,000
1	0	350	3,200
1	10	220	2,100
1	20	34	1,800
1	30	17	1,300
1	45	5	1,200
2	0	0	870
2	15	1	530
2	30	0	360
2	45	----------	330
3	0	0	320
3	15	----------	240
3	30	----------	160
3	45	----------	130
4	0	0	90

In spite of the fact that the water deficit of the air of the cold room was greater than that of the hood, the bacilli remained alive longer in the cold room. The only interpretation of this result is that *B. prodigiosus* resists death from drying longer at low temperatures than at high ones, even when the rate of drying is the same in both instances. It seems highly probable that this is also true of the plague bacillus; if so, the bearing of the phenomenon is an additional factor in the longer persistence of living plague bacilli in droplets of sputum, and hence upon the more rapid spread of pneumonic plague in cold climates is obvious.

SUMMARY.

It is shown that when spread on glass slides and exposed to the air, plague bacilli occupy an intermediate position between the cholera vibrio and *B. prodigiosus* with regard to resistance to death from drying. Sarcina resists much longer than *B. prodigiosus*. When suspended in saline solution and sprayed into the air, the living cholera vibrio disappears with surprising rapidity, *B. prodigiosus* persists for a longer time, and sarcina much longer than *B. prodigiosus*. The relative length of time that these organisms remain alive when sprayed into the air agrees strikingly with their survival on glass slides. This suggests that their disappearance from the air is also due to death from drying.

This was shown to be in fact the case by spraying the same cholera suspension into a comparatively dry atmosphere and then, under similar conditions, into an atmosphere nearly saturated with moisture; living cholera vibrios remained in the air much longer in the latter instance. A similar experiment was performed with *B. prodigiosus* with the same result.

By spraying sarcina and immediately thereafter cholera vibrios, so that the droplets containing these organisms were subjected to identical conditions, living sarcina was found to persist in the air long after the living cholera vibrios had disappeared. Since the sarcina is a larger organism than the cholera vibrio, it follows that the disappearance of the latter was not due to settling.

We believe we are justified in concluding from these experiments that were the plague organisms sprayed under similar conditions they would persist longer than cholera vibrios, but a shorter time than prodigiosus bacilli. Hence, it seems probable that the plague bacilli contained in fine droplets of pneumonic-plague sputum would suffer death from drying in a few minutes unless they were suspended in an atmosphere with an extremely small water deficit. Infection in pneumonic plague follows the inhalation of droplets of pneumonic sputum and obviously the longer these droplets remain suspended in the air, the greater is the danger of infection. As has just been stated, these fine droplets disappear very quickly except when they are suspended in an atmosphere with a very small water deficit. Such an atmosphere is under ordinary circumstances of common occurrence in very cold climates, whereas it is extremely rare in warm ones. Hence, since the droplets of sputum persist longer, the plague bacilli remain alive longer in the air, and there is a greater tendency for the disease to spread in cold climates than in warm ones.

In harmony with the above ideas, we find that the only great epidemic of pneumonic plague of modern times occurred in Manchuria during the winter of 1910 to 1911, when the atmospheric temperature was many degrees below zero Centigrade. The disease spread with amazing rapidity. Furthermore, although during the past fifteen years there have been millions of plague cases in India and 2 to 5 per cent of these have been cases of plague pneumonia, yet this form of the disease has not assumed epidemic proportions. The largest epidemic of pneumonic plague in India (1,400 deaths) occurred in Kashmir in northern India at an elevation of 1,524 meters above the sea level during very cold weather.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

IV. PORTAL OF ENTRY OF INFECTION AND METHOD OF DEVELOPMENT OF THE LESIONS IN PNEUMONIC AND PRIMARY SEPTICÆMIC PLAGUE: EXPERIMENTAL PATHOLOGY.

By Richard P. Strong and Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

For the purpose of studying experimentally the question of the portal of entry of the organism and the method of the development of the lesions in pneumonic plague, animals were placed in closed glass cages, and agar-cultures of virulent pneumonic strains of the plague bacillus suspended in saline solution were sprayed for a period of from about two to three minutes into the surrounding air which they breathed. Thirty-four normal guinea pigs and 55 normal monkeys were so infected with plague bacilli, and all succumbed to plague infection. The animals were necropsied in each instance, and the lesions present observed and studied. It would be very tedious to record here the individual necropsy reports, since the lesions found were so often similar. Therefore, only a general description of the lesions will be undertaken, and the different types of lesions emphasized.

In the guinea pigs so infected, the following changes were encountered at necropsy. In general there was marked evidence of plague infection about the cervical and laryngeal tissues. The subcutaneous tissues showed extensive œdema, and there was swelling of the cervical lymphatic glands and of those about the trachea. Usually the glands were not only swollen but more or less hæmorrhagic and presented the appearance of small early buboes. Throughout the body marked evidences of septicæmia were usually present. There were frequently extensive hæmorrhages in the intestinal wall. The spleen sometimes showed the typical changes encountered in bubonic-plague in-

fection with miliary abscesses. Distinct evidences of pneumonia were present in only about 23 per cent of the guinea pigs. Plague bacilli were frequently not very abundant in the lungs, unless pneumonic areas were encountered, but were always present in the heart's blood. The lungs were sometimes reddened, congested, and œdematous, and sometimes contained hæmorrhagic infarcts. Small areas of primary bronchial pneumonia were encountered in some of the cases, and in one a whole lobe of the lung showed pneumonic engorgement. In two instances either red or early gray hepatization was present. Numerous miliary abscesses were occasionally encountered in the lungs. (See Plate VII.) The areas of bronchial pneumonia were firm, contained no air, and were usually irregular in outline and red, reddish yellow, or yellow in color. On cut section they were sometimes wedge-shaped. In those instances in which hæmorrhagic infarcts, miliary abscesses, and in addition reddish-yellow or yellow areas of lobular pneumonia are present (see Plate VII), we must conclude that the infection of the lung is secondary, and that in these instances we are not dealing with primary pneumonic plague, in which infection enters through the bronchi, but with secondary infection of hæmotogenous origin. Such a conclusion is supported by the microscopical study of these lesions. A section of the lung in the vicinity of one of the hepatized areas, pictured in Plate VII, shows the bacteria in very large numbers both about and within the small blood vessels, and in places infarctions have occurred; numerous hæmorrhages from the vessels have also taken place; in the neighborhood of the pneumonic areas the bacteria are also plentiful in the lung alveoli and in the perivascular spaces.

Therefore, these changes suggest that the primary point of infection did not always occur in the bronchi or alveoli of the lung. From a study of all the lesions in guinea pigs, it would appear that these animals, under the conditions of the experiments in which the spraying was carried on, did not frequently develop primary plague pneumonia, but that infection occurred through the mucous membranes of the mouth and throat, resulting in a general septicæmia generally preceded by the formation of early buboes of the cervical glands and sometimes followed by the development of secondary areas of plague pneumonia. It would appear that in guinea pigs, either on account of too shallow respiration or the small size of the larynx and trachea, the bacteria are not so likely to penetrate to the smaller bronchi by means of the inspired air. Instead, they are apparently

deposited largely upon the mucous membranes of the mouth and throat.

The experiments performed on monkeys seem to throw much more light upon the mode of pneumonic-plague infection in man. The lesions in 55 monkeys infected by spraying were studied at necropsy. There was a marked similarity in general in the pathological changes encountered. In practically all of the animals there was absence of any sign of plague infection about the cervical tissues. The submaxillary and cervical lymphatic glands and those about the trachea were not swollen, nor was there any œdema of the cervical tissues, as was practically always seen in the experiments with guinea pigs. In none of the cases examined did the tonsils show evidence of primary disease, though in a number of instances they were sectioned and stained. In some instances they were moderately congested. Plague bacilli were scanty in them and when present were not more numerous than in the heart's blood and never so numerous as they were in the lungs or spleen.

There was frequently œdematous fluid in the trachea, and in a few cases the trachea was slightly reddened. The larynx and vocal cords were not as a rule injected. There was not such marked evidence of septicæmia as seen in the experiments with guinea pigs, but plague bacilli could always be recovered from the heart's blood by culture. No hæmorrhages were noted in the intestines and omentum. The spleen and liver showed no miliary abscesses. There were no cervical, axillary, nor inguinal buboes. The lungs showed primary pneumonic changes in every case. There was always much œdema. In those animals which succumbed a shorter time after infection, the lobular type of pneumonia was much more frequently encountered. In those which survived a longer period, whole lobes of the lung usually showed pneumonia. The progress of the lesions is well shown in Plate VII, figs. 2 and 3. The process evidently begins as a lobular bronchial pneumonia. By the fusion of a number of the areas of lobular pneumonia, the whole lung may become involved. The large pneumonic areas were either in the stage of engorgement or of red or early gray hepatization. In a number of cases a pleuritic exudate was observed over the hepatized areas. In no case were miliary abscesses observed in the lungs. In the cases with the *early lesions,* the plague bacilli were always most numerous in the lungs, and in section were found in greatest profusion about the bronchioles, in the peribronchial lymph spaces and alveoli, and beneath the pleura. In some instances the cells

lining the alveoli appear normal even when they contain large numbers of bacilli. Although the blood vessels between the lobules and septa were dilated, and hæmorrhages sometimes occurred, practically no bacteria were found within them.

From these observations, it is obvious that the infection in monkeys occurred by inhalation and resulted in primary plague pneumonia.

It also is evident that in some instances in which monkeys are exposed to infection by inhalation, the primary point of infection may be not only the lungs, but also the mucous membranes of the mouth and throat. That plague infection may occur through the mucous membranes of the mouth and throat *alone* in monkeys was demonstrated by placing a small quantity of plague bacilli upon the posterior portion of the throat by means of a glass rod. The following experiments are given as examples of such infection.

EXPERIMENT I.

Monkeys Nos. 5882, 5883, and 5884 were all infected in the following manner on November 7.

A necropsy was performed upon monkey No. 5876 which had just died of experimental pneumonic plague and a portion of the pneumonic lung was cut into small pieces in a Petri dish. A glass rod with the end rounded in a flame was dipped into the œdematous fluid in the Petri dish and passed over the tongue and rubbed against the pharynx of each of the three monkeys (Nos. 5882, 5883, 5884). The monkeys held their tongues so that the glass rod was squeezed between the soft palate and the tongue and most of the material on the rod was evidently caught there. All three of the monkeys were treated in the same way and then the rod was dipped into the same fluid and touched to the shaved skin of a guinea pig as a control. The control guinea pig, No. 5885, died November 14, seven days after, with typical lesions of plague.

Monkey No. 5882 was found dead on Nov. 13, six days after infection. *Necropsy*: The superficial cervical glands are swollen on both sides. Both submaxillary glands are swollen and hæmorrhagic. The changes are more marked on the left side. The deep cervical glands on both sides are also swollen and hæmorrhagic; the process is more advanced on the left side. The axillary lymph nodes are also swollen and hæmorrhagic. The lesions in these glands are more marked on the right side. The tonsils on both sides are swollen and reddened. The larynx shows slight injection. The trachea contains a small amount of pale, frothy fluid; its mucosa is not injected. The bronchial lymph nodes at the bifurcation of the trachea are very small. There is no evidence of pneumonia in either lung. The spleen is much swollen and very soft. Smears from the spleen and blood show innumerable plague bacilli. Smears from the cervical and axillary glands show very numerous plague bacilli. Smears from the lung show fair numbers of plague bacilli. Sections of the tonsils show no evidence of primary plague infection and but few bacilli.

Monkey No. 5883 was found dead on November 15, eight days after infection. *Necropsy:* The tonsils are pale; they contain few pest bacilli and many cocci. The submaxillary, deep cervical, and axillary glands are small and deep red in color. A gland at the bifurcation of the bronchi is enlarged and reddish black in color and contains many plague bacilli. The pharynx and larynx are slightly reddened. The trachea contains some pale, frothy fluid. The lungs are pale and show no pneumonic areas. Cultures made. The spleen is enlarged, deep red, firm, and contains large numbers of plague bacilli. The blood also contains large numbers of plague bacilli.

Guinea pig No. 5902 inoculated with the spleen of monkey No. 5883. Died in four days with large numbers of plague bacilli in its spleen and with well-marked buboes.

Guinea pig No. 5901 inoculated with the lung of monkey numbered 5883. Died in seven days with large numbers of plague bacilli in its spleen and with well-developed buboes.

Monkey No. 5884 was found dead on November 14, seven days after infection. *Necropsy:* (By Dr. Crowell.) The tonsils and pharynx are considerably reddened and covered with frothy fluid. The tonsils are small and pale, show no hæmorrhages, and are probably not enlarged. The submaxillary glands are slightly enlarged and deep red. The deep cervical glands are somewhat enlarged and deep red, redder than the submaxillary. The glands in both axillæ are enlarged and hæmorrhagic, those in the left being larger than in the right. A gland at the bifurcation of the trachea is small, but deep red in color. The larynx and trachea are slightly reddened throughout their extent and contain abundant frothy, slightly blood-tinged fluid. The lungs show on the surface only a few small red areas. No pneumonia is present. On section, the cut surface is dark red and very moist. The spleen is enlarged and fairly firm.

EXPERIMENT II.

Culture No. 32 isolated from a pneumonic-plague case at Mukden was passed through a series of guinea pigs and a fresh culture from one of these passage guinea pigs was suspended in saline solution. A glass rod was dipped into this suspension and touched against the pharynx of three monkeys (Nos. 5927, 5928, 5929) as in the preceding experiment. The following necropsy reports show that the bacilli from artificial cultures brought about the same result as those inoculated directly from the pneumonic lung.

Monkey No. 5927.—Bacillus pestis placed on mucosa of mouth December 5. Found dead six days later. *Necropsy:* (By Dr. Crowell.) The axillary glands in the right axilla are slightly reddened, in the left they are pale. The tonsils show no visible change. There is no pneumonia present. The spleen is somewhat enlarged. Smears from the heart show numerous bipolar organisms. The spleen contains involution forms. The liver contains numerous bipolar organisms which are less numerous in the lungs than in the blood.

Monkey No. 5928.—Bacillus pestis placed on mucosa of mouth December 5. The animal died December 14. *Necropsy:* (By Dr. Crowell.) The tonsils, deep cervical, submaxillary, and axillary glands are only slightly swollen and reddened. The lungs are somewhat œdematous and a little

reddened. There is no consolidation. The trachea is only slightly reddened. The spleen slightly, if at all, enlarged. Smears from the heart's blood show very numerous pest bacilli, while the organisms in the lung, liver, and spleen are numerous.

Monkey No. 5929.—Inoculated on December 5, died on December 10. *Necropsy:* (By Dr. Crowell.) Smears from the spleen show very few, if any, pest bacilli. The heart shows two or three to a field. Few are found in the lung, while the liver shows numerous bacilli. The lesions are practically the same as those encountered in monkey No. 5928.

Therefore, these animals all died of plague septicæmia with or without bubonic infection of the cervical glands; that is, in the case in which the infection was severe and the susceptibility of the animals more marked, they succumbed to septicæmia before cervical buboes developed. In none of these instances was pneumonia present. Primary plague pneumonia only results when infection by inhalation has in addition taken place.

It has been claimed by several observers and more recently by Koulecha[1] that pneumonic plague in man is primarily a septicæmic disease, the lungs becoming secondarily involved by way of the blood circulation. According to this observer, the infection is supposed to spread from the perivascular spaces to the neighboring lung alveoli. He further believes that the bacilli enter the blood by the lymph vessels through the lesions in the tonsils and are deposited in the interstitial tissues around the lung alveoli, the tonsils being regarded as the primary point of infection. In some instances he assumes it to be possible for the plague bacilli to pass from the mucous membranes of the trachea and bronchi to the neighboring lymphatic glands and from them to enter the blood and in this way later to reach the lung. Albrecht and Ghon have shown that by the intravenous injection of plague bacilli in animals, pneumonic plague did not result.

In our opinion, the view that pneumonic plague is primarily a septicæmic disease and that the lungs become secondarily involved by way of the blood circulation and that the tonsil is first infected is not acceptable.

From our study of pneumonic plague both in man[2] and animals, we feel justified in concluding that infection in epidemic pneumonic plague results from inhalation, the primary point of

[1] Report of the International Plague Conference held at Mukden, April, 1911. Manila (1912), 154.

[2] For a description of the human lesions, see VII, p. 210 of this report.

infection being not in the tonsils[3] but some portion of the bronchi, the organism either passing along the bronchioles directly to the alveoli or through the walls of the bronchioles to the contiguous tissue of the lungs, giving rise, first, to peribronchial and perivascular inflammation in the surrounding tissues, and then to more diffuse inflammatory processes throughout the lung. Having reached the lung tissue, the bacilli rapidly multiply and produce at first pneumonic changes of the lobular type and shortly afterward more general lobar involvement of the lung tissue.[4]

The blood becomes quickly infected and a true bacteræmia results in every case. The fact that the bronchial glands at the bifurcation of the trachea are always much more severely affected than any of the other lymphatic glands also argues against the theory that epidemic pneumonic plague is primarily a septicæmic disease and that the lungs are infected secondarily from the blood. Moreover, in the earliest stage of the disease, the blood may be free from plague bacilli as we have shown by cultures.

It is true that in some instances the bacteræmia occurs early in the course of the disease and before hepatization of the lung may have taken place. However, microscopical examination will reveal enormous numbers of plague bacilli in the engorged lung tissue from which it appears that the origin of the bacteræmia is clear.

The tonsils may become secondarily infected in pneumonic plague just as other lymphatic glands—for example, the bronchial ones—become so infected. However, in pneumonic plague death usually occurs before any marked macroscopic changes occur in the tonsils. There is no doubt also that the tonsils may become primarily infected in epidemics of pneumonic plague just as has occurred in sporadic cases in epidemics of bubonic plague; such cases have been previously reported. This, however, is not the common channel of primary infection, and in such cases involvement of the glands of the neck occurs early in the course of the disease. Such cases are really instances of bubonic plague in which the lungs may, or may not, become secondarily infected.

In some instances plague infection may occur directly through

[3] See also under pathological anatomy, p. 215 of this report for the condition of the tonsils in the human cases and Plates XI and XVIII.

[4] See Plate VII, figs. 2 and 3, and Plates IX and X.

the mucous membranes of the mouth and throat. Primary septicæmia may then result. In those instances in which the infection is virulent and severe and the susceptibility of the host marked, death may sometimes occur before bubonic involvement is apparent. In other instances, bubonic involvement of the glands of the neck and septicæmia are present. No true pneumonia occurs unless infection by inhalation has in addition taken place. The German and the Austrian Plague Commissions concluded that primary plague septicæmia probably does not exist. However, these commissions made their observations only during epidemics of bubonic plague. From our studies made upon human beings, during the Manchurian epidemic, as well as from the animal experiments quoted above, we must conclude that primary plague septicæmia does sometimes take place and that death may occur, though rarely, before visible lesions have taken place either in the lungs or lymphatic glands.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

V. CLINICAL OBSERVATIONS.

By Richard P. Strong and Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

CONTENTS.

TYPES OF THE DISEASE MET WITH DURING THE MANCHURIAN EPIDEMIC.

The cases throughout the epidemic were almost entirely those of primary pneumonic plague, only two or three undoubted cases of primary bubonic infection having been reported at the International Plague Conference.[1] However, in a number of instances death occurred before there were any clinical manifestations that pneumonic plague was present, and in some of these cases only at necropsy was it discovered that early involvement of the lungs existed. This led to the belief that many of the cases were primarily septicæmic in character. One observer at the Conference, Doctor Christie,[2] estimated from a clinical standpoint that about 5 per cent of the cases was of the septicæmic variety without pneumonia. However, from the post-mortem studies made during the epidemic, we must conclude that the cases with no involvement of the lungs were exceptional ones. Nevertheless, in a few instances in which infection did not occur by inhalation but probably through the tonsils or the mucous membranes of the mouth or throat, it seems unquestionable that the lungs were either not involved or only very slightly so. Thus,

[1] Report of the International Plague Conference held at Mukden, April, 1911. Manila (1912), 428.

[2] *Ibid.*, p. 166.

in one instance of this nature, occurring during the epidemic and reported by Fujinami,[3] the lymphatic glands of the neck showed enlargement with hæmorrhages, and the surrounding tissues of the pharynx and larynx were very much affected, while the lung was only very slightly involved. Obviously, this case should be regarded as primarily of bubonic character. Both the German and the Austrian plague commissions concluded that primary plague septicæmia probably does not exist. However, as has already been called attention to elsewhere in this report, these commissions made their observations only during epidemics of bubonic plague. From the studies made upon human beings during the Manchurian epidemic, as well as from the animal experiments performed in this laboratory,[4] we must conclude that primary plague septicæmia does sometimes occur, death resulting from this cause before lesions, which are macroscopically recognizable, are present in the lymphatic glands or in the lungs.

Several cases of primary intestinal plague were reported at the Conference in which bloody diarrhœa appeared to be the most prominent symptom. None of these cases was studied at necropsy. It appears that no definite evidence of the occurrence of primary intestinal infection during the epidemic was produced. In the few instances in which plague bacilli had been found during the epidemic in the fæces, infection had evidently occurred secondarily from the blood. Albrecht and Ghon in the report of the Austrian Commission have reported the only suggestive case of primary intestinal plague occurring during a bubonic epidemic of plague, and even in this case the evidence of such infection is not conclusive. However, it seems established that primary intestinal plague has been produced in rats by feeding large quantities of virulent plague bacilli. In many instances during the Manchurian epidemic, the patients with pneumonic plague must have swallowed enormous numbers of plague bacilli in the saliva and sputum. Nevertheless, in none of the necropsies performed during the epidemic were evidences of primary intestinal infection present nor was serious involvement of the intestine encountered. This fact certainly speaks strongly against the existence of primary intestinal plague in man and would seem to show that even if the intestines are sometimes secondarily involved, this condition in human beings must be also a very rare one.

[3] *Ibid.*, p. 150.

[4] See IV, p. 173 of this report.

SEX, AGE, AND INCUBATION PERIOD.

Both sexes seem equally susceptible, but the proportion of females and children attacked during the epidemic was comparatively small, as women and children were evidently not so frequently exposed to infection. The disease prevailed particularly among the poorer classes, coolies, etc., the majority of whom were between 20 and 40 years of age. The incubation period varied from two to five days, though usually it was not over two or three days.

SYMPTOMS.

The following summary of the clinical features of the disease has been made largely from personal observations during the epidemic in Mukden and also from evidence presented at the International Plague Conference.

The onset of the disease is usually somewhat abrupt; prodromal symptoms are rare. The disease usually begins with chilly sensations, but a distinct rigor generally does not occur. Epistaxis is generally not present. There is headache, loss of appetite, an increase in the pulse rate, and fever. Vomiting rarely occurs. Within from twenty-four to thirty-six hours after the onset, the temperature usually has reached 103° or 104° F., and the pulse 110 to 130 or more beats per minute. Cough and dyspnœa usually appear within twenty-four hours after the onset of the first symptoms. The cough is usually not painful. The expectoration is at first scanty, but soon becomes more abundant. The sputum at first consists of mucus which shortly becomes blood-tinged. Later the sputum becomes much thinner and of a bright-red color; it then contains enormous numbers of plague bacilli in almost pure culture. The typical rusty sputum of croupous pneumonia has not been observed. The conjunctivæ become injected, and the tongue coated with either a white or brownish layer. The expression is usually anxious, and the face frequently assumes a dusky hue. Labial herpes has never been observed. The patients sometimes complain of pain in the chest, but usually this is not severe. Apart from the disturbances due to the dyspnœa and their anxiety for their condition, they usually appear to suffer but little and usually do not complain of pain. In the later stages of the disease, the respirations become greatly increased and the dyspnœa usually very marked, the patients frequently gasping for air for several hours before death. Cyanosis is then common.

The signs of cardiac involvement are always marked in the

advanced cases, the pulse becoming gradually more rapid, feeble, and running; finally it can not be felt.

Gallop rhythm of the heart sounds are frequently observed. Death takes place from cardiac paralysis and exhaustion. The patients frequently succumb after slight physical exertion, such as sitting up in bed to take nourishment or on being moved. A few hours before death the temperature often declines to below normal. Delirium and coma are frequently present before death.

The urine in the later stages may show the presence of albumin. The diazo and indican reactions have not been observed in the few cases in which the urine was tested. Extravasations of blood have been found in the pelves of the kidneys at post-mortem examination.

The spleen is usually not palpable, and the lymphatic glands not enlarged. Petechiæ or larger hæmorrhages of the skin are usually not present. Bloodly diarrhœa is occasionally observed. Plague bacilli frequently may be present in the blood in such numbers that a simple, microscopical examination suffices for their detection; in other cases, cultures are necessary for their discovery. A marked leucocytosis may occur, though in some cases the leucocytes are not increased. In the *primary septicæmic* cases the course of the disease is very rapid. There may be no manifestations of disturbances of the lung. The cardiac symptoms are very prominent. The patients soon pass into a comatose condition and die.

PHYSICAL SIGNS.

The physical signs in the lungs are often slight, even in cases well advanced in the disease. On percussion, dulness is often absent, and the vocal fremitus and resonance unchanged. In a small proportion of cases, however, smaller or larger areas of dulness may be discovered. On auscultation râles are frequently not present, except shortly before death. When present early in the disease, they are usually of the fine variety. Numerous moist râles are heard late in the disease, and are due to the œdematous condition of the lungs. The character of the râles is in accordance with what one would expect from the condition of the lungs and bronchi and the character of the exudate observed at necropsy. Coarse râles such as occur in cases of catarrhal bronchitis usually are not present. Feeble, respiratory sounds, tubular modification, or pure tubular respiration over small areas are the conditions found most commonly on auscultation. Not infrequently a dry, pleuritic rub is heard.

The limits of dulness of the heart are sometimes increased

to the right of the sternum. The heart sounds are rapid and usually become feeble or embryocardiac in character toward the end. In the early stages the secondary pulmonic sound may be accentuated, but it soon becomes much less distinct.

DIAGNOSIS.

The diagnosis is usually clear from the bacteriological examination of the sputum in which the bacillus is found in enormous numbers and in almost pure culture. A rise in temperature and an increased pulse rate are usually the earliest symptoms observable, but before the sputum appears the diagnosis may be doubtful. An examination of the blood, either microscopically or by culture, may reveal the diagnosis, since during the past epidemic all the cases became septicæmic. The blood should always be examined early, by cultural methods, as in the primary septicæmic cases involvement of the lungs may not occur. The bacteriological diagnosis is the only certain one for excluding pneumonic infection due to microörganisms other than *Bacillus pestis,* but from the general condition of the patient, in connection with the absence of marked physical signs in the lungs, the diagnosis of pneumonic-plague infection is often particularly suggested. Labial herpes has not been observed in primary pneumonic plague. The presence of numerous coarse, piping or sibilant bronchial râles in the lungs is an argument against pneumonic-plague infection. The sputum in pneumonic plague is not purulent as it frequently is in catarrhal bronchitis or in bronchial pneumonia, and it is not so tenacious and has not the rusty appearance of the sputum so often seen in croupous pneumonia. The cough is usually not so painful as in croupous pneumonia.

The duration of the disease is usually less than two days, though many cases did not live longer than sixteen hours after the onset of symptoms. Cases sometimes survived for three, and, more rarely, for four days. In no case reported was the duration over one week.

PROGNOSIS AND TREATMENT.

The prognosis is unfavorable. No cases in which the bacteriological diagnosis was complete were known to have recovered during the Manchurian epidemic.

No method of treatment appeared in any way to have been successful. Treatment with serum seemed, in a few instances, to have prolonged the duration of the illness.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

VI. BACTERIOLOGY.

By Richard P. Strong and Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

CONTENTS.

CHARACTERS OF THE PNEUMONIC STRAIN OF "BACILLUS PESTIS."

During the epidemic in Manchuria the idea became rather general that the organism of pneumonic plague differed, in some respects at least, from *Bacillus pestis* of bubonic plague. Apart from cultural variations, some physicians believed that while the bacillus of bubonic plague on inoculation into guinea pigs gave rise to buboes, the bacillus of this epidemic, on injection into these animals, caused only pneumonia and septicæmia. Also, it was claimed by some, that the virulence of the organism of pneumonic plague was much greater than that of the bacillus of bubonic plague. These ideas were erroneous, as is apparent from a consideration in detail of the properties of the pneumonic strain arrived at from the study of numerous microscopical preparations and cultures obtained from the sputum and from necropsies performed during the epidemic.

MORPHOLOGY.

From a morphological standpoint, the causative organism of the Manchurian epidemic of pneumonic plague apparently differs in no respect from other strains of *Bacillus pestis* isolated during

many epidemics of bubonic plague. In stained microscopic preparations made from the organs at necropsy it appears in its most characteristic form as a short bacillus, more or less ovoid in form, swollen in the center, and rounded at the ends. It exhibits marked bipolar staining, the central portion either remaining uncolored or staining lightly. Such preparations and those made from sputum often show, besides these bipolar forms, great variation in the morphology of the organisms present. Involution forms, consisting of longer, thicker, deeply staining rods, or of organisms which have assumed a spherical or orbicular outline, or, occasionally even appearing very much as yeast cells, may be encountered. Many of these forms stain poorly, or sometimes only a portion of the organism is stained, and in the shorter bacilli the appearance of ring forms is thus produced. In agar-cultures, and particularly in 3 per cent salt agar, these large involution forms and degenerating organisms of very different shapes are very numerous and characteristic: long and slender or thick bacilli and also boat-shaped, dumb-bell, ring-shaped, and spherical organisms may all be observed. The organism generally appears in preparations from agar-cultures as a short or longer rod, and does not so frequently reveal the marked bipolar appearance when stained. In hanging-drop preparations no true motility is exhibited. No flagella are visible in properly-stained preparations, and no spores have been demonstrated. It stains easily with all the anilin dyes, and particularly well with dilute carbol-fuchsin solution, and is easily and completely decolorized by Gram's stain.

CULTURAL CHARACTERISTICS.

The cultural characteristics of the bacillus also are practically identical with those of many bubonic strains. The bacillus grows well upon neutral, or slightly alkaline, moist agar at a temperature of from 25° to 35° C., and is aërobic. After twenty-four to forty-eight hours on agar-cultures inoculated with the pneumonic strain, usually small, delicate, transparent, dewdrop-like colonies appear, which after forty-eight to seventy-two hours have increased in size, are more raised, and have become less translucent. After this time many of these colonies do not perceptibly increase in diameter, while others later become much heavier and larger, so that the two types of colonies are frequently observed in the same culture: the one smaller and more or less translucent, and the other much larger (four or five times the

diameter of the smaller ones) and whiter and more opaque in character. The organism grows more slowly when first transplanted from the animal body to agar than in subsequent transplantations on agar. Microscopically, the colonies exhibit a lighter peripheral band and a thicker, raised, slightly granular center which, when examined by direct light, gives a considerably darker appearance than the periphery.

In gelatin, somewhat similar, though slightly more delicate, colonies to those on agar are formed. In stab-cultures the gelatin is not liquefied. It was pointed out by some observers at the Conference that some of the freshly-isolated pneumonic cultures caused no turbidity when grown in bouillon, the growth rapidly falling to the bottom of the media and leaving the supernatant fluid clear. However, this is not invariably the case, as other pneumonic cultures cause slight turbidity. These variations in the different cultures evidently depended more upon the amount and manner of inoculation of the organisms and the character of the media than upon any particular characteristic of the culture itself.

In Manila, we have, since the Conference, studied three different bubonic cultures recently isolated—one from Shanghai, one from Hongkong, and one from Mariveles, Philippine Islands—and three cultures from different pneumonic cases. These were each inoculated in tubes of bouillon and grown side by side at room temperature. No difference in growth as to the cloudiness of the bouillon, amount of sediment, etc., could be observed in the different tubes. In one of the pneumonic cultures and in one of the bubonic ones the growth and flocculi seemed somewhat heavier than in the other tubes. The growth in all of the cultures became visible, about the second day, in the form of fine flocculent masses which later greatly increased in size and became deposited partly along the sides and at the bottom of the tubes. The bouillon in all was slightly clouded. Microscopical specimens from the different cultures revealed chains of coccoid bacilli.

MUCUS PRODUCTION.

The production of mucus by the pneumonic strain when grown upon agar slants has been marked, but varies greatly, as is also the case with bubonic strains, according to the temperature at which the cultures develop. Grown at ice-box temperature, the culture forms a crumbly mass when collected upon the platinum loop and, when this mass is placed in saline solution, it is ex-

tremely difficult to break up the small clumps and to obtain a homogeneous and durable suspension. When grown at 37° C., the bacilli, when collected upon the platinum loop, form a homogeneous, moist, mucoid mass which readily forms a homogeneous suspension when shaken in saline solution. At 30° C., the growth results sometimes more like the growth at 37° C. just described, at other times more like the growth at the temperature of the ice-box, depending upon the strain employed; most strains cultivated at 30° C. produce more mucus than is usually seen in cultures developed in the ice-box and less than is seen in cultures grown at 37° C.

Another factor, which in our experience has exerted an important influence upon the mucus production of a plague strain, is the length of time it has been cultivated upon artificial media. Freshly-isolated strains, whether from human subjects or from our experimental animals, produce more mucus than strains which have been cultivated on agar for some time.

We cultivated a number of strains at 32° C. upon sugar-free agar, glucose-agar, saccharose-agar, and starch-agar, and did not observe that these carbohydrates caused an increase in the mucus production.

The age of the culture is a factor influencing the amount of mucus present. A twenty-four-hour culture will contain less mucus than the same culture several days later.

We have pointed out that the readiness with which the strains form homogeneous suspensions appears to run parallel with their mucus production and hence the former serves as a good index of the latter. There are, however, other factors which bring about the formation of homogeneous suspensions, notably the presence of alkali. The addition of a few drops of alkali to a suspension of a culture grown at ice-box temperature and shaking quickly brings about the disappearance of the clumps, and a homogeneous suspension results. It is for this reason difficult to determine whether or not the reaction of the culture-medium exerts an influence upon the mucus-production of plague organisms; we can only affirm that this influence, if present, is not marked.

To sum up, in our opinion the two factors of paramount importance with regard to the mucus production of plague bacilli are the temperature at which the cultures are grown and the length of time that the organisms have been cultivated on artificial media since their isolation from the animal host.

Bearing these facts in mind, we have not observed with regard

to mucus production that our pneumonic-plague strains in any way differ from the bubonic strains.

VIRULENCE.

The organism seems to have retained a maximum virulence throughout the epidemic, at least all of the cultures isolated and studied by inoculation into animals possess this very high degree of virulence. Cultures isolated near the close of the epidemic showed an equally high virulence to those isolated near its beginning. However, the idea that this epidemic of pneumonic plague was due to the fact that the strain possessed an abnormally high virulence—much greater than that possessed by the organism of bubonic plague—and that this accounted for the very high mortality during the epidemic appears to be erroneous. The very acute course of the disease, the very high death rate during the epidemic as compared with that of bubonic plague, and the apparently increased virulence of this pneumonic strain may be satisfactorily explained by the fact that the portal of entry of the organism and the location of the primary points of infection in pneumonic plague and in bubonic plague are different. The plague organism finds in the pulmonary tissues a much more favorable and extensive medium for its multiplication and diffusion than it does in the lymphatic glands. In bubonic plague, the lymphatic glands may be said to act as filters against the general invasion of the organism by the plague bacillus, while in primary pneumonic plague there is no such mechanism for the defense of the host, the bacilli spreading rapidly throughout the lung and invading the circulation in every instance in a comparatively short time and apparently before the organism has had time to produce any appreciable quantity of immune substances. The bronchial lymphatic glands in primary pneumonic plague offer resistance to the invasion of the plague bacillus, and in every case of this disease these glands are very acutely inflamed and frequently almost of a black color from the resulting toxic hæmorrhages in the glandular substance. However, by the time the bronchial glands have become involved, the bacteria have already spread so extensively throughout the lung substance that a bacteræmia has usually occurred. Microscopical preparations made at necropsy from the lungs of these pneumonic cases invariably contain enormous numbers of plague bacilli. In no other disease are the organisms found in such great abundance. In primary pneumonic plague, the bacilli are found in very much greater number in the lung than in the spleen,

even though an advanced bacteræmia is present. This fact, also, suggests that the lung tissue offers a more favorable location for the growth and multiplication of the bacilli than does the spleen. The bacteria are also present in far greater numbers in the lung than they are ever found in the buboes or spleen in bubonic-plague cases. It is, also, evident that in pneumonic plague the infected lung (which may be said to correspond to the primary bubo of bubonic plague) contains, by reason of the size of the infected area, a far greater number of plague bacilli than the primary bubo in bubonic plague. During epidemics of bubonic plague, there are occasionally small epidemics of pneumonic plague in which the same high mortality and acute course of the disease is observed as occurred in the Manchurian epidemic of pneumonic plague. This is another argument in favor of the fact that during epidemics of bubonic plague the causative organism may show the same high virulence. As examples may be cited the epidemic of bubonic plague in Japan—in Kobe and in Osaka in 1899 to 1900—in which 13 cases of primary pest pneumonia all terminated fatally after a very rapid course, and the epidemic of bubonic plague in 1898 in Bombay in which, toward its close, 11 cases of pneumonic plague also all quickly succumbed one after the other.

All this evidence is in favor of the supposition that the organism giving rise to the present epidemic is of no greater virulence than in the case of many bubonic strains; furthermore, definite proof of this fact has been obtained from comparative inoculations made in animals with different pneumonic and bubonic cultures. Many of our experiments have been reported in the testimony of the Conference, and will not be given in detail here;[1] the results of others performed by us since that time are recorded in Table I.

The guinea pigs were all inoculated in the following manner: An area of the abdomen, about 2 centimeters square, was shaved and scraped with the razor until petechial hæmorrhages appeared in the skin. A 42-hour agar-slant-culture of each organism was suspended in 5 cubic centimeters of peptone solution and 5 *œsen* of each suspension were rubbed over the shaved area of the guinea pig's abdomen. At necropsy the animals showed the usual lesions of bubonic plague. These guinea pigs were inoculated on June 8. The pneumonic strains were isolated during the month of March, the bubonic strain "Hongkong" on May 20, and the bubonic strain "Mariveles" on May 27. The bubonic strain sent from Shanghai had been on artificial media at least for several months.

[1] Report of the International Plague Conference held at Mukden, April, 1911. Manila (1912), 75, and Index under Virulence.

TABLE I.—*Showing virulence of various cultures of plague.*

Number of guinea pig.	Weight of guinea pig.	Number of culture.	Number of days before death.
	Grams.		*Days.*
5258	400	1	3½
5259	390	2	4
5261	350	5	6½
5262	360	7	7½
5263	340	8	7
5264	400	9	3
5265	360	10	7
5266	350	21	6
5267	390	22	5½
5292	350	16	8
5293	380	23	6½
5294	390	25	6
5295	390	26	5
5297	330	28	3
5298	350	29	5½
5300	370	31	5½
5325	330	11	5
5326	350	12	7
5327	380	13	5½
5328	360	14	10
5329	380	15	5½
5330	360	17	5
5331	380	18	4½
5332	370	19	5
5334	350	Shanghai.	(a)
5335	360	Mariveles.	5½
5336	340	Hongkong.	5
5415	340	32	9

[a] Developed buboes, but recovered.

These experiments and those already referred to (*loc. cit.*) have shown that the pneumonic cultures have not possessed any greater virulence than that possessed by many virulent bubonic ones of the organism. Mice, rats, guinea pigs, and monkeys inoculated with virulent bubonic cultures die within the same period of time and from the same doses as do the corresponding animals inoculated with the pneumonic cultures. The same lesions are observed in animals after inoculation of the pneumonic strain as after the inoculation of the bubonic strain. Both strains when inoculated cutaneously, or subcutaneously, into guinea pigs and monkeys give rise to bubonic-plague infection. When the animals are infected by inhalation with either strain, similar lesions are also produced. In guinea pigs, after inhalation, infection results through the mucous membrane of the throat and upper portion of the respiratory tract, resulting in buboes of the cervical glands and septicæmia and in primary or secondary pneumonia; in monkeys, after infection by inhalation, primary pneumonic infection of the lung with secondary septicæmia results.

However, while during epidemics of bubonic plague reports

have been made that there is often a marked difference in virulence in the different cultures isolated, during this epidemic of pneumonic plague the organism seems to have retained a very high degree of virulence throughout. The cultures isolated from a number of cases near the close of the epidemic, upon inoculation into animals, proved to be fully as virulent and to kill animals as quickly and in the same doses as did those cultures isolated near the beginning. That the organism retained such a stable virulence throughout the epidemic is, perhaps, not surprising when one considers that infection occurred directly from man to man or, frequently one might say, from lung to lung and without the passage of the organism through rodents as ordinarily occurs in bubonic-plague infection. Morever, from the results of previous experiments relating to infection of animals with pneumonic plague by inhalation, we would expect that the organism would have retained its maximum virulence throughout this epidemic.

For these reasons and, also, from the fact that the acute course and mortality of the disease were not changed toward the close of the epidemic and especially, from the experimental proof furnished by the inoculation of animals with cultures isolated near the beginning and near the close of the epidemic, we must conclude that the sudden decline and cessation of the epidemic was not due to any marked change in the virulence of the strain. Such a decline and cessation must have depended upon other causes. The plague bacillus, whether isolated from pneumonic or from bubonic epidemics, usually exhibits marked stability in virulence. While it is not a very resistant organism in nature and easily becomes destroyed under certain conditions, it usually does not become markedly attenuated in passage through the animal body, and even on artificial culture-media, after many months, its virulence is usually fully retained. Instances of spontaneous loss of virulence in culture-media have been reported, but this is not usually the case with fresh, virulent cultures. This quality of stability of virulence of the plague bacillus, so different, for example, from that of the cholera vibrio, is of particular interest from an epidemiological standpoint.

AGGLUTINATION TESTS.

Theoretically the agglutination test has two applications in plague: (1) The diagnosis of the disease by the demonstration of antibodies in the patient's serum and (2) the identification of the organism cultivated from a suspected case by means of the serum of an animal immunized against the plague bacillus.

In pneumonic plague, the agglutination test has no clinical value, for the patients succumb to the disease before antibodies are produced or at least produced in any quantities that are capable of detection.

With regard to the second application of the method, as there seemed to be some difference of opinion as to the value of the agglutination test in identifying plague bacilli, we decided, after our return to Manila, to carry out a series of experiments in the hope of throwing further light upon this subject. The result of our experiments in this direction will be described briefly.

For obtaining an agglutinating serum, rabbits were used and large doses of the bacilli were injected intravenously. Repeated inoculation of *living avirulent* plague bacilli administered in this way called forth a very satisfactory serum, but *killed virulent* bacilli failed to do so in every instance. All of the rabbits lost weight rapidly during immunization.

After obtaining a satisfactory serum, the various pneumonic strains which we had brought back with us from Mukden, together with three bubonic strains and three strains from experimental animals, were all subjected to the agglutination test with the same plague serum. The organisms were grown at 32°C. In order to avoid spontaneous sedimentation, the bacteria were suspended in distilled water and the dilutions of the sera made with 0.1 per cent sodium chloride solution.

The greatest dilution of the immune serum, which caused complete or almost complete agglutination, is recorded for each strain tested in the following table:

TABLE II.—*Showing limit of agglutination in plague strains.*

Strain.	Limit of agglutination.	Strain.	Limit of agglutination.
Pneumonic plague:		Pneumonic plague—Continued.	
No. 1	160	No. 22	1,280
No. 5	160	No. 23	1,280
No. 7	640	No. 25	320
No. 8	320	No. 26	320
No. 9	160	No. 28	320
No. 10	160	No. 29	320
No. 12	640	No. 32	320
No. 13	160	Shanghai	320
No. 14	640	Hongkong	640
No. 15	320	Mariveles	320
No. 16	160	Avirulent plague	(?)
No. 17	320	Guinea pig:	
No. 18	640	No. 5635	80
No. 19	640	No. 5769	80
No. 21	640	No. 5745	80

Two points are strikingly obvious from this series of experiments: (1) There is great variability in the limits of agglutination of the different strains and (2) the strains freshly isolated from experimental animals agglutinate only at relatively low dilutions of the serum. It is also to be noted that both pneumonic strains and bubonic ones are agglutinated by the same serum.

It was next decided to select certain of these strains in order to make a careful study of the influence of various factors upon their agglutinability.

One of the difficulties in performing agglutination tests, particularly with strains which have been grown on artificial media for long periods of time, has been the tendency of the bacilli to form clumps spontaneously. We found that very small amounts of alkali would prevent this spontaneous flocculation and sedimentation of the suspensions, but on performing tests with such suspensions these extremely small amounts of alkali inhibited all agglutination.

It has already been mentioned that we performed a series of tests in the presence of only a small amount of electrolytes (0.1 per cent sodium chloride instead of 0.8 per cent). This served well to render the suspensions homogeneous and durable and agglutination was not inhibited, but there was frequently a disturbing flocculation with normal serum within very narrow limits, such as is often seen when one colloid is flocculated by another. As only two or three tubes of a long series were so affected, it was possible to distinguish between this phenomenon and the true specific agglutination. Nevertheless, the method was abandoned and in the tests to be described below both the bacterial suspensions and the dilutions of the serum were prepared with 0.5 per cent sodium chloride solution.

The following tables, selected from a number of similar ones with other strains of plague bacilli, demonstrate clearly the results of our experiments.

TABLE III.—*Showing agglutination of culture No. 26.*

	Grown at 37° C.			Grown at 32° C.			From guinea pig. Grown at 37° C.			From guinea pig. Grown at 32° C.			From guinea pig. Grown at 12° C.		
	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.	2 hours.	3 hours.	20 hours.
Serum of immunized rabbit:															
1/20	++	+++	+++	+	++	+++	++	+++	+++	+	++	+++	trace	+	+++
1/40	++	+++	+++	+	++	+++	++	+++	+++	+	++	+++	trace	+	+++
1/80	+	+++	+++	+	++	+++	—	—	+	+	++	+++	trace	+	+++
1/160	—	—	trace	+	++	+++	—	—	—	+	++	+++	trace	+	+++
1/320	—	—	trace	+	++	+++	—	—	—	+	++	+++	trace	+	+++
1/640	—	—	—	+	++	+++	—	—	—	trace	++	+++	trace	+	+++
1/1280	—	—	—	+	++	+++	—	—	—	—	trace	++	trace	+	+++
1/2560	—	—	—	trace	++	+++	—	—	—	—	trace	++	trace	+	+++
1/5120	—	—	—	trace	+	+++	—	—	—	—	trace	++	trace	+	+++
1/10240	—	—	—	—	+	+++	—	—	—	—	trace	+	—	+	+++
Salt solution	—	—	—	—	trace	+++	—	—	—	—	trace	+	—	+	+++
Normal rabbit serum:															
1/20	—	—	—	—	—	+++	—	—	—	—	—	trace	—	+	+++
1/40	—	—	—	—	—	+++	—	—	—	—	—	trace	—	+	+++
1/80	—	—	—	—	—	+++	—	—	—	—	—	trace	—	+	+++
1/160	—	—	—	—	—	+++	—	—	—	—	—	trace	—	+	+++
1/320	—	—	—	—	trace	+++	—	—	—	—	—	trace	—	+	+++
1/640	—	—	—	—	trace	+++	—	—	—	—	—	trace	—	+	+++
1/1280	—	—	—	—	trace	+++	—	—	—	—	—	trace	—	+	+++
1/2560	—	—	—	—	trace	+++	—	—	—	—	trace	+	—	+	+++
Salt solution	—	—	—	—	trace	+++	—	—	—	—	trace	+	—	+	+++

TABLE IV.—*Showing agglutination of culture No. 12.*

	Grown at 37° C.			Grown at 32° C.			From guinea pig. Grown at 37° C.			From guinea pig. Grown at 32° C.			From guinea pig. Grown at 12° C.		
	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.
Serum of immunized rabbit:															
1/20	++	+++	+++	++	++	+++	++	+++	+++	+	++	+++	+	+	+++
1/40	++	+++	+++	++	++	+++	++	+++	+++	+	++	+++	+	+	+++
1/80	++	+++	+++	++	++	+++	−	+	++	+	++	+++	+	+	+++
1/160	trace	+	++	++	++	+++	−	−	−	trace	++	+++	+	+	+++
1/320	trace	+	++	+	++	+++	−	−	−	trace	+	+++	+	+	+++
1/640	trace	+	++	+	++	+++	−	−	−	−	trace	++	+	+	+++
1/1280	trace	+	+	+	++	+++	−	−	−	−	−	trace	+	+	+++
1/2560	trace	+	+	+	++	+++	−	−	−	−	−	trace	+	+	+++
1/5120	−	−	−	+	+	+++	−	−	−	−	−	trace	trace	+	+++
1/10240	−	−	−	+	+	+++	−	−	−	−	−	trace	trace	+	+++
Salt solution	−	−	−	−	trace	++	−	−	−	−	−	trace	trace	+	+++
Serum of normal rabbit:															
1/20	−	−	−	trace	trace	+	−	−	−	−	−	−	trace	+	+++
1/40	−	−	−	trace	trace	+	−	−	−	−	−	−	trace	+	+++
1/80	−	−	−	trace	trace	+	−	−	−	−	−	−	trace	+	+++
1/160	−	−	−	trace	trace	++	−	−	−	−	−	−	trace	+	+++
1/320	−	−	−	+	+	++	−	−	−	−	−	trace	trace	+	+++
1/640	−	−	−	+	+	++	−	−	−	−	−	trace	trace	+	+++
1/1280	−	−	−	trace	trace	++	−	−	−	−	−	trace	trace	+	+++
1/2560	−	−	−	−	trace	++	−	−	−	−	−	trace	trace	+	+++
Salt solution	−	−	−	−	trace	++	−	−	−	−	−	trace	trace	+	+++

TABLE V.—*Showing agglutination of culture "Hongkong."*

	Grown at 37° C.			Grown at 32° C.		
	2 hours.	4 hours.	20 hours.	2 hours.	4 hours.	20 hours.
Serum of immunized rabbit:						
1/20	++	++	+++	+	+	+++
1/40	++	++	+++	+	+	+++
1/80	+	++	+++	+	+	+++
1/160	+	++	+++	+	+	+++
1/320	+	++	+++	+	+	+++
1/640	+	++	+++	+	+	+++
1/1280	+	++	+++	+	+	+++
1/2560	+	+	++	+	+	+++
1/5120	trace	+	++	+	+	+++
1/10240	trace	+	++	+	+	+++
Salt solution	—	+	+	+	+	+++
Serum of normal rabbit:						
1/20	—	—	—	—	trace	++
1/40	—	—	—	—	trace	++
1/80	—	—	—	—	+	++
1/160	—	—	+	—	+	+++
1/320	—	—	+	—	+	+++
1/640	—	+	+	+	+	+++
1/1280	—	+	+	+	+	+++
1/2560	—	+	+	+	+	+++
Salt solution	—	+	+	+	+	+++

In Table III it is seen that the strain used agglutinates at greater dilutions when grown at 32°C. than when grown at 37°C. The control tubes with normal serum show in the case of the bacteria grown at 37°C. no agglutination whatsoever, even after twenty hours, while in the cases of the bacilli grown at 32°C., the bacteria have all settled out in twenty hours.

The same strain, after passage through an animal, does not agglutinate at as great dilutions as before. When grown at 32° C., it also shows less tendency toward spontaneous sedimentation than previous to the passage through the guinea pig. When grown at 12°C., flocculation begins almost as soon in the tubes with normal serum as it does in those containing immune serum, so that it is difficult to determine whether or not specific agglutination has taken place; however, after twenty hours, on shaking the tubes, the sediment in those with normal serum readily forms a homogeneous suspension, while in the first few tubes, at any rate of those containing immune serum, the sediment is seen to consist of coarser flocculi.

These same observations apply in a general way to the strain used in Table IV. This strain, however, when cultivated at

37°C. agglutinates at much greater dilutions of the same immune serum than does the previous strain when grown at this same temperature. Furthermore, the differences in agglutinability before and after passage through an animal are more marked.

The strain of Table V, when grown at 37°C., agglutinates at still greater dilutions. When cultivated at 32° C., flocculation takes place almost as quickly with normal serum as with immune serum, and it is difficult to decide whether or not specific agglutination has taken place.

Our strain of *avirulent plague* may be cited as the extreme of this series, showing varying grades of agglutinability. Even when cultivated at 37°C., spontaneous sedimentation takes place so rapidly that it is impossible to say that specific agglutination has occurred. Although this strain was used in producing the immune serum, we have in no single instance been able to show that it was agglutinated specifically by the serum.

The same immune serum was used for the tests recorded in Tables III, IV, and V.

We have previously noted that the plague bacillus forms more mucus when cultivated at 37°C. than when grown at 32°C. or even lower temperatures and that more homogeneous and more durable suspensions result in the former instance. We now see that the bacillus when grown at 37°C. is agglutinated with greater difficulty by a specific serum. It, therefore, seems not unlikely that the decrease in agglutinability is due to the increase in mucus production. In harmony with this view is also the fact that strains freshly isolated from experimental animals produce more mucus and are less readily agglutinated by a specific serum than are strains which have been cultivated for months upon artificial media, though the factor of possible difference in virulence also must be considered in this instance.[2]

Finally, we may add that during the course of these experiments we have been able to identify promptly by the agglutination test two strains which were isolated from bubonic cases of plague dying upon ships in the harbor of Manila.

While one of the difficulties in the performance of the agglutination test with the plague bacillus is the tendency toward spontaneous flocculation, we are inclined to believe that, under proper conditions, spontaneous flocculation usually does not occur in freshly-isolated strains; in most strains which have been grown upon artificial media for long periods of time it can be avoided by

[2] Strong, *Journ. Exp. Med.* (1905), 7, 229.

cultivating them at 37°C. The greater difficulty sometimes is, in our opinion, to obtain a satisfactory immune serum. We gave several rabbits repeated intravenous injections of large doses of killed virulent cultures without obtaining more than a trace of agglutination with their sera. We can strongly recommend the use of the living avirulent culture for the preparation of the immune serum.

In conclusion, we can only warn against the use of cultures grown at ice-box temperature as recommended by Shibayama[3] for the agglutination tests. Although such cultures are readily agglutinable, flocculation in the control tubes is apt to be very confusing. If one has a satisfactory immune serum, the culture grown at 32°C. or even at 37°C. will be agglutinated promptly and the control tubes will remain practically unchanged. Controls with normal serum should always be prepared in performing the test.

INFECTIVITY OF THE EXCRETA.

In no other disease is the infecting organism found in such abundance in the sputum as it is in pneumonic plague. When the disease is well developed, *Bacillus pestis* is present in almost pure culture. In pneumonic plague as in bubonic plague, when the disease becomes septicæmic, the organisms are sometimes found in the urine and even sometimes in the fæces. When once the sputum of pneumonic-plague cases becomes thoroughly dried it is no longer infectious, but when the sputum becomes frozen and pulverized, particles of it may be blown about and remain infective for long periods of time or until the sputum is again thawed.

BACTERIOLOGICAL DIAGNOSIS OF PNEUMONIC PLAGUE.

EXAMINATION OF THE SPUTUM.

A bacteriological diagnosis from the sputum can not be made at the onset of the disease, and not until after the fever has developed does the sputum appear. Shortly after the appearance of the sputum, the plague-organism, even if not visible from the microscopical examination, may be isolated by culture. When the sputum becomes bloody, the organism is usually present in large numbers and in almost pure culture. Sometimes the organism might be mistaken morphologically for *Diplococcus pneumoniæ*, and bipolar-staining organisms, other than plague bacilli, may

[3] *Centralbl. f. Bakt. etc.*, Orig. (1905), 1 Abt. 38, 482.

sometimes be encountered in the sputum. While in the microscopical examination of the sputum Gram's stain is a very valuable aid in arriving at a diagnosis of the organism, nevertheless, Gram-negative bacilli have been encountered in the sputum, which proved later not to be plague bacilli. However, usually if the sputum is blood-stained, from the microscopical examination, with the aid of Gram's stain, there is no difficulty in arriving at a diagnosis, since the plague organism is usually present in such very large numbers. In the later stages of the disease, involution forms are commonly encountered in the sputum. The organisms are constantly found in great abundance up to the time of death.

BACTERIOLOGICAL EXAMINATION OF THE BLOOD.

In the early stages of the disease, cultures from the blood are frequently negative. Sometimes, however, the organism could be cultivated from the blood from twenty-four to forty-eight hours before death, and it could always be obtained from the blood a few hours before death. In many instances the bacteria are present in very large numbers in the blood, so that a diagnosis can often be made from a simple, microscopical examination. In no other disease is so marked a bacteræmia present. In the early stages of the disease, cultures from the blood should be made in bouillon, as much as 1 cubic centimeter of blood being employed. The agglutination test is of no value in making a diagnosis, as the course of the disease is too acute and the patient has succumbed before the agglutinins appear in demonstrable quantities. The reaction of the deflection of the complement is also not to be recommended for the same reason; the examination of the sputum and blood for the presence of the bacillus gives much greater and more valuable information. In cases where no necropsy is permitted and a post-mortem bacteriological diagnosis is advisable, microscopical examination of material, obtained by lung puncture with a syringe, may often be conclusive of pneumonic plague, *Bacillus pestis* being present in the microscopical preparation, in enormous numbers, in pneumonic-plague cases.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

VII. PATHOLOGY.

By Richard P. Strong, B. C. Crowell, and Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

Although bubonic plague is a disease that has occurred in large and protracted epidemics and has been widely studied, epidemics of pneumonic plague, even of moderate size, have not been frequent and very few contributions to the literature upon the pathological anatomy of primary pneumonic plague have hitherto been made. Moreover, none of these articles has been based upon the study of extensive material during a large epidemic, and some of the cases described in the literature as those of primary pneumonic plague are really instances of secondary infection of the lung. Therefore, the subject of epidemic pneumonic plague is one of particular importance in connection with the Manchurian epidemic.

Hitherto, our ideas regarding the pathology of pneumonic plague have been based largely upon several cases described by Childe in 1897–1898, and upon three cases reported by Albrecht and Ghon in 1898. The German Plague Commission (Gaffky, Pfeiffer, Dieudonné, Sticker) in the report of their investigations in India, during the same year, described 7 cases of pneumonia in plague, but when one reads the description of these, it is found that but two were cases of primary pneumonic plague, and in both of them the infection was complicated by the presence of other bacteria, in addition to the plague bacillus.

Childe,[1] in 1897 and 1898, describes the post-mortem lesions in two cases of pneumonic plague. In the first case the necropsy was performed seven hours after death and the lesions encountered are described as follows:

"The lungs showed much general engorgement and œdema, with serosanguineous frothy fluid in the bronchi, but no pus; the usual appearances of acute bronchitis were absent. There was one small pneumonic patch, the size of a walnut, in the early second stage, situated below the apex

[1] *Brit. Med. Journ.* (1897), 1, 1215.

on the front of the right lung, and two similar but smaller patches at the same part of the left lung; these patches stood out a little from the surface, and were airless, friable, and sank in water, each was surrounded by a dark ring of engorgement, which merged into the healthy lung, and there was recent pleurisy over the pneumonic areas. All the other organs were examined, and showed considerable engorgement, but no special lesion was observed. The cervical, the axillary, and the lumbar lymphatic glands were slightly enlarged; the left iliac slightly enlarged, red, and soft; all the other glands, including the bronchial, looked absolutely normal."

Childe states that he had performed 12 post-mortem examinations on pneumonic-plague cases all presenting appearances similar to those described in the one above.

In his later publication in 1898,[2] he describes the pneumonic form of plague as follows:

"In this form of plague, the only marked evidences of disease are found in the lungs; the lymphatic glands and other organs are scarcely affected at all.

"*The Condition of the Lungs.*—There was general engorgement with considerable œdema, a reddened condition of the mucous membrane of the bronchi, but no marked evidences of bronchitis, and frothy watery fluid, sometimes blood-stained, could be squeezed from the bronchi. (Pus in the bronchial tubes was only found on one occasion.) A number of pneumonic patches were found scattered through the lungs, varying in size from a pea to an egg. They were light pink or red-grey in colour, solid, airless, and sank in water; they were rounded in shape, and usually separated by a distinct ring of engorgement from the crepitant lung around. Some, instead of being pink, were of a deep blood colour throughout, and less solid, and some of these had a small, greyish, more solid centre. Those of the patches which were situated on the surface of the lung were prominent, and projected distinctly from the surface; whilst the pleura over them was roughened, and showed signs of early inflammation. These patches had, in fact, the appearance of the first and second stages of lobular pneumonia, but no patches were found which had passed on to the third stage of softening and breaking down. In a few cases larger masses of pneumonic lung than these were found, and once about half the lower lung was found in this condition. Petechial hæmorrhages were usually found on the surface of the lung; the bronchial glands were either enlarged, swollen, œdematous, soft, and distinctly engorged, or else they were small and of the usual appearance, perhaps a little engorged. The remaining lymphatic glands throughout the body showed none of the appearances of either the bubonic or septicæmic form of plague; most of them looked absolutely normal, and the only noticeable change was that the axillary, and sometimes the cervical, chains were a little engorged.

The description of the remaining internal organs already given applies equally to this form of plague, except that the large hæmorrhages were absent, but petechiæ on the surface of the heart, in the pelvis of the kidney, bladder, stomach, and intestines were commonly present. Petechiæ in the skin were not observed in this form of plague. * * *

"A section of lung tissue, apart from a pneumonic area, shows great engorgement of all large blood vessels, and of the alveolar capillaries as

[2] *Ibid.* (1898), 2, 859, 860.

well, and patches of hæmorrhage into the alveoli around these engorged vessels are seen scattered about. In a pneumonic area three zones can be made out. At the circumference there is intense engorgement of all vessels including alveolar capillaries, the alveoli are full of blood, and the hæmorrhage is so intense that many of the alveolar septa are broken down, entirely absent, or represented by mere shreds. Within the circumference is seen a zone in which the alveoli are intact and are completely filled with well-stained cells, so that there is no interval between the alveolar walls and their contents; and at the centre is one universal mass of similar cells, and the cellular infiltration is so extreme that the walls of the alveoli are scarcely visible. Such is the general arrangement of the pneumonic patch, although there may be alveolar hæmorrhage in parts of either the middle or central zone. Under a higher power the alveoli of the circumference are seen to be completely filled with blood corpuscles, and there is scarcely an appearance of fibrin, or none at all; in the middle zone the alveolar contents consist for the most part of catarrhal epithelium with some white and a few red blood corpuscles, and a little fibrin or none at all, whilst the dense central mass of the cells consist of catarrhal epithelium and leucocytes with some granular *débris*. Thus the pneumonic area has the appearance of very extreme lobular or catarrhal pneumonia. The walls of the bronchial tubes, as well as of the large veins, show great engorgement and there are hæmorrhages into the vein walls. Blood and catarrhal cells may be seen in the finer bronchi, but the bronchial mucous membrane is scarcely altered, there being at most a little cellular proliferation. There are the appearances of acute pleurisy over those pneumonic areas which project upon the surface of the lung, with hæmorrhages beneath the pleura. The bronchial glands show engorgement of blood vessels, some hæmorrhage into the gland tissue and distended lymphatic vessels; but in some cases these conditions are only slightly marked and the glands looked nearly normal."

Albrecht and Ghon[3] in their report upon bubonic plague describe three cases of primary plague pneumonia. From the study of these cases, they concluded that the primary plague pneumonia represents a typical lobular pneumonia or bronchopneumonia which involves either a single lobe, or several lobes (in some cases bilateral), or an entire lung.

They further state: On the cut section one can, as a rule, still make out the confluence of the separate infiltrated lobules, since their boundaries can still be partially distinguished. The posterior portions of the lung tissue are most often attacked by the inflammation. It has already been remarked that the primary as well as the secondary plague pneumonias both have a very characteristic and, in this sense, specific appearance, since the finer anatomic picture resembles that of no other inflammatory disease of the lungs with which we are acquainted. Even in the pleura the peculiar conformation and color of such foci is striking. The pleura is either only slightly cloudy, injected to a bright color, and dotted with numerous small hæmorrhages, or it is covered with or penetrated by a yellowish, fibrinous, exudative membrane. This fresh pleurisy is, as in every pneumonia, a regular part of the inflammatory process.

[3] Ueber die Beulenpest in Bombay im Jahre 1897. K. Akad. d. Wiss. (1898), II. B., 429.

One sees beneath the pleura fine yellow and red dots and spots caused by numerous yellow nodules or bands upon a bright red background. The picture resembles exactly the one encountered in many lymph glands which contain numerous bacilli. Microscopical sections show that this picture is due above all to the fact that the distended alveoli are filled with enormous masses of bacilli or with blood and with these almost alone; the cut section shows a similar, generally mixed yellow-red color, appears as though most finely shagreened but never really granular, and yields an abundant, somewhat viscid juice.

The changes in the septa of the alveoli are very characteristic and indeed as well in the primary as in the secondary pneumonias. The septa are very strikingly broadened and changed into a glistening frame-work which is sometimes coarser, sometimes more thread-like, and stains well with eosin. Between the bands of this frame-work are enclosed, in scant numbers, cells or cell nuclei or red blood-cells: the thick cords are lined by small and most minute granules standing close together and by cell nuclei, irregular, pear-like, or spermatozoon-like in shape.

The complete agreement with the changes in the vessels of primary buboes and with the multiple foci in the spleen is obvious at the first glance. The large numbers of plague bacilli in the alveoli lead also in this case to that peculiar coagulation of the tissue-fluid and the cellular elements of the septa of the alveoli and the vessel-walls; at the same time coagulation takes place in the blood within the vessels. The finer or coarser bands, which thus arise, do not give the fibrin-staining reaction of Weigert.

In addition to these changes in the septa of the alveoli, which are to be regarded as due to necrosis, there appears at places a complete disappearance of the septa, so that only spur-like remnants of the same are left. The bronchioles are also markedly dilated and filled with enormous masses of bacilli, which occur also in just as large numbers in the large bronchi and are of course expectorated. However, fibrinous exudation is everywhere almost completely lacking, only a scant fibrin network being found here and there. The amazingly large number of plague bacilli is also evident from cover-slip preparations and from cultures from the pneumonic lungs. In primary plague pneumonias, we found plague bacilli twice in pure culture and once mixed with a small number of diplococci (*Diplococcus pneumoniæ*), in the metastatic foci only once in pure culture and three times with diplococci, which were also in these cases not numerous. We, of course, found a mixture of different bacteria in the pneumonic foci due to aspiration.

With regard to the frequency of the occurrence of pneumonic foci due to the plague bacillus, among 44 acute plague cases we found such foci nine times; viz., 3 primary plague pneumonias, 4 metastatic or secondary plague pneumonias, and 2 aspiration pneumonias in which we could demonstrate numerous plague bacilli. The metastatic plague foci in the lungs hence occur rather seldom if one considers that undoubtedly the circulation is flooded with plague bacilli, either only for a short time or frequently several days before death.

The Anglo-Indian Plague Commission[4] report "that the lesions in pri-

[4] Report of the Indian Plague Commission (1901), 5, 435.

mary pneumonic plague, when contrasted with those occurring in *Pestis major*, are less intense in the other organs, with the exception of the lungs.

"The lymphatic glands are only slightly affected, and external buboes having the specific characteristics seen in *Pestis major* are seldom, if ever, encountered. Congestion and enlargement of organs and even hæmorrhage in mucous and serous membranes may be present, but they do not assume the proportions attained in *Pestis major*. On the other hand, the lungs are conspicuously affected. The whole substance is engorged, the large as well as the small blood vessels being distended; and hæmorrhagic zones are seen scattered throughout the lungs, filling the alveoli and often breaking down their walls. Within the hæmorrhagic zones are areas in which the alveoli are completely filled with leucocytes, epithelial cells, and granular débris, constituting, with the surrounding zones of hæmorrhage, blood-congested areas of catarrhal pneumonia. In these areas, as well as in the fluid matter contained in the trachea and bronchi, plague bacilli are abundantly present. Greyish necrotic patches have also been found containing large numbers of plague bacilli. The bronchi are engorged with blood, and catarrhal cells are found in their terminations. Over affected areas at the surface of the lungs, the pleura may be acutely inflamed. In most cases, the bronchial glands were congested, and there was a little hæmorrhage into the gland substance; but in some cases, their appearance was normal.

"While, however, a catarrhal inflammation of lobular distribution has most frequently been regarded as the characteristic type of primary plague pneumonia, several observers have denied its existence, and have asserted that croupous (lobar) pneumonia is the form that most frequently occurs. Major Evans, I. M. S., and Captain Elphick considered that all cases of typical plague pneumonia come under the latter category, and Major Jones expresses the opinion that "lobar pneumonia is common." Major Evans stated that the pneumonia is distributed in small detached patches, constituting lobular areas, only when the inflammation has not advanced far; but that it is lobar to the extent of involving a whole lobe or the greater part of a lobe when the lung inflammation has advanced further. Captain Elphick, I. M. S., described several autopsies in which individual lobes or even an entire lung was consolidated, and he stated that "every case of pneumonic plague examined showed lobar condensation." It may further be stated that in many cases only slight changes were found in the bronchi. It is therefore possible that the pneumonia is lobular in patients who have died at an early stage of the disease, and lobar in those who have survived to a later period; or, otherwise, that lobar pneumonia occurs when the toxin is most virulent and most widely distributed throughout the lung, and lobular pneumonia when it is less virulent and less widely diffused.

"* * * [The] microscopic examination has mainly shown general dilatation and engorgement of the veins and smaller blood vessels and numerous capillary and larger hæmorrhages in almost every structure and organ of the body."

Dürck[5] and Herzog[6] have reported at some length upon the general

[5] Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie (1904–5), Supp. 6–7.

[6] *Pub. Bur. Govt. Labs.* (1904), No. 23, 9.

pathological anatomy of bubonic plague, but neither of these observers had any special opportunity for the study of the primary pneumonic form.

During the Japanese epidemic of 1899, reported by Kitasato, Takaki, Shiga, and Moriya,[7] 13 cases of primary pneumonic plague occurred, but no necropsies were made. Sata[8] has recently reported upon the pathological anatomy of a single case of pneumonic plague in which, however, the lesions were complicated by the presence of other bacteria, besides the plague bacillus.

On account of this absence in the literature of observations upon the pathological anatomy of *epidemic* pneumonic plague, the results of the study of this subject made by us during the Manchurian epidemic will be reported in detail.

Our observations upon the human pathology of this disease are based upon the study of 25 complete necropsies performed at the plague hospital at Mukden. All of the material was fresh, many of the necropsies having been performed immediately or within a few hours after death.

The histological examination of the tissues has been performed in Manila since our return. Zenker's fixation with alcohol preservation of sections was employed in all cases, while primary alcohol fixation of sections from some cases was also used in order to facilitate bacterial investigation. It was necessary in a few cases to resort to the study of the material which had been preserved in Kaiserling's fluid. All tissues were sectioned in paraffin and stained with Böhmer's hæmotoxylin and eosin; in addition Weigert's stain for fibrin, Unna's methylene blue and eosin, the Gram-Weigert stain, and Mallory's iron hæmotoxylin were used as differential stains in nearly all of the cases.

It has been deemed advisable to consider the gross and histological lesions under the description of each organ.

External appearance.—The bodies with one exception were those of robust, well-nourished individuals and showed no emaciation. Two of the subjects showed evidences of old syphilitic infection and one had early carcinoma. None of them was tuberculous. The superficial lymphatic glands were not enlarged, and carbuncles, vesicles of the skin, or buboes were not observed. Small punctiform hæmorrhages in the skin about the bends of the elbows and over the chest occurred in two cases and were apparently the result of needling.[9] *Livor mortis* was not as a

[7] Bericht über die Pestepidemie in Kobe und Osaka. Tokio (1900).

[8] Quoted by N. Masuyama, *Ztschr. f. klin. Med.* (1910), 70, 498.

[9] A method of treatment of the disease employed by certain Chinese physicians of the old school.

rule very extensive or marked owing to the freshness of the cases; in three it was extensive over the shoulders and the dependent parts and was of a dark, brownish-red color. *Rigor mortis* in some of the cases had not developed. In others it was very strong. In degree it was, perhaps, when compared with the rigor mortis occurring in other acute infectious diseases, only surpassed by that seen in Asiatic cholera. The muscles were usually of a bright-red color; hæmorrhages were not observed in the abdominal ones, but small extravasations of blood were on one occasion noted in the thoracic muscles in stripping them from the thoracic wall and ribs.

Pericardial cavity, heart and blood vessels.—In the anterior mediastinum in the tissues surrounding the thymus gland usually much œdema and frequently extensive hæmorrhages occurred. On the visceral surface of the serous layer of the pericardium, petechiæ often occurred and larger punctiform hæmorrhages were sometimes encountered. On the epicardium varying numbers of petechiæ were observed in most of the cases. The right chambers of the heart were usually distended with blood and in a number of cases showed acute dilatation and thinning of the wall, particularly of the right auricle. The muscle was in some instances soft but usually of a fairly firm consistency. Cloudy swelling was almost invariably noted; early fatty degeneration was observed in a few instances. The bronchial veins sometimes showed hæmorrhages in the intima, and numerous extravasations of blood occurred about the vessels posterior to the peritoneum and in the region of the kidneys, omentum, and mesentery. In the omentum, hæmorrhages were particularly observed in the fat around the larger veins.

Histological examination of the heart.—The changes in the heart consist chiefly in a cloudy swelling of the muscle fibers with some œdema between the fibers in some cases. The fibers are, however, usually closely packed. In some cases slight hæmorrhage was present beneath the epicardium. In some there was infiltration of the epicardial fat into the muscle, and in one or two cases slight infiltration of this fat between the muscle bundles.

Fatty degeneration of the fibers to any marked degree was not noted, but lesser degrees could not be determined on account of the fact that the method of preservation of the tissues did not permit of the satisfactory use of selective stains for fat.

Fragmentation of the fibers was a constant feature in all of the cases examined. No exudation from the vessels was encountered, although the vessels were constantly engorged.

Pleuræ.—The parietal pleura covering the thoracic wall, diaphragm, and pericardium in many instances showed numerous ecchymoses in the region of the infected lung, and very often delicate, fibrinous adhesions were observed between the parietal and visceral pleuræ. In some instances many of the hæmorrhages were punctiform in character, but in others they were confluent and formed diffuse, larger, dark-red patches.

Lungs.—Numerous ecchymoses beneath the pleura were almost always encountered, though they varied greatly in extent and in number. The appearance of the lungs varied according to the stage of the disease at the time of death. Generally the lungs were dark red, voluminous, very rich in blood, and very œdematous. From a careful study of the lesions of the lungs we can conclude that plague pneumonia is an anatomically defined type of disease different from other varieties of pneumonia.

Fresh, fibrinous pleurisy was observed in every case, extending over the more marked areas of pneumonia. (See Plates IX and X.) In some instances the delicate membrane was reddish and slightly roughened; in other cases, grayish or grayish white or yellowish, and could be easily peeled from the surface of the lung. Rarely a gelatinous, œdematous exudate was present. In two instances, the pleural cavity contained between 100 and 200 cubic centimeters of a serous hæmorrhagic exudate in which large numbers of plague bacilli were present.

Some portion of the lung showed either inflammatory engorgement or pneumonic infiltration. The seat of the pneumonia varied greatly. The upper lobes appeared to be quite as frequently involved as the lower.

On section of the lung, the tissues adjacent to the areas showing pneumonic involvement usually revealed very marked congestion and œdema. Such areas were firmer than the normal lung and tore more easily. On pressure, a reddish, serous fluid exuded from the cut surface in great abundance. Sometimes in these areas the œdema was so great as to give to the lung tissue a jelly-like consistency.

While in croupous pneumonia the first stage of inflammatory engorgement as an independent condition is almost never, or certainly very rarely, encountered, as the patient does not succumb within twenty-four to thirty-six hours from the origin of the disease, in our cases of plague infection of the lung the early stages of inflammatory engorgement were frequently met with and often death occurred before the lesion had progressed further, so that indeed in some instances no true pneumonia was yet

visible. In the stage of inflammatory engorgement, the plague-infected lung was voluminous, firmer, and less crepitant than the normal lung, and either dark red or reddish blue in color. Upon section, the tissues were found to be very œdematous, and a thin, reddish serum escaped in great abundance.

The pneumonic areas, when present, were either lobular or lobar in type. (See Plates VIII, IX, and X.)

In the lobular type, one or several nodules varying from about three to five centimeters in diameter might be found in the lobe. They were rather sharply circumscribed from the surrounding lung tissue by a more or less marked ring of engorged pulmonary tissue and were either circular in outline or wedge-shaped. In one instance, on section of the lung, six areas in the stage of early gray hepatization were observed in one lobe situated near the base. Three of these measured 2, 1.5, and 1 centimeters in diameter and were all arranged along the same bronchus. About one-half centimeter from the tip of the base of the lobe on the same bronchus were three more hepatized patches measuring 5 or 6 millimeters in diameter. The mucous membrane of the bronchi was dark red in color. The other lobe and the right lung in this case showed only congestion and œdema. Sometimes these pneumonic areas are situated on the surface of the lung, when they project distinctly from the surrounding lung tissue, and the pleura over them is roughened and shows other signs of early inflammation. Such areas of broncho-pneumonia as just described no longer contained air. On cut section the surface was rather dry, grayish red in color, and finely granular in appearance. No muco-purulent secretion was visible in the smaller bronchi, and, on pressure, mucus plugs were not expressed from the bronchi as is frequently the case in bronchial pneumonia due to infection with other microörganisms. The granular appearance of these areas is not identical with that observed in croupous pneumonia. The granules are irregular and coarser, and, on scraping the surface of these areas with the knife, no fibrin plugs are observed to escape from the air cells, but the juice so expressed is grayish white, slightly sticky, and evidently highly albuminous. The alveolar septa sometimes appear broader than normal. The mucous membrane of the bronchi leading to such areas was bright red in color. Occasionally several pneumonic areas might be arranged along one bronchus somewhat as the flowers of the hydrangea are placed on the stalk of the plant.

While a careful study of the human lungs, as well as of those

of numerous monkeys and guinea pigs, in which pneumonic plague had been produced by inhalation of plague bacilli, has shown that the pneumonia is primarily bronchial in origin and of the lobular type,[10] nevertheless, very early lobar involvement was very much more frequently encountered in the human cases at necropsy.

In the lobar type, the whole lobe or a portion of it showed either only early inflammatory engorgement or a portion of the lobe early red, with beginning gray hepatization. Plate X illustrates a section of the lung in the stage of gray hepatization. We have not seen an entire lobe in the stage of gray hepatization such as is frequently observed in ordinary croupous pneumonia due to the *Diplococcus pneumoniæ,* as the patients with primary pneumonic plague evidently die before this stage is ever reached. Large areas of red hepatization are also rare. However, a smaller area of gray hepatization, adjoining one of red hepatization and this in turn shading into an area showing only engorgement, was sometimes observed. Very frequently death evidently occurred before any apparent hepatization had taken place and only a portion of a lobe showed engorgement. Even in these instances, however, enormous numbers of plague bacilli were present in the lung tissue. In but comparatively few of the cases had the stage of gray hepatization been reached, and evidences of resolution were not encountered.

Rarely one lung was practically normal in appearance. However, in these cases in which one lung only showed pneumonic infiltration, the other usually showed congestion and œdema. In other instances single lobes, or all the lobes of one lung, might show early inflammatory engorgement. In some of the cases both types of pneumonia were encountered. In one lung the lobular areas might be observed while in the other the appearance of a lobar type was present. Or in the same lung a smaller area of gray or red hepatization might be encountered while the remainder or some part of the lobe showed pneumonic infiltration in the stage of engorgement. The differentiation of the so-called lobar type of pneumonic plague from other varieties of pneumonia may not be as easily accomplished as in the case of the lobular type. The cut surface of the pneumonic lung, however, in the stage of early gray or red hepatization, usually seems less granular; the condition of the bronchi and

[10] See also IV, p. 173 of this report.

the character of the exudate also renders assistance in arriving at a diagnosis. Also the absence or scarcity of fibrin in the alveolar exudate in pneumonic plague is in striking contrast to the condition observed in croupous pneumonia. The alveoli are frequently filled with plague bacilli. The gross lesions of the human lung are illustrated in Plates VIII, IX, and X.

Histological examination.—No cases in the series were found in which the lungs exhibited no alteration and no part of any lung examined was free from at least some pathological changes. In the earlier cases (1) the presence of bacteria, (2) the changes in the blood content of the vessels, and (3) the changes in the bronchi and bronchioles constitute the prominent features.

(1) The bacteria occur in enormous numbers and frequently appear as dense blue clouds in thin sections stained by hæmotoxylin and eosin and examined even with a low magnification. In general, this method of examination gives the most satisfactory evidence of the distribution of the bacteria, and the higher magnification with the oil-immersion objective is only necessary when the bacteria must be searched for.

In the earliest cases the bacteria are especially numerous about the bronchioles, in the peribronchial lymph spaces, and adjoining alveoli. Here they frequently form masses completely encircling the bronchioles, and are also present in large numbers in the interlobular septa and beneath the pleura. In the lungs which are the seat of anthracotic deposits, wherever anthracotic pigmentation is found, there are enormous masses of the bacteria, and the distribution of the bacilli about the bronchioles, in the interlobular septa, and beneath the pleura is recognized as the usual distribution of anthracotic pigments. In these earlier cases there are but few bacilli in the blood contained within the vessels and also few in the neighborhood of the vessels. The alveoli in this stage also contain bacilli when there is no recognizable change in their lining epithelium.

(2) The blood vessels in the interalveolar and interlobular septa are widely distended with blood and occasionally small hæmorrhages have taken place from these vessels into the alveoli. Very few, if any, bacteria can be found in the blood vessels in the earlier cases.

(3) The smaller bronchi and bronchioles are in the condition of catarrhal inflammation. The lining cells are swollen and frequently desquamated, and there are some few red blood-cells and leucocytes among the lining cells and in the lumina of the bronchioles. Mucus in the form of granular flakes is also con-

tained in the bronchi, as well as very large numbers of bacilli. The distribution of the bacilli about the bronchioles has already been described.

The condition of the lung alveoli in the early stage of the disease varies in different areas. The septa have already been referred to as engorged and the alveoli about the bronchi as filled with bacilli. The alveolar epithelium is swollen and frequently desquamated in the form of large cells often containing abundant pigment. The contents of the alveoli consist of a few of these desquamated cells, serum, bacilli, and an occasional leucocyte or red blood-cell.

The pleura may be the seat of a slight fibrinous exudate, and small hæmorrhages from the vessels may have occurred.

As the process passes on to the later stages of the disease, the added features are those of exudation and more extensive hæmorrhages.

The exudation consists in the passage into the alveoli of red blood-cells and leucocytes, the stage where the red cells predominate probably preceding that of the mixed red and white exudate, so that a red and a white stage can be differentiated. But in no case does the latter condition proceed so far as in the ordinary pneumonia due to *Diplococcus pneumoniæ* and the leucocytes are never so abundant. That is to say, there is not a pure white stage, as a good proportion of red cells is always present and the red appearance of the lung is also more prominent on account of the frequency of hæmorrhages which may be small or involve a large portion of the lung. The leucocytes are chiefly of the polymorphonuclear neutrophile type, although some mononuclear cells are present. Few, if any, eosinophiles are present in the exudate. Fragmentation of the nuclei of the leucocytes is not infrequent. A peculiarity of the leucocytes when seen under high magnification is that they are very frequently surrounded by a clear zone. The possibility of specific staining for fat was precluded by the method of preservation of the tissues. Phagocytosis was seldom observed.

The presence of fibrin in the exudate is an unusual occurrence, and in those cases where careful staining showed it to be present, the amount was in no way comparable to the amount found in ordinary pneumococcus pneumonia and when present was only at the immediate periphery of the alveoli in the neighborhood of the vessels.

In the later stages of the disease, the bacteria are very numerous and here, in contrast to what was described in the

earlier cases, they are in greatest number about the medium-sized vessels and can also be seen in the blood contained within the vessels. They are also present in large numbers immediately beneath the pleura and in the fibrinous exudate which always covers the pleura over a consolidated area. Where sections were taken through the interlobar septa, the presence of a leucocytic exudate can be seen in the groove between the pleural surfaces. (See Plates XIII to XVII illustrating histological changes.)

The bronchi.—(See Plate VIII.) The mucous membrane of the bronchi was in every case of a bright-red color which varied in the different instances only in intensity. Often in the bronchi near the bifurcation, the deeper red portions appeared as closely placed, parallel, longitudinal stripes in the bronchial wall. The bronchi contained a red, frothy, bloody serous fluid or more rarely a reddish mucus exudate. The yellow or whitish muco-purulent exudate frequently seen in cases of catarrhal bronchitis or in other forms of pneumonia was never observed, nor were fibrinous plugs encountered. In one case in which the lesions in the lung as well as the changes in the other organs were not very far advanced, the diagnosis of primary lung infection with plague bacilli was suggested from this condition in the bronchi and the character of the exudate. This diagnosis was confirmed by bacteriological examination.

Pharynx, larynx, and trachea.—(See Plate XI.) The anterior surface of the tongue was usually coated with a brown, buff, or pinkish-gray layer. The papillæ at the base of the tongue and the lymphoid follicles here and on the posterior wall of the pharynx were swollen. The tonsils were in every instance of about normal size or slightly swollen. On cut section the surface was usually reddish or reddish gray and in a few instances bluish in color. In only one case were there small areas of necrosis and hæmorrhages in the tonsil. The mucous membrane of the mouth and throat over the base of the tongue, uvula, tonsils, and adjacent structures was in all cases somewhat swollen and generally appeared of a more or less congested, dark-red color or in a few instances of a reddish-purple hue. From the pharynx to the larynx the mucous membrane as a rule gradually assumed a brighter red color. Over the epiglottis, vocal cords, cartilages, and whole larynx it was generally markedly hyperæmic and red in color, but in a few instances of a whitish-pink or pink hue. When the color was not bright red the injected vessels could be seen more plainly upon the pink background just described. The

mucous membrane just above the vocal cords in a few cases was not so markedly hyperæmic, but below them, in every instance, it appeared of a bright-red color. Throughout the entire length of the trachea the hyperæmia was always more marked below the vocal cords, whatever the condition above them was. This hyperæmic condition continued in every instance throughout the trachea and bronchi, though it was sometimes less marked in the smaller tubes which led to normal lobes of the lung. In no case was there noticeable œdema of the glottis. In a single instance, in which the epiglottis and surrounding structures showed no injection, the hyperæmia and injection of the vessels did not begin until about 3 centimeters below the cords. In a few cases there were small hæmorrhages measuring several millimeters in diameter in the mucous membrane of the trachea. Over the surface of the trachea a small quantity of blood-stained serous exudate, sometimes frothy in character, was present. There was always much œdema of the tissues surrounding the lower portion of the trachea, and the lymphatic glands in this region were swollen to a greater or less degree. In one instance two of them measured as much as 3 centimeters long by 1½ wide. (See Plate XI.) On cut section they were usually red or bluish in color and showed many hæmorrhages. The glands at the bifurcation of the trachea were always greatly swollen, generally anthracotic, and in all instances were of an almost black-red color from resulting hæmorrhages in the glandular substance.

Histological examination of the tonsils.—The morphological changes in the tonsils are not prominent. The majority of the tonsils examined did show very marked congestion and in some œdema was present. Small hæmorrhages were noted in a few cases. The crypts frequently contained mucus in which very moderate numbers of pest bacilli were present. The epithelium and follicles for the most part showed no change. Some of the tonsils were the seat of old inflammatory changes which were unrelated to the plague infection. One case showed very active proliferation of the lymphoid follicles. This case showed very few plague bacilli in the tonsil itself but the greatest numbers observed were present in the blood contained within the vessels of the tonsil. The majority showed very few bacilli at any place in the tonsil.

One showed very large numbers of pest bacilli in the crypts and scattered throughout the parenchyma, without any definite distribution, except that the follicles were practically free.

Another case showed a remarkable apparent leucocytosis judging from the number of leucocytes in the blood within the vessels.

The remarkable feature about the tonsils as a whole was their comparative freedom from anatomical changes. Congestion, sometimes œdema, sometimes hæmorrhages, occasionally slight lymphoid activity constituted the main features. (See Plate XVIII.) The bacilli were present in small numbers with one exception, and never bore any comparison to the number in the lungs.

The *œsophagus* was in every instance normal, no hyperæmia of the mucous membrane being observed.

Stomach and intestines.—The mucosa of the stomach was frequently somewhat swollen and showed numerous, small ecchymoses. In a few instances small erosions were present. In a few cases the peritoneal surface of the small intestine was reddened and in a few others hæmorrhages were observed on the peritoneal surface of both the large and small intestines. These hæmorrhages were of two types—the first dark, almost black in color, measuring from ½ to 1 centimeter in diameter and suggesting in their appearance *œsophagostomum* infection; and the second appearing as fine, bright-red, linear hæmorrhages. The mucous membrane in these cases was reddened and showed a catarrhal condition, with a pinkish mucous layer covering the surface, beneath which were innumerable, bright-red, pin-point-sized areas.

Lymphatic glands.—The bronchial glands near the bifurcation of the trachea always showed more advanced changes than any of the other lymphatics; they were always swollen, rich in blood, and frequently almost black in color from resulting hæmorrhages. The lymphatics along the lower portion of the trachea were also usually swollen and sometimes contained hæmorrhages. In a few cases the mesenteric lymphatics showed simple inflammatory swelling, but in the majority of the cases they were normal. The largest ones measured about 2½ centimeters in diameter. On section the surface was pink or of a grayish-red or dark-red color, but showed no hæmorrhages or necrotic areas, although in one case in the veins about them the blood had frequently escaped from the vessel walls. In one instance the glands showed small hæmorrhages. In the other lymphatics of the body, no special changes were observed.

Spleen.—The spleen was distinctly enlarged in 56 per cent of the cases. In bubonic plague the percentage with distinct anatomical enlargement of the spleen is considerably higher, but the spleen is by no means always enlarged in bubonic plague, as has frequently been stated. In the present cases it was usually

firmer than the typical, infectious splenic tumor, a condition depending upon the increase of red pulp and blood in the organ. On cut section the red pulp was greatly increased and the follicles were usually either small or invisible. In two cases the follicles appeared as white, pin-point areas inclosed by dark-red, pin-head-sized areas, which in turn were surrounded by the lighter red splenic parenchyma. Small, punctiform hæmorrhages occurred beneath the capsule in one instance and scattered through the substance of the spleen in others. The trabeculæ were prominent in only one instance in which the age of the subject was apparently between 50 and 60 years. In one case a reddish-white infarct 4 millimeters in its greatest width was encountered.

Histological examination of the spleen.—The chief lesion in the spleen is found in a marked congestion and hyperplasia of the pulp tissue with small hæmorrhages occurring beneath the capsule and throughout the pulp in a very large percentage of cases. The degree of the congestion varies. It is frequently especially marked at the immediate periphery of the lymphoid follicles. These lymphoid follicles are for the most part both relatively and absolutely small and seldom show any signs of proliferation. The bacteria in the follicles are very scarce. Some cases show fairly large areas of necrosis of the pulp in the areas of the hæmorrhage. The swelling of the endothelial cells of the lymph sinuses is by no means an infrequent occurrence, although evidence of their multiplication is not seen.

Kidneys.—Punctiform hæmorrhages measuring several millimeters in diameter were frequently observed in the capsules of the kidneys, which usually stripped easily from the surfaces of the organs. The kidneys were usually rich in blood, and in a number of instances after the removal of the capsule a red, granite-like appearance was observed due to the deeply injected vessels in contrast to the yellowish parenchyma of the organ. The stellate veins were usually deeply injected. Small hæmorrhages about the surface vessels of the kidneys were unusual, but were observed in three cases. On cut section either parenchymatous or early fatty changes were almost invariably evident. The glomeruli were frequently swollen and often appeared as fine, reddish, pin-point-sized areas. Petechiæ were frequently seen in the pelves and upper portion of the ureters.

Histological examination of the kidneys.—Extreme degeneration of the parenchyma of the kidney is a constant feature. The degeneration is in the form of an extreme cloudy swelling and

granular degeneration which is especially marked in the cells of the convoluted tubules but also involves the epithelium covering the glomerular tufts. It is not infrequent for this degeneration to have proceeded so far as to constitute a necrosis. The most striking changes in the glomeruli consist in the degeneration of the epithelium of the tufts which has already been referred to. Intense congestion of the glomerular vessels is practically always present and, in a few cases, a small amount of fluid exudate into Bowman's capsule is found. In no case was the leucocytic exudate into Bowman's capsule excessive. No evidence of proliferation of the cells lining Bowman's capsule was seen. In two cases of the series, fibrin thrombi as described by Herzog [11] constituted a very prominent feature in the sections of the glomeruli. Œdema of the kidney is evident in the sections, and very numerous, small hæmorrhages which were chiefly situated beneath the capsule were often seen. Some of the cases were the seat of an old chronic interstitial process on which the changes above indicated had been superimposed. The finding of casts in the tubules was rare, but the presence of a coagulated fluid exudate or transudate was not at all infrequent. Sections of the mucosa of the pelvis of the kidney were not obtained.

Liver.—The liver also invariably showed either cloudy swelling or early fatty degeneration. A few small hæmorrhages about 2 to 3 millimeters in diameter situated beneath the capsule were observed in two cases, in one of which the hæmorrhages were also linear in character, measuring as much as one-half centimeter in length and about 1 or 2 millimeters in width. Small metastatic abscesses such as are occasionally observed in bubonic plague were not encountered in either the liver or the kidney.

Histological examination of the liver.—The sections show practically always an extensive congestion, and cloudy swelling is a constant feature. While no large areas of necrosis are found, many of the specimens show small areas where one or two or three cells at one place have undergone necrosis. Extensive fatty changes were not noted, although selective stains for fat were impossible. Hæmorrhages beneath the capsule occurred, but hæmorrhages in the substance of the organ were scarcely ever noted and were never of any extent. In some places the liver cells were considerably compressed by the engorged vessels. In some of the cases rather extensive bile-stasis was manifest by the abundance of biliary pigment contained within the liver cells.

[11] *Pub. Bur. Govt. Labs.* (1904), No. 23, 9.

The *adrenals* sometimes showed congestion. No pathological changes were observed in the *pancreas, thyroid,* or *thymus gland,* though the tissues about the latter were usually markedly œdematous. In the *uterus,* hæmorrhages were frequently observed; in the other *sexual organs* or *bladder,* no special changes were noted. The central nervous system in the instances we had occasion to examine showed no gross anatomical changes with the exception of hyperæmia and sometimes œdema of the meninges.

Bacteriology.—Microscopical preparations and cultures were made from the organs in every case. In each instance the pest bacillus was present in the blood. The bacilli were always much more numerous in the lungs and in the bronchial lymphatic glands at the bifurcation of the trachea than in any of the other organs or in the blood. In the lungs they were found frequently packed together in great masses and were usually present in pure culture. In but two instances were diplococci encountered in small numbers. The plague bacilli were always more numerous in the spleen than in the blood. In no other disease are such enormous masses of bacteria encountered in the lung. In the tonsil, with but one exception, the number of plague bacilli found was small, usually not more than was observed in the blood. Staphylococci and streptococci and even Gram-positive bacilli were seen in preparations from the tonsils in several cases. In scrapings from the mucosa of the bronchi, plague bacilli were often abundant, but not always so.

Conclusions.—From the study of the human lesions and those produced experimentally in animals, [12] it would appear that epidemic plague pneumonia results from inhalation, the primary point of infection being the bronchi. Along the bronchioles the infection extends by continuity directly into the infundibulum and air cells, or by contiguity through the walls of the bronchioles to the contiguous tissue of the lung, and gives rise to a consecutive peribronchial inflammation in the tissues immediately surrounding the bronchioles. From these areas the infection rapidly spreads to the adjacent pulmonary tissue and visceral pleura. The bacilli rapidly multiply and produce at first pneumonic changes of the lobular type, and shortly afterwards from the fusion of several rapidly spreading areas more general lobar involvement of the lung tissue. The blood becomes quickly infected, and a true bacteræmia results in every case. Secondary pathological changes occur, particularly in the spleen, bronchial glands, heart, blood vessels, kidneys, and liver. The

[12] See IV, p. 173 of this report.

fact that the bronchial glands at the bifurcation of the trachea are always much more severely affected than any of the other lymphatic glands argues against the theory that epidemic pneumonic plague is primarily a septicæmic disease, and that the lungs are infected secondarily from the blood. Moreover, in the earliest stage of the disease, the blood may be free from plague bacilli.[13] The conditions observed in the trachea and bronchi in epidemic pneumonic plague, together with the character of the pulmonary exudate, is pathognomonic of this condition. From the appearance of the mucous membranes of the throat, larynx, and trachea, a diagnosis of pneumonic plague may sometimes be suggested. The tonsils may become secondarily infected in pneumonic plague, just as other lymphatic glands—for example, the bronchial ones—become so infected. However, in pneumonic plague, death occurs before any very marked macroscopic changes occur in the tonsils. There is no doubt also that the tonsils may become primarily infected in epidemics of pneumonic plague, just as has occurred in sporadic cases during epidemics of bubonic plague. This, however, is not the common channel of primary infection, and in such cases involvement of the lymphatic glands of the neck occurs early in the course of the disease. The fact that the œsophagus was found to be normal in every case examined and that the intestines showed only slight lesions constitutes another argument against the idea of the occurrence of primary intestinal plague infection in man, since in many of the pneumonic cases plague bacilli must have been repeatedly swallowed in the bronchial secretions and in the saliva.

[13] See p. 202 of this report.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

VIII. SUSCEPTIBILITY OF ANIMALS TO PNEUMONIC PLAGUE.

By Richard P. Strong and Oscar Teague.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

Many cultures isolated by us during the Manchurian epidemic from the lungs at necropsy have demonstrated the same pathogenicity for animals as virulent bubonic strains of the plague bacillus. The pneumonic cultures have shown themselves to be particularly pathogenic for mice, rats, guinea pigs, and monkeys (*Cynomolgus philippinensis* Geoff.), these animals dying from the same doses and succumbing within the same period after inoculation as has been observed after infection with bubonic strains. Some evidence was introduced at the Conference held at Mukden that suggested that when the pneumonic strains were injected subcutaneously into the guinea pigs, usually septicæmia was produced very quickly and typical buboes were not obtained. Moreover, it was affirmed that the guinea pigs died within a shorter time after inoculation than in the cases in which bubonic strains were employed. However, in these instances it appears that the results were dependent upon the size of the dose inoculated, as much as one-half of an agar-culture having been employed in the infection. We showed in Mukden that the cutaneous or subcutaneous inoculation of very small doses of the pneumonic strain into guinea pigs gave rise to the typical lesions observed in these animals after inoculation with virulent bubonic strains, particularly to typical buboes, to miliary abscesses in the spleen, and to secondary septicæmia with hæmorrhages in the different organs. Our statements at the Conference in this respect have since been borne out by extensive experiments performed by us in Manila and it has been conclusively shown, in addition, that when guinea pigs are inoculated with the pneumonic cultures by inhalation, they develop primary infection of the glands of the

neck, with secondary septicæmia and occasionally secondary pneumonia or, in some cases, primary pneumonia with secondary septicæmia. Very rarely does the spleen show miliary abscesses in such cases, the animals dying before such lesions develop.

In *monkeys* (*Cynomolgus philippinensis* Geoff.), also, the cutaneous or subcutaneous injection of the pneumonic cultures causes typical bubonic infection. Monkeys infected by the same cultures by inhalation develop primary pneumonic plague with secondary septicæmia and without involvement of the glands of the neck.

Tarbagans.—There has been considerable evidence brought forward during the past in support of the view that plague has existed in epizoötic form among a species of marmot, the tarbagan (*Arctomys bobac* Schreb.).[1] (See Plate VI.) However, there has been no direct bacteriological proof of this fact, and we have known nothing definite before in regard to the susceptibility of this animal to plague infection, though, according to Preble, *loc. cit.*, Tchaoushow showed these animals were susceptible to plague infection. Our own experiments on tarbagans were carried out in Mukden where, by the kindness of the Hon. Alfred Sze, imperial commissioner to the Plague Conference, we were supplied with these animals for experimental purposes. From our experiments we were able to show for the first time that cutaneous or subcutaneous infection of the tarbagan with virulent cultures of the pneumonic strain gives rise in these animals either to an acute bubonic or to subacute and chronic forms of plague infection. In some instances we have shown by comparative experiments that the tarbagan seems as equally susceptible to cutaneous or subcutaneous infection as the guinea pig, these animals dying in about the same time (two and one-half to five days after infection) and from the same doses of the organism. In these instances there are hæmorrhages about the point of inoculation, typical buboes, and swelling of the spleen. In other instances, after infection with the same organism and with the same doses, the tarbagans may suffer from subacute and chronic forms of plague infection. In three of these animals killed by chloroform from ten days to two weeks after infection,

[1] For evidence of this fact, see Report of the International Plague Conference *under* Tarbagans. *Also,* The Tarbagan and Plague. By Paul Preble. Reprint from the United States Public Health Reports (1912), No. 68. This latter article entirely omits our own experiments on tarbagans while giving other observations on these animals reported at the International Plague Conference.

there were found at necropsy abscesses measuring several millimeters in diameter in the subcutaneous tissues or in the abdominal muscles, near the point of inoculation, and swelling of the inguinal glands, while the liver and spleen showed indurated, yellowish nodules also measuring several millimeters in diameter. (See Plate XII, fig. 2.) Plague bacilli were present in small numbers in the abscesses and in the nodules in the spleen and liver. These animals, judging from their condition at the time they were killed, would probably have lived at least several weeks longer. The lesions present were similar to those which have been described in rats which have succumbed to chronic plague infection. We have also shown that the tarbagan is also susceptible to primary pneumonic plague when infection has taken place by inhalation. Death then occurs three or four days after infection from primary pneumonia and secondary septicæmia. These experiments were performed with the species *Arctomys bobac* Schreb.[2] We also showed that another species of marmot (*Spermophilus citillus* Linn.), very common about Mukden and the vicinity, was susceptible to acute plague infection, these animals dying in from three to seven days after cutaneous or subcutaneous inoculation of small doses of the pneumonic strain and exhibiting at necropsy hæmorrhages about the point of inoculation, typical buboes, and acute, splenic tumor.[3]

DONKEYS.

Some evidence was introduced at the International Plague Conference to show that donkeys became infected with pneumonic plague during the epidemic. Dr. W. S. Yang reported to the Conference [4] the death of 10 donkeys, the first of which died with cough and expectoration of blood. In the case of one of these animals, a necropsy was performed and cultures were made from the heart, spleen, lungs, and liver. All of these cultures were said to show plague bacilli. It was also announced that Doctor Otsuki in Fushun had observed at necropsy 2 donkeys in which there was hepatization of the lungs, in one in the right and in the other in the left caudal lobe. The pathological

[2] Petrie has shown (Report of the International Plague Conference, p. 235) that *Arctomys bobac* Schreb. found in Manchuria may be infected with the flea, *Ceratophyllus silantievi* Wagner, and that this flea will bite man. Tiraboschi and D-Kolbasenko have also described fleas on the tarbagan in Russia.

[3] For the details of these experiments, see Report of the International Plague Conference, pp. 237 and 385.

[4] *Ibid.*, p. 440.

changes in the lungs were said to be similar to those seen in the cases of human infection. In regard to the question of plague infection in donkeys, the Conference resolved that the question of the occurrence of pneumonic plague in these animals should be made the subject of a special study with regard to their liability to the infection. We, accordingly, have attempted to infect donkeys experimentally with pneumonic plague by spraying suspensions of virulent strains of pneumonic-plague bacilli into a closed canvas bag, fastened about the donkey's head in such a manner that it was necessary for the animal to inhale the bacteria in breathing. The experiments were performed as follows:

Experiment 1.—September 16. Two 48-hour agar-slant-cultures of a virulent pneumonic strain of the plague bacillus (isolated a few days previously from monkey No. 5635, which died of pneumonic plague) were suspended in saline solution and two-fifths of this suspension sprayed into the sacks surrounding the head of each of 2 donkeys. One of the donkeys coughed several times while the spraying was continued. The time of the spraying occupied from three to four minutes. The remaining quantity of the suspension of the agar-cultures, used in attempting to infect the donkeys, was sprayed into a closed glass cage containing 6 guinea pigs, and 5 loops of the same suspension were rubbed over the shaved abdomen of another guinea pig. All of these guinea pigs died of plague infection, the first six either of pneumonia or septicæmia with involvement of the cervical glands and the seventh guinea pig of bubonic infection. Both of the donkeys remained entirely healthy.

Experiment 2.—September 29. One 48-hour agar-culture of a virulent pneumonic strain of *Bacillus pestis*, isolated a few days before from animal No. 5741, which died of plague infection, was suspended in about 10 cubic centimeters of salt solution and about two-thirds of this suspension sprayed into both nostrils of a third donkey. The remainder of the suspension of this culture was then sprayed into a closed glass cage, containing 6 control monkeys (Nos. 5771 to 5776). All of the monkeys died later of pneumonic-plague infection. The third donkey remained healthy.

Experiment 3.—October 7. A large pneumonic area of the left lower lobe of a monkey that had just succumbed to pneumonic-plague infection was cut into small pieces and crushed with a pair of forceps in salt solution and the lung thoroughly broken to pieces. The suspension amounted in volume to about 20 cubic centimeters. One-half of this suspension was sprayed into a canvas sack surrounding the nostrils and head of one donkey and nearly all of the other half into a second sack over the nostrils and head of a second donkey. Guinea pig (No. 5802) was also inoculated cutaneously with 5 *œsen* of this same suspension. The guinea pig died three days later with typical bubonic-plague infection. The two donkeys remained entirely healthy.

Therefore, although we never failed to infect guinea pigs and monkeys with pneumonic plague by the same cultures which were sprayed into the nostrils of the donkeys, we were entirely

unable to infect the donkeys, even when they were made to inhale air charged with the most virulent cultures of pneumonic strains of the plague bacillus for a period of as long as five minutes at a time. We, therefore, do not consider donkeys susceptible to pneumonic-plague infection, and these experiments render it doubtful that these animals played any part in the dissemination of pneumonic plague during the Manchurian epidemic, and suggest that in the reported cases of pneumonic plague in donkeys the infecting organism was not *Bacillus pestis*, but, perhaps, some other organism of the hæmorrhagic septicæmia group.

DOGS.

At the Mukden Conference,[5] 1 case of pneumonic-plague infection in a dog, observed by Doctor Takami, was referred to in which there was pneumonia in the caudal lobe of the left lung. This dog was found in a house where 7 people had died of plague infection. The Conference also resolved that the question of the occurrence of pneumonic plague in dogs should be made the subject of special study with regard to their liability to this infection. Accordingly, we also performed experiments with this object in view. The results were as follows:

On November 4, 2 fully grown dogs were placed in a closed glass cage and a suspension of two 48-hour agar-cultures of a virulent pneumonic strain of the plague bacillus was sprayed into the cage for two periods of two and one-half minutes, each after a brief interval between them. The first dog, No. 5880, died on November 9, five days after infection. The necropsy showed there was pneumonia of both lungs. In the right lung all the lobes were involved. Only a small portion at the apex of the upper lobe did not show pneumonia. In the left lung, both lobes, with the exception of the apex of the upper lobe, were also involved. The pneumonia was in the stage of engorgement with the exception of small bronchial areas scattered throughout the lung, measuring from about 2 millimeters to 1 centimeter in diameter. These areas of bronchial pneumonia were grayish in color on the surface of the lung, and on section they were grayish at the periphery and in the center red and slightly granular. The areas were not wedge-shaped, but were circular in outline (see Plate XII, fig. 1). Smears from the lungs showed comparatively few plague bacilli and a few streptococci. The large bronchi were not reddened. There was much mucus in the

[5] *Loc. cit.*

trachea, but the mucous membrane here was also not reddened. The cervical glands appeared normal. There was no œdema of the cervical tissues. The spleen was swollen, but contained no miliary abscesses. The liver showed cloudy swelling, and also contained no miliary abscesses. Microscopical preparations from the spleen showed a few plague bacilli. Cultures from the heart and lung developed numerous colonies of the plague bacillus.

The other dog (No. 5881) died March 21, seventeen days after infection. He was considerably emaciated. The necropsy showed that the lymphatic glands were nowhere swollen. There were no hæmorrhages or œdema in the tissues about the neck. The trachea and larger bronchi contained frothy, reddish mucus. The left lung was normal throughout. The upper lobe of the right showed advanced hepatization throughout and sank when placed in water. Two grayish wedge-shaped infarcts, measuring from 1 to 1.5 centimeters at the base, were present in this lobe. The whole lobe showed reddish-gray hepatization with beginning resolution. The middle and lower lobes were somewhat congested, but contained no pneumonic areas. Microscopical preparations from the lung showed fair numbers of *Bacillus pestis*. No other organism was present in the lung, as was demonstrated by cultures. Microscopical preparations from the spleen showed a few bipolar forms and a number of involution forms of the plague bacillus.

Therefore, our experiments upon dogs show that these animals are only moderately susceptible to pneumonic plague but that, when exposed to severe infection, they may contract primary pneumonic plague and die of the disease.

Shibayama [6] showed that dogs were not very susceptible to subcutaneous infection with the pneumonic strain, but that they sometimes succumbed from the subcutaneous inoculation of large doses or from intraperitoneal inoculation.

Pigs.—It was stated that over 300 pigs had died during the epidemic at Harbin, but there was no evidence presented which showed that the disease from which they succumbed was bubonic or pneumonic-plague infection, nor was any evidence submitted which showed that the disease was not hog cholera or swine plague.

[6] *Ibid.*, p. 46.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

IX. PROTECTIVE INOCULATION AGAINST PNEUMONIC PLAGUE.

By Richard P. Strong and Oscar Teague.

(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

The epidemic of pneumonic plague, which raged in Manchuria and northern China during the winter of the year 1910–1911 and which caused the death of over 50,000 people, brought before us, among other problems, one of particular importance, namely, that of protective inoculation against the disease.

The Chinese Government spent over 100,000 dollars (Mexican) on plague prophylactics during the epidemic, but, at its close, their efficacy was doubted.

Inoculations with killed cultures were alone employed during the epidemic. One hundred and thirty-two people were inoculated at Harbin; 22 of these contracted plague, 13 after one injection, 8 after two injections, and 1 after three injections. Of the 8 who fell sick after two injections, 2 contracted plague six days, 2 ten days, 2 fourteen days, 1 twelve, and 1 twenty-seven days after the inoculation. Of the 13 who contracted plague after one injection, 12 contracted plague after two weeks and one after six days.

Unfortunately, it was not possible to ascertain how many of those inoculated were afterward exposed to pneumonic-plague infection or how many, when exposed, protected themselves by the wearing of masks. Dr. Wu [1] reported to the Conference the case of Mr. Liu, a medical student who worked with pneumonic-plague patients for a whole month with no other precaution than masking. On January 2 he was inoculated, and eight days after he contracted pneumonic plague and died. He also reported the case of Dr. Hsu who was inoculated on January 4 and contracted pneumonic plague on January 22, and stated in addition

[1] Report of the International Plague Conference held at Mukden, April, 1911. Manila (1912), 332.

that of 20 other individuals who were inoculated at the same time none became infected.

At Fuchiatien, 439 individuals were inoculated with Haffkine's vaccine and with antiplague serum. Sixteen individuals received three inoculations, two of Haffkine's vaccine and one of serum. None of these became infected. Thirty individuals received two injections, either with Haffkine's vaccine or with Haffkine's vaccine and serum. None of these, also, became infected. Of 393 individuals who were vaccinated once with Haffkine's vaccine, 4 died of plague, 1 eight days, 1 ten days, 1 eighteen days, and 1 thirty-two days after inoculation. The same comment applies to these statistics, namely, that we have no evidence as to how many of the 439 individuals who were inoculated were subsequently exposed to infection and how many protected themselves by the use of masks.

Approximately 14,000 individuals were inoculated with killed cultures of the plague bacillus, during the epidemic, but the great majority of these individuals were never exposed to plague infection. Therefore, we have no positive evidence as to what protection was conferred upon them by inoculation. The only definite conclusion which, it appears, we were justified in drawing from the statistics obtained from the epidemic is that prophylactic inoculations, by means of dead cultures, have sometimes been ineffective in preventing pneumonic-plague infection. Some individuals, inoculated twice, and some even three times, have contracted the disease.

From the evidence presented before the International Plague Conference, held in Mukden in April, 1911, it was resolved by the Conference that the statistics, which were collected during the epidemic, did not allow of any definite conclusion about the value of active prophylactic inoculation against pneumonic plague. Nevertheless, the Conference further resolved that, as the statistical evidence pointed to the conclusion that some degree of protection is conferred against bubonic plague by the use of prophylactics, therefore, there were *a priori* grounds for the use of protective inoculation against pneumonic plague.

The Conference, therefore, advised that experiments on the protective inoculation of animals should be carried on and the immunity of the animals tested by their exposure to infection to pneumonic plague by inhalation, in order to find out which prophylactic could be best used against pneumonic plague, and, if another outbreak of this disease should occur, that dead bacillary prophylactics, Lustig and Galeotti's nucleo-proteid, and Strong's method of vaccination, with a living attenuated culture,

should be tried in selected communities, under rigorous scientific conditions.

At the time the Conference was in session, there was no experimental evidence whatever as to the protection afforded by prophylactic inoculations against pneumonic plague, and no experiments of this nature in animals, other than the ones which will be discussed in this paper, hitherto have been reported. The reason for this appears to be obvious from the fact that there has been no other great epidemic of pneumonic plague within modern times, and the question of prophylactic inoculation in man, as a practical means of protection against this disease, during an epidemic, has not hitherto arisen. We, therefore, determined to investigate this question experimentally. The assumption that, because prophylactic inoculations furnish some degree of protection against bubonic plague they also would be protective against pneumonic-plague infection hardly would seem warranted, since the portal of entry of the infecting agent is so different in the two conditions. Moreover, the plague organism finds in the pulmonary tissues a much more favorable and extensive medium for its multiplication and diffusion than it does in the lymphatic glands. In bubonic plague, the lymphatic glands may be said to act as filters against the general invasion of the body by the plague bacillus, while in primary pneumonic plague there is no such mechanism for the defense of the host, the bacilli spreading rapidly throughout the lung and invading the circulation in every instance in a comparatively short time and apparently before the host has had time to produce any appreciable quantity of immune substances. The bronchial lymphatic glands in primary pneumonic plague offer resistance to the invasion of the plague bacillus, and in every case of this disease these glands are very acutely inflamed and frequently almost of a black color from the resulting toxic hæmorrhages in the glandular substance. However, by the time the bronchial glands have become involved, the bacteria have already spread so extensively throughout the lung substance that a bacteræmia has usually occurred.

The infection or immunity of the host, for certain bacteria, sometimes depends solely upon the portal of entry of the organism; for example, the same quantity of cholera vibrios, injected subcutaneously in man or administered by the mouth, may produce entirely different results. In the former instance, a local and general reaction is obtained, but the bacteria quickly die, while in the latter instance, the vibrios may pass to and multiply in the intestines and Asiatic cholera result.

As another example of the importance of the portal of entry of the organism in relation to infection and immunity may be cited the fact that the tetanus bacillus, which frequently resides normally as a harmless commensal in the intestine of the horse, when injected beneath the skin of this animal, may produce tetanus and death.

These examples serve to emphasize the importance of experimental work upon the subject of protective inoculation against pneumonic-plague infection, and show that it does not follow that, because there is evidence that protective inoculation is sometimes successful in the case of bubonic plague, it will necessarily also be efficient in the case of pneumonic plague.

In our experiments in immunization, we used both guinea pigs and monkeys. In selecting a method of prophylactic inoculation for the production of the immunity, we naturally chose the one of *vaccination;* that is, inoculation with a living attenuated organism, as this method unquestionably has been shown to produce a much higher immunity against bubonic-plague infection than any other in which killed cultures of the plague organism or its extracts are employed.

The accompanying Table I, taken from the previous experiments of one of us (Strong),[2] shows the comparative value of the different methods of immunization employed against cutaneous and subcutaneous plague infection in animals.

TABLE I.—*Combined table comparing efficiency of different methods of immunization.*

KILLED PEST CULTURES.

Kind of animal and series No.	Number inoculated.	Number dead before immunity tested.	Immunized.	
			Number.	Percentage.
Monkeys:				
Bouillon-cultures—				
Series 5	8		3	37
Series 49	9		2	22
Agar-cultures—				
Series 9	3			
Series 25	20	3	4	23
Series 48	15	1	4	28
Total	55	4	13	25
Guinea pigs (killed agar-cultures):				
Series 50 (total)	15		4	26

[2] *This Journal, Sec. B* (1907), 2, 238.

TABLE I.—*Combined table comparing efficiency, etc.*—Continued.

LIVING PEST AVIRULENT STRAIN I.

Kind of animal and series No.	Number inoculated.	Number dead before immunity tested.	Immunized.	
			Number.	Percentage.
Monkeys:				
Series 4	6		5	83
Series 11	5		1	20
Series 12	8		4	50
Series 18	10		5	50
Series 51	15		8	53
Total	44		23	52
Guinea pigs:				
Series 32	11	5	5	83
Series 37	9	2	6	85
Series 39	15		8	53
Series 41	21		15	71
Series 46	15		12	80
Total	71	7	64	72

LIVING PEST AVIRULENT STRAIN II.

Monkeys:				
Series 17	4		3	75
Series 21	12		8	66⅔
Series 24	18	4	13	92
Series 52	15	1	7	50
Total	49	5	31	70
Guinea pigs:				
Series 33	10	3	7	100
Series 38	7	1	4	66⅔
Series 40	15	1	11	78
Series 47	15	1	14	100
Total	47	6	36	88

EXTRACTS OF PLAGUE BACILLUS (FREE RECEPTORS).

Monkeys:				
Series 7	4		1	25
Series 26	5		1	20
Total	9		2	22

ARTIFICIAL AGGRESSIN.

Monkeys:				
Series 29 (total)	32		4	12½
Guinea pigs:				
Series 29	2		0	0
Series 30	2		0	0
Series 31	6		1	16⅔
Series 36	12		0	0
Series 42	4		2	50
Total	26		3	11

TABLE I.—*Combined table comparing efficiency, etc.*—Continued.

NATURAL AGGRESSIN.

Kind of animal and series No.	Number inoculated.	Number dead before immunity tested.	Immunized.	
			Number.	Percentage.
Guinea pigs:				
Series 35	15		4	26
Series 44	12		4	33⅓
Total	27		8	30

KLEIN'S METHOD.

Guinea pigs:				
Series 54	6		2	33⅓
Series 56	7		2	28
Total	13		2	30

It is demonstrated that in the case of guinea pigs, vaccinated with an avirulent culture, about 80 per cent are protected against a severe cutaneous plague infection, and in monkeys, vaccinated in the same way, about 61 per cent are so protected against subcutaneous infection.

It was possible to immunize against the same severe cutaneous test but 26 per cent of the guinea pigs with killed cultures. Kolle and Otto, in numerous previous experiments on guinea pigs, were never able to immunize more than 10 per cent of these animals by means of repeated inoculations of killed cultures. It will be noted also in the accompanying table that in the experiments in which living attenuated cultures were used for the immunization of guinea pigs, in one series 72 per cent and in another 88 per cent were protected against cutaneous infection. These experiments are confirmatory of the statement that the living attenuated culture gives a much higher degree of immunity against cutaneous plague infection than a killed one.

In order to retest the value for immunization against cutaneous infection of the culture used for the vaccination in the experiments recorded in this paper, the following experiment was performed:

EXPERIMENT NO. 1.

Twenty-four guinea pigs each received subcutaneously on June 9, 1911, one 48-hour agar-slant-culture of living avirulent plague. One died (intraperitoneal inoculation) in less than twenty-four hours after vaccination and the others survived. Two weeks later, 11 of these vaccinated guinea pigs were subjected to infection with virulent plague bacilli by cutaneous

inoculation in order to retest the value for immunization against cutaneous infection of the culture used for the vaccination in the experiments recorded in this paper. The 12 remaining vaccinated guinea pigs were subjected to infection by inhalation on the same day. The virulent culture used was isolated from our human case (No. 9) of pneumonic plague at Mukden. The culture was passed through a guinea pig and a monkey, and fresh cultures on agar from the monkey's blood were employed in the experiment.

The 11 vaccinated guinea pigs, together with 12 normal guinea pigs as controls, were subjected to cutaneous inoculation in the following manner: The growth of one agar slant of the virulent culture just described was suspended in 5 cubic centimeters of peptone solution and 5 *œsen* of this suspension were rubbed over the shaved and scarified abdomen of each of the guinea pigs. The result was as follows:

Cutaneous infection.

Vaccinated guinea pigs.[a]	Normal guinea pigs.[b]
No. 5281 survived.	No. 5360 died in 5 days.
No. 5282 died in 13 days.	No. 5361 died in 10 days.
No. 5283 survived.	No. 5362 died in 3 days.
No. 5284 survived.	No. 5363 died in 10 days.
No. 5285 died in 14 days.	No. 5364 died in 8 days.
No. 5286 died in 7 days.	No. 5365 died in 6 days.
No. 5287 died in 6 days.	No. 5366 died in 9 days.
No. 5288 survived.	No. 5367 died in 4 days.
No. 5289 died in 7 days.	No. 5368 died in 6 days.
No. 5290 survived.	No. 5369 died in 5 days.
No. 5291 survived.	No. 5370 died in 3 days.
	No. 5371 died in 6 days.

[a] Total: 6 survived; 5 died.
[b] Total: 0 survived; 12 died.

Fifty-five per cent of the vaccinated guinea pigs and none of the controls survived. This experiment merely demonstrated the immunizing value of the culture against cutaneous or bubonic infection. It is desired to emphasize again the fact that guinea pigs can usually *only* be successfully immunized against cutaneous or bubonic infection by means of a living attenuated culture. Only a very few of the animals inoculated with killed cultures, when exposed to infection, survive.

For the purpose of testing the immunity of the remaining 12 vaccinated guinea pigs against pneumonic infection, the growth of two agar slants of the virulent culture described above was suspended in 30 cubic centimeters of normal saline solution. This was placed in a glass receiver of an ordinary nasal spray. Air was supplied by a hand-force-pump and rubber tubing connection. The suspension could, in this manner, be sprayed in a fine vapor for a distance of several feet. Six vaccinated and six normal

guinea pigs were placed together in a closed glass cage about .75 meter square, the nozzle of the spray introduced at one side of the cage, and the suspension sprayed into the cage for about one minute. The position of the nozzle was then changed to the opposite side of the cage, and the suspension then sprayed for another minute. The animals remained in the closed cage about ten minutes after the spraying was discontinued. The other 6 vaccinated guinea pigs with 6 controls were sprayed in like manner in a similar cage. While performing all of the spraying experiments referred to in this article, we always wore masks[3] and goggles, such as we employed when working with pneumonic-plague patients during the recent epidemic in Manchuria. Rubber gloves were also worn in handling the animals.

The result in this first series of animals was as follows:

SERIES I.—*Infection by inhalation.*

Vaccinated guinea pigs.[a]	Normal guinea pigs.[b]
No. 5268 died in 6 days.	No. 5348 died in 4 days.
No. 5269 died in 6 days.	No. 5349 died in 4 days.
No. 5270 survived.	No. 5350 died in 4 days.
No. 5273 survived.	No. 5351 died in 5 days.
No. 5274 survived.	No. 5352 died in 11 days.
No. 5275 survived.	No. 5353 died in 13 days.
No. 5276 survived.	No. 5354 died in 4 days.
No. 5277 survived.	No. 5355 died in 3 days.
No. 5278 died in 6 days.	No. 5356 died in 4 days.
No. 5279 survived.	No. 5357 died in 4 days.
No. 5280 survived.	No. 5358 died in 3 days.
	No. 5359 died in 3 days.

[a] Total: 8 survived; 3 died.
[b] Total: 0 survived; 12 died.

In this series 72.7 per cent of the vaccinated animals survived, while all of the unvaccinated control ones died of plague infection.

EXPERIMENT NO. 2.

On August 10, 1911, each of 24 guinea pigs of a second series was vaccinated with one agar slant of a 48-hour culture of avirulent plague and 23 survived the treatment; one died of an injury. Four weeks later, these vaccinated guinea pigs, together with 24 controls, were subjected to infection by inhalation with a virulent strain of plague. The culture used was originally obtained from a pneumonic-plague necropsy at Muk-

[3] The experiments of Barber and Teague, see XII, p. 255 of this report, demonstrate that this mask (the Mukden type) was not a safe protection while carrying on these inhalation experiments. Fortunately, we escaped pneumonic-plague infection, probably because the spray was not directed toward us but into the cage.

den. After passage through a number of guinea pigs, a monkey was infected with the strain by inhalation. The monkey died of pneumonic plague, and a guinea pig was inoculated cutaneously with a portion of the pneumonic lung of the monkey. The culture sprayed was obtained from the blood of this guinea pig. The growth of two agar-slant-cultures was suspended in about 40 cubic centimeters of normal saline solution and about two-thirds of the suspension was sprayed into the cages as in the preceding experiment. The result was as follows:

SERIES II.—*Infection by inhalation.*

Vaccinated guinea pigs.[a]	Normal guinea pigs.[b]
No. 5568 died in 4 days.	No. 5617 died in 8 days.
No. 5569 survived.	No. 5618 died in 4 days.
No. 5570 died in 4 days.	No. 5619 died in 4 days.
No. 5571 survived.	No. 5620 died in 3 days.
No. 5572 died in 3 days.	No. 5621 died in 4 days.
No. 5573 survived.	No. 5622 died in 3 days.
No. 5574 died in 10 days.	No. 5623 died in 4 days.
No. 5575 survived.	No. 5624 died in 3 days.
No. 5576 survived.	No. 5625 died in 6 days.
No. 5578 survived.	No. 5626 died in 4 days.
No. 5579 survived.	No. 5627 died in 4 days.
No. 5580 survived.	No. 5628 died in 3 days.
No. 5581 survived.	No. 5629 survived.
No. 5582 survived.	No. 5630 died in 3 days.
No. 5583 survived.	No. 5631 died in 3 days.
No. 5584 survived.	No. 5632 died in 4 days.
No. 5585 survived.	No. 5633 died in 5 days.
No. 5586 survived.	No. 5634 died in 4 days.
No. 5587 survived.	No. 5635 died in 3 days.
No. 5588 died in 7 days.	No. 5636 died in 3 days.
No. 5589 survived.	No. 5637 died in 3 days.
No. 5590 died in 5 days.	No. 5638 died in 4 days.
No. 5591 died in 7 days.	No. 5639 died in 4 days.
	No. 5640 died in 3 days.

[a] Total: 16 survived; 7 died.
[b] Total: 1 survived; 23 died.

Sixteen, or 69.6 per cent, of the vaccinated animals survived, while all but one of the control ones (that is, 4.1 per cent) died of plague infection. This one control animal probably screened itself in some way behind the other guinea pigs and thus avoided infection.

Summary of all inhalation experiments upon guinea pigs.

Guinea pigs.	Total.	Survived.	Percentage of survivals.
Vaccinated	34	24	70.6
Normal	36	1	2.8

Therefore, from these two series of experiments, we see that 70.6 per cent of the vaccinated animals proved immune when exposed to infection by means of spraying virulent plague bacilli into the air which they breathed, and hence were immune to this method of infection. However, it is necessary to examine closely into the nature of this immunity.

It is seen that of *36 control unvaccinated* guinea pigs, all except one succumbed to the infection induced by spraying. Upon post-mortem examination, the following changes, which applied to practically all of the *control* animals, were encountered. In general, there were marked evidences of plague infection about the tissues of the neck and throat. The subcutaneous tissues showed extensive œdema, and there was swelling of the lymphatic glands of the neck and of those about the trachea. Usually the glands were not only swollen but more or less hæmorrhagic, and had the appearance of small buboes. Throughout the body, marked evidence of septicæmia was usually present. There were frequently extensive hæmorrhages in the intestinal wall. The spleen sometimes showed the typical changes encountered in plague infection with miliary abscesses. Pneumonia was present in only about 23 per cent of the control animals. These changes suggest that the primary point of infection evidently was located in the mucous membranes of the throat and that it did not usually occur in the bronchi or alveoli of the lung. From these lesions it would appear that normal guinea pigs, under the conditions of the experiment in which the spraying was carried on, do not usually develop primary plague pneumonia, but that infection occurs through the mucous membranes of the mouth and throat and infection and sometimes buboes of the glands of the neck and septicæmia result. It would appear that in guinea pigs, either on account of too shallow respirations or the small size of the larynx and trachea, the bacteria are not so likely to penetrate to the smaller bronchi by means of the inspired air. Instead, they are apparently arrested by the mucous membrane of the throat. Attention must be called to the fact that the spray employed was not so fine a one as that used in the subsequent experiments on monkeys and that the bacteria were, therefore, sprayed in larger particles in the first two series of experiments. Whatever the reason, however, the fact remains that primary pneumonic infection in the guinea pigs did not usually result. Therefore, the conclusions that can be drawn regarding the vaccinated guinea pigs

are that 70 per cent of these animals appeared to be immune against plague infection entering through the mucous membranes of the mouth and throat, but one can not conclude that this same percentage of animals would have proved to be immune if the organism really had been introduced directly into the lung by the bronchi.

Let us consider the experiments in relation to monkeys which give us much clearer information regarding immunization against pneumonic plague. Three series of experiments were performed as follows:

EXPERIMENT NO. 3.

Eleven[4] monkeys were vaccinated on June 23, 1911, each with one 48-hour agar-culture of avirulent plague. They were subjected to infection by inhalation as follows: Two vaccinated monkeys with two controls on July 7; 5 vaccinated ones with 5 controls on July 12; 5 vaccinated ones with 6 controls on July 14. The general mode of procedure was the same as in the preceding experiments. The result was as follows:

SERIES III.—*Infection by inhalation.*

Vaccinated monkeys.[a]	Normal monkeys.[b]
No. 5404 died in 5 days.	No. 5437 died in 4 days.
No. 5386 died in 5 days.	No. 5438 died in 4 days.
No. 5384 died in 6 days.	No. 5439 died in 5 days.
No. 5394 died in 5 days.	No. 5440 died in 5 days.
No. 5393 died in 5 days.	No. 5501 died in 5 days.
No. 5400 died in 4 days.	No. 5424 died in 3 days.
No. 5401 survived.	No. 5425 died in 3 days.
No. 5387 died in 3 days.	No. 5491 died in 4 days.
No. 5389 died in 5 days.	No. 5492 died in 3 days.
No. 5403 died in 5 days.	No. 5493 died in 4 days.
No. 5390 died in 4 days.	No. 5494 died in 3 days.
	No. 5495 died in 3 days.

[a] Total: Survived, 1; died, 10.
[b] Total: Survived, 0; died, 12.

Only one of the vaccinated monkeys, or 9 per cent, survived, while all of the controls died of pneumonic infection.

EXPERIMENT NO. 4.

On September 15, 1911, twenty-two monkeys were vaccinated each with one 48-hour agar-culture of living avirulent plague bacilli. Two weeks later they, together with 22 unvaccinated monkeys, were subjected to

[4] Additional monkeys were vaccinated in this and the following series but died in a cachectic condition before the date for testing their immunity arrived. In no instance were we able to show that they died of plague.

infection by inhalation with a pneumonic strain which had been passed through a series of guinea pigs. The growth from 3 agar-slant-cultures was suspended in about 40 cubic centimeters of normal saline solution and all of this suspension was used for the spraying. Only three or four vaccinated monkeys with the same number of controls were placed in a cage at a time during the spraying. They were then, of course, placed in separate cages. The result of the experiment was as follows:

SERIES IV.—*Infection by inhalation.*

Vaccinated monkeys.[a]	Normal monkeys.[b]
No. 5704 survived.	No. 5771 survived.
No. 5706 died in 6 days.	No. 5772 died in 5 days.
No. 5707 survived.	No. 5773 died in 5 days.
No. 5708 died in 4 days.	No. 5774 died in 6 days.
No. 5709 died in 6 days.	No. 5775 survived.
No. 5710 died in 5 days.	No. 5776 died in 5 days.
No. 5711 died in 5 days.	No. 5777 died in 5 days.
No. 5712 survived.	No. 5778 died in 6 days.
No. 5713 died in 7 days.	No. 5779 died in 6 days.
No. 5714 died in 8 days.	No. 5780 died in 5 days.
No. 5715 survived.	No. 5781 died in 5 days.
No. 5716 died in 6 days.	No. 5782 died in 5 days.
No. 5717 died in 5 days.	No. 5783 died in 8 days.
No. 5718 died in 6 days.	No. 5784 survived.
No. 5719 died in 8 days.	No. 5785 died in 6 days.
No. 5720 survived.	No. 5786 died in 4 days.
No. 5721 survived.	No. 5787 died in 4 days.
No. 5722 survived.	No. 5788 died in 5 days.
No. 5724 survived.	No. 5789 died in 4 days.
No. 5725 died in 6 days.	No. 5790 died in 5 days.
No. 5726 died in 6 days.	No. 5791 survived.
No. 5727 survived.	No. 5792 died in 5 days.

[a] Total: Survived, 9; died, 13.
[b] Total: Survived, 4; died, 18.

Nine, or 40.5 per cent, of the vaccinated monkeys survived, while 4, or 18.1 per cent, of the unvaccinated control ones also survived. In this experiment, evidently the method of producing the infection was not satisfactory, since four of the control unvaccinated monkeys did not develop plague infection. The results obtained in Series IV, therefore, do not give as valuable information as do the results obtained in Series III and V.

EXPERIMENT NO. 5.

On October 18, 1911, twenty-one monkeys were each vaccinated subcutaneously with one 48-hour agar-slant-culture of living avirulent plague bacilli. On November 2, these animals and 21 control unvaccinated ones were exposed to infection by inhalation in the same manner as in the preceding experiments. The result may be tabulated as follows:

SERIES V.—*Infection by inhalation.*

Vaccinated monkeys.[a]	Normal monkeys.[b]
No. 5818 died in 5 days.	No. 5854 died in 2 days.
No. 5819 died in 6 days.	No. 5855 died in 5 days.
No. 5820 died in 5 days.	No. 5856 died in 5 days.
No. 5822 survived.	No. 5887 died in 7 days.
No. 5823 died in 5 days.	No. 5858 died in 5 days.
No. 5824 died in 2 days.	No. 5859 died in 5 days.
No. 5825 died in 6 days.	No. 5860 died in 5 days.
No. 5826 died in 6 days.	No. 5861 died in 5 days.
No. 5827 died in 6 days.	No. 5862 died in 5 days.
No. 5828 died in 5 days.	No. 5863 died in 5 days.
No. 5829 died in 5 days.	No. 5864 died in 5 days.
No. 5830 died in 5 days.	No. 5865 died in 5 days.
No. 5831 died in 5 days.	No. 5866 died in 2 days.
No. 5832 died in 2 days.	No. 5867 died in 5 days.
No. 5833 died in 9 days.	No. 5868 died in 2 days.
No. 5834 survived.	No. 5869 died in 5 days.
No. 5835 died in 6 days.	No. 5870 died in 2 days.
No. 5837 died in 5 days.	No. 5871 died in 5 days.
No. 5838 died in 4 days.	No. 5872 died in 5 days.
No. 5839 died in 5 days.	No. 5873 died in 5 days.
No. 5840 died in 6 days.	No. 5874 died in 5 days.

[a] Total: Survived, 2; died, 19.
[b] Total: Survived, 0; died, 21.

Only 2, or 9.5 per cent, of the vaccinated animals survived, while all of the control monkeys died of pneumonic-plague infection.

Summary of all experiments upon monkeys.

Series.	Vaccinated monkeys.			Normal monkeys.		
	Survived.	Died.	Percentage of survivals.	Survived.	Died.	Percentage of survivals.
IV	9	13	41	4	18	18
V	2	19	9.5	0	21	0
III	1	10	9	0	12	0
Total	12	42	22	4	51	7.3

As we have done in the case of the unvaccinated guinea pigs, so it will be advisable in the case of the unvaccinated normal monkeys to examine into the character of the infection. The following observations apply to practically all of these control animals. At necropsy, there was absence of any sign of plague infection about the tissues of the neck. The submaxillary and cervical lymphatic glands and those about the trachea were

not swollen, nor was there any œdema of the cervical tissues, as was practically always seen in the control guinea pigs. In a number of cases, the tonsils were examined and found to be normal. There was frequently œdematous fluid in the trachea. The larynx and vocal cords were, as a rule, not injected. In a few cases the trachea was slightly reddened. There were not such marked evidences of a septicæmia as seen in the control guinea pigs. No hæmorrhages were noted in the intestines and omentum. The spleen and liver showed no miliary abscesses.

There were no cervical, axillary, nor inguinal buboes. *The lungs showed primary pneumonia in every case.* There was always much œdema of the lung. The pneumonia was either in the stage of engorgement or of red or early gray hepatization. In a number of the cases, a pleuritic exudate was observed over the hepatized areas. The plague bacilli were always most numerous in the lungs.

From these observations, it is obvious that the infection in monkeys occurred by inhalation and resulted in primary plague pneumonia. It also is evident that in some instances, in which monkeys are exposed to infection by inhalation, the primary point of infection may not only be the lungs but also the mucous membranes of the mouth and throat. That plague infection may occur through the mucous membranes of the mouth and throat in monkeys was demonstrated by placing a small quantity of plague bacilli, by means of a glass rod, on the posterior portion of the throat.[5]

These animals all died of plague septicæmia, with or without infection of the glands of the neck. That is, in the cases in which the infection was severe and the susceptibility of the animals more marked, the animals succumbed to septicæmia before cervical buboes developed. In none of these instances was pneumonia present. Primary plague pneumonia only results when infection by inhalation has in addition taken place.

Therefore, experiments performed with monkeys in the vaccination and subsequent infection of the animals by inhalation give us much more valuable information in regard to the protection afforded by vaccination against pneumonic plague than do those performed with the guinea pigs. In the instances where the infection was severe and all of the control unvaccinated monkeys succumbed to pneumonic-plague infection, only 9 per cent of the vaccinated monkeys survived.

[5] See IV, p. 176 of this report.

In conclusion, our experiments have demonstrated that vaccination does not afford the same protection against pneumonic plague that it does against bubonic plague in experimental animals. They indicate strongly that prophylactic inoculation can not be relied upon as even a reasonable means of protection against pneumonic infection in man. It would appear that a proper mask furnishes the only reliable method of protection.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

X. IMMUNIZATION OF GUINEA PIGS BY VACCINATION WITH AVIRULENT PLAGUE BACILLI MIXED WITH AGAR.

By M. A. Barber.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

The object of this research was to test the behavior of doses of an avirulent organism when mixed with agar and to compare the immunizing effect of such doses with that of the organism alone. Plague was chosen as a convenient test organism since it grows well in agar and has been shown by Strong [1] and Kolle and Otto [2] to immunize about 70 to 83 per cent of guinea pigs when given alone in doses of 1 to 2 agar-slant-cultures.

The mixture of the avirulent organism with agar aims at the following possible advantages:

1. A very small initial dose may be given, lessening the dangers of anaphylactic or other intoxication; 2, the gradual absorption of agar, and with it the growing colonies of bacteria and their products insures dosage that is gradual and, for a time, gradually increasing; 3, one inoculation may insure a dosage extending over considerable time; 4, a local reaction is set up by the agar which, in some cases, might favorably affect immunization.

The technique is simple. Nutrient agar of the ordinary sort, or, in some cases, made somewhat stiffer than usual, was melted, cooled to about 43°C., and a known amount of bacilli thoroughly mixed with it. Quantities of the still liquid mixture, varying

[1] *This Journal, Sec. B* (1907), 2, 155.

[2] *Ztschr. f. Hyg. u. Infectionskrankh.* (1903), 45, 512; 48, 399.

from 0.25 to 6 cubic centimeters, were inoculated both subcutaneously and intraperitoneally by means of an ordinary syringe. Especial precautions were taken against contamination; for a contaminating organism might develop rapidly under protection of the agar. The escape of the still liquid agar could be prevented by applying ice or cold water to the point of inoculation after withdrawing the needle.

It was found that if the agar mass was deposited immediately under the skin, necrosis of the overlying skin sometimes occurred. This could be avoided by depositing the agar well into the subcutaneous tissues. Few cases of death due to a contaminating organism occurred.

In order to observe the behavior of the inoculations, animals, some of them inoculated with agar alone and some with the agar pest mixture, were sacrificed at the following periods after inoculation: three and one-half hours, twenty-one hours, forty-eight hours, three days, four days, five days, six days, seven days, twenty-one days, and twenty-nine days. In all cases the agar mass with the surrounding tissues was studied in frozen sections.

The agar mass examined soon after inoculation was found to be permeated by connective tissue fibers more or less stretched by the agar. Within a few hours leucocytes begin to invade the mass, following the larger strands of connective tissue. They become more and more abundant as time goes on, and within two or three days part of the mass may become semifluid. This was more marked in the agar and pest inoculations. Areas of agar could be detected up to the twenty-ninth day, at least. Colonies of plague, some of them 30 $\mu\mu$ in diameter, were found scattered in the agar mass as early as twenty-one hours after inoculation and as late as five days. As the time went on the agar became more and more invaded by leucocytes and the zone of granulation tissue encroached more and more on the agar, until nothing but a small hard lump of scar tissue could be felt. In some cases this lump could be felt as late as two months after inoculation. In a few cases a softer abscess persisted many weeks.

The contents of the agar mass was examined for plague bacilli in all sacrificed animals and in some living animals by withdrawing some of the mass by means of a glass capillary pipette. Living plague bacilli were detected in practically all sacrificed

animals, and in 3 cases of living animals twenty-five days after inoculation in pure culture. On account of the lack of virulence of this strain of plague, it was impossible to identify it by guinea pig inoculations; but the morphology, staining, and characteristic growth on various media, including the growth in broth covered with sterile vaseline, served to identify the organism satisfactorily. The fact that several tests showed the same plague-like organism in pure culture helped to confirm the identification. One animal inoculated with 3 cubic centimeters of agar with avirulent plague bacilli died from some unknown cause twenty-nine days after inoculation. In it the avirulent plague bacillus in apparently pure culture was found at the point of inoculation, while no growth of any sort was obtained from the spleen, liver, lungs, or peritoneal cavity. There was still a small mass of agar remaining. This case is the more remarkable since there had been some necrosis of the skin over the inoculated agar. This had entirely healed at the time of the death of the animal.

It was demonstrated then that, following a small initial dose of avirulent pest bacilli in agar, pest colonies form in the agar, a portion of agar remains as long as twenty-nine days, and that pest bacilli may be recovered in pure culture after that interval. Gradual dosage over a long period of time may, therefore, be attained by this method.

To test for immunity, the animals inoculated with the agar-avirulent-pest were subjected to infection with virulent plague bacilli. In the first group, included under Table I, relatively small amounts of pest bacilli were mixed with the agar and various quantities of agar were inoculated. The test dose in all animals included in Table I was 0.5 cubic centimeter of a suspension of a 24-hour culture made directly from an infected guinea pig. This strain had been kept at a high degree of virulence by long passage through guinea pigs and was regularly fatal to guinea pigs, inoculated cutaneously, in three to five days. The number of bacteria in the test dose was estimated by means of the Thoma Zeiss counting chamber at 750,000, counting each element of a chain as one. By plating dilutions, the test dose gave 390,000 colonies, a lower number than that obtained by counting, since a chain or united pair could give but one colony. The test dose was given subcutaneously.

TABLE I.

Number of guinea pigs inoculated.	Previous treatment.	Died of plague.	Recovered.	Average number of days of survival after inoculation in fatal cases.	Remarks.
1	Recovered from infection with virulent plague.	0	1	----------	Marked infiltration at point of inoculation.
2	Recovered from infection with plague strain "Shanghai."	0	2	----------	Marked infiltration at point of inoculation.
16	No previous immunization -------	16	0	4.8	
2	Avirulent pest alone (about $\frac{1}{10}$ slope).	2	0	11.0	
2	About $\frac{1}{50}$ loop of avirulent pest in $\frac{1}{2}$ and $\frac{1}{4}$ cc. agar.	2	0	6.5	Immunizing doses given from 30 to 60 days before test dose.
4	About $\frac{1}{100}$ loop in 1 cc. ordinary agar.	3	1	5.3	
2	About $\frac{1}{100}$ loop in 1 cc. 4 per cent agar.	1	1	3	
1	About $\frac{2}{100}$ loop in 2 cc. 4 per cent agar.	1	0	6	All agar and pest given subcutaneously except in last-mentioned group of 5 where inoculation was intraperitoneal.
1	About $\frac{3}{100}$ loop in 3 cc. 4 per cent agar.	1	0	3	
9	About $\frac{1}{100}$ loop in 3 cc. 4 per cent agar.	6	3	8.8	
5	About $\frac{1}{100}$ loop in 1 cc. ordinary agar.	2	3	5	

In the series represented by Table I, all nonimmunized controls died of plague within six days after inoculation, except one which survived nine days. The 16 in this group include 6 which were inoculated without infection some two to three months previously with single small doses of 2 to 100 plague bacilli, either virulent or of the "Shanghai" strain—a somewhat attenuated race. There was apparently no immunizing effect of these single small doses. Of the immunized group, the two which received avirulent pest bacilli alone in a considerable dose (about 1 cubic centimeter of a thin suspension) died in thirteen and nine days after the test dose. Of the 24 which had received avirulent pest in agar, 8 recovered from the test dose.

In Table II are given the results for a second group of guinea pigs. Here all animals received in immunization a much larger amount of avirulent plague in a larger amount of agar and the doses were given intraperitoneally. The test dose was in all cases given thirty-seven days after the avirulent pest agar. This test dose consisted of about 500,000 bacteria of the same highly virulent strain as that used in the first group, and was

taken from an 18-hour culture made directly from an infected guinea pig and inoculated subcutaneously.

TABLE II.

Number inoculated.	Previous treatment.	Died of plague.	Recovered.	Average number of days of survival after inoculation; fatal cases.	Remarks.
8	Highly immunized survivors of test dose, Table 1.	0	8	----------	Slight local infiltration.
7	Nonimmunized ----------	7	0	5.4	
5	Avirulent pest alone. 1 slope----	1	4	11.0	
2	Avirulent pest alone. ½ slope----	2	0	4.5	
1	Avirulent pest alone. ¼ slope----	1	0	7.0	
3	Avirulent pest 1 slope in 5 to 6½ cc. ordinary agar.	2	1	6.5	
2	Avirulent pest ½ slope in 5 cc. ordinary agar.	0	2	----------	
5	Avirulent pest $\frac{3}{16}$ slope in 5 cc. ordinary agar.	3	2	6.3	

In Table II it is seen that of this group all highly immunized animals survived with but little reaction, all nonimmunized controls died, and of the 8 receiving avirulent pest alone and of the 10 receiving agar and avirulent pest one-half survived in each group. The results of this series were somewhat less favorable than that done with the smaller doses.

Summarizing the results of the two groups, it is seen that the proportion of recoveries following an immunization with this strain of avirulent plague mixed with agar (one-third in group 1 and one-half in group 2) is rather less than the proportion obtained by Strong with avirulent pest alone. In the series described here the number of controls which received avirulent pest alone was too few and the doses, for the most part, too small to give a fair comparison. These series were at first intended to serve only as preliminary ones, but the results did not seem favorable enough to warrant a further series with this strain of avirulent plague. The relative inefficacy of this method is shown especially by 3 animals inoculated subcutaneously with agar and avirulent plague. These three showed avirulent plague at the point of inoculation in pure culture twenty-five days after inoculation, yet 2 of the 3 succumbed to the test dose of three-fourths million virulent plague.

As regard the relative immunizing power of single small initial doses of avirulent plague in agar compared with much larger

doses given alone, the above series show more decisive results. While in no case was immunization to the test dose effected by less than one 24-hour agar-slant-culture of avirulent pest bacilli alone, the 22 which received only 1/10,000 to 3/10,000 of a loop mixed with agar gave 8 recoveries. This result, taken with the proof obtained of the long survival in animals of avirulent pest when inoculated with agar, gives some encouragement of success with a series inoculated with a slightly more virulent strain of plague in agar. Experiments with agar and organisms other than plague are now in progress.

Summarized briefly, the results obtained demonstrate: 1, The long persistence of ordinary nutrient agar mixed with avirulent plague bacilli and inoculated subcutaneously in guinea pigs (twenty-nine days); 2, the long survival of avirulent plague bacilli in pure culture in such inoculation (twenty-five days and twenty-nine days); 3, the possibility of immunizing a proportion of animals with very small initial doses of avirulent plague bacilli in agar (1/10,000 loop).

The results indicate that as good or better success may be obtained in immunizing with living avirulent plague bacilli alone as with doses mixed with agar. This is true of the strain of avirulent plague used. The method might give better results with another strain of avirulent plague or in immunization with some other organisms.

ADDENDUM.

It was noted that even with highly immunized animals which had survived a severe infection with virulent plague some local reaction followed the test doses of avirulent plague. This was especially true of the animals in Table I receiving a test dose of three-fourths million. It was thought worth while to ascertain if a smaller dose would give in highly immunized animals such local reaction. Ten animals of the series described in Table I, which had survived an infection following a dose of three-fourths million avirulent bacilli, were inoculated subcutaneously with doses of from 45 to 80 virulent plague bacilli. A similar dose was fatal to 7 out of 10 nonimmunized controls. None of the three noninfected controls or of the 10 immunized animals showed a local reaction greater than that which could be accounted for by the prick of the very fine capillary pipette used in inoculating.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

XI. THE INFECTION OF GUINEA PIGS, MONKEYS, AND RATS WITH DOSES OF PLAGUE BACILLI, RANGING FROM ONE BACILLUS UPWARDS.

By M. A. Barber.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

The method of isolation and inoculation of minute doses of bacilli has been described in various papers[1] by the writer and needs but a short description here.

The organisms to be manipulated are suspended in hanging drops of liquid under a large cover glass. This cover is placed over a moist chamber consisting of a glass box open at one end, and the whole is mounted on the stage of the microscope. A glass pipette, the end of which is drawn into a microscopically fine capillary point, is attached to a special holder clamped to the stage of the microscope. The capillary point, bent upward at right angles, is raised by the holder into the hanging drop containing the bacilli, both bacilli and point being kept in view in the field of the microscope. The bacilli enter the point by capillarity and may then be discharged on a sterile part of the cover, or on a new cover, by blowing through a rubber tube attached to the outer end of the pipette. Doses thus isolated are taken up by a new sterile pipette and inoculated. The point is made to pierce the skin of the animal, and the dose is injected by blowing into the rubber tube attached to the pipette. Enough salt solution is drawn into the inoculation-pipette before taking up the dose to wash out the bacilli during the discharge, and just before inoculation, enough sterile salt solution is drawn in to wash the bacteria some distance back from the tip. This is done to prevent the loss of the dose by the breaking off of

[1] *Sci. Bull.*, Kansas Univ. (1907), 4, 3. *Journ. Infect. Dis.* (1907), 5, 380; (1906), 6, 634; (1911), 8, 348.

the more delicate part of the tip during inoculation. That the bacteria pass into the animal with the inoculating fluid and do not remain behind in the pipette has been shown by a series of controls where organisms were discharged into a suitable culture-medium instead of into the animal.

Most of the inoculations were made with a virulent strain of plague which has been fatal to guinea pigs usually in three to five days after cutaneous inoculaton. In the series "Shanghai," a strain of somewhat less virulence was used.

Bacilli were taken immediately from the blood or spleen of infected animals or from the first cultures made from these sources. In most cases bacilli from the heart's blood or organs were grown for a few hours in hanging drop or test-tube in a mixture of body fluid and water of condensation of ordinary agar. When the formation of chains showed that the organisms were multiplying, they were isolated and inoculated at once.

Doses of 50 or less were carefully counted and larger doses were counted or closely estimated; but in the summary given here all doses are arranged in convenient groups. The doses of one-half and three-fourths million were estimated by the Thoma Zeiss counter. In the column giving the dosage, a pair of very short elements clinging closely together were, in some cases, reckoned as a single bacillus; though probably each element was capable of individual growth.

All animals were inoculated subcutaneously, the guinea pigs and monkeys under the skin of the abdomen, the rats at the root of the tail.

TABLE I.—*Guinea pigs and virulent plague.*

Dose in number of bacilli.	Number of animals inoculated.	Result.			
		Infected and died.	Infected and recovered.	Not infected.	Average number of days between inoculation and death.
1	9	6	0	3	9.7
2 to 10	7	3	0	4	9.0
11 to 50	14	10	0	4	8.6
51 to 100	1	1	0	0	7.0
101 to 200	3	2	1	0	9.0
201 to 500	2	2	0	0	9.0
2,000	1	1	0	0	12.0
½ million	4	4	0	0	6.5
¾ million	16	16	0	0	4.8

Total number receiving doses of 1 to 500, 36. Per cent of fatal infections, 63.9.

TABLE II.—*Guinea pigs and plague strain "Shanghai."*

Dose in number of bacilli.	Number of animals inoculated.	Result.			
		Infected and died.	Infected and recovered.	Not infected.	Number of days between inoculation and death.
1	1	0	0	1	
2 to 10	6	1	0	5	14
11 to 50	1	0	0	1	
51 to 100	1	1	0	0	12
101 to 200	1	0	1	0	
201 to 500	3	1	2	0	8
Total	13	3	3	7	

TABLE III.—*Monkeys and virulent plague.*

Dose in number of bacilli.	Number of animals inoculated.	Results.			
		Infected and died.	Infected and recovered.	Not infected.	Number of days between inoculation and death.
1	12	2	0	10	8 and 15
2 to 10	10	1	0	9	17
11 to 50	4	1	0	3	5
101 to 200	2	2	0	0	20 and 9
201 to 500	3	0	0	3	
Total	31	6	0	25	

TABLE IV.—*Rats and virulent plague.*

Dose in number of bacilli.	Number of animals inoculated.	Results.			
		Infected and died.	Infected and recovered.	Not infected.	Number of days between inoculation and death.
1	2	0	0	2	
2 to 10	7	2	0	5	9 and 13
11 to 50	4	2	0	2	9 and 19
51 to 100	1	0	0	1	
Total	14	4	0	10	

It will be noticed from Table I that the percentage of fatal infections in the guinea pigs receiving a dose of one bacillus of the virulent strain is nearly the same as that of the entire 36 which received 1 to 500; namely, 63.9 per cent and 66.7 per cent respectively.

The "Shanghai" strain, though evidently less infective, was in one case fatal in a dose of 5 bacilli. These results illustrate how large a part varying susceptibility of animals plays in infection, and emphasize the necessity of inoculating a series of animals in any test of virulence of a microörganism.

In some guinea pig inoculations, one or few bacilli were washed with salt solution before inoculating and some of these washed doses resulted in fatal infection. Since a most minute quantity, if any at all, of the original body fluid was then inoculated, it does not seem probable that aggressins played any part in these infections. In the experiments on monkeys few succumbed to the small doses, though in two cases fatal infection followed a dose of one bacillus.

In the rat series the wild gray rat was used. One animal succumbed to a fatal infection following a dose consisting of one chain of four small elements, another to a dose of three bacilli, each divided into two still adherent elements. Two other rats succumbed to doses of 50 and 60, respectively, of such pairs. These results render more plausible the view that sufficient bacilli for infection may enter the abraded skin from the fæces of a flea or a crushed flea. The English Plague Commission has shown that flea fæces or flea bodies may contain very large numbers of plague bacilli.

On the average, animals infected with minute doses survived nearly twice as long as those infected with three-fourths of a million or more.

In summary, these results show conclusively that the smallest possible dose of virulent plague bacilli may infect fatally the more susceptible guinea pigs, monkeys, or rats.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

XII. SOME EXPERIMENTS TO DETERMINE THE EFFICACY OF VARIOUS MASKS FOR PROTECTION AGAINST PNEUMONIC PLAGUE.

By M. A. Barber and Oscar Teague.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

During the epidemic of pneumonic plague which raged in Manchuria during the winter of 1910 to 1911, it was believed and, toward the close of the epidemic, was experimentally demonstrated, by Strong and Teague, that sputum in the form of invisible droplets containing viable plague bacilli was frequently suspended in the air near the coughing pneumonic-plague patients. A Petri dish, containing solidified agar-culture-medium, held for a minute or two before the mouth of a patient and closed after a single cough did in some instances on incubation show numerous colonies of plague bacilli, although no visible particles of sputum had been thrown against it.[1] There was every reason to believe that even the smallest number of these bacilli inhaled into the lung would lead to infection and that this was, in fact, the common mode of infection in pneumonic plague. The obvious method to protect against such infection was to interpose a barrier to the passage of these droplets into the mouth and nostrils. With this object in view, masks were worn quite generally by physicians and attendants when in the presence of plague patients or suspected cases. That protection was afforded by the masks apparently went unquestioned and, without the sense of security that their use gave, the mental strain in connection with the work would have been almost unbearable.

The total number of deaths that occurred among physicians,

[1] Report of the International Plague Conference held at Mukden, April, 1911. Manila (1912), 83. See also II, p. 137 of this report.

nurses, attendants, and inspectors during the recent epidemic of pneumonic plague in Manchuria will never be known. The following death roll at Fuchiatien, the Chinese city near Harbin, shows that the total must have been extremely high.

List of deaths of antiplague staff at Fuchiatien.[2]

Doctors	1	out of	20
Students	1	out of	29
Native practitioners	4	out of	9
Police inspectors	2	out of	31
Police	30	out of	688
Sanitary police	11	out of	206
Mounted police	5	out of	80
Firemen	5	out of	20
Coolies	102	out of	550
Cooks	4	out of	60
Ambulance parties	69	out of	150
Soldiers	63	out of	1,100
Total	297	out of	2,943

In South Manchuria the plague sanitary corps suffered a loss of 122 persons among whom were 1 Japanese, 1 English, and 40 Chinese physicians. This represents 2.66 per cent of the total plague mortality in the districts concerned.[3]

The presumption is that all of the members of the sanitary corps wore masks. The masks were, however, not worn constantly nor were they always properly adjusted; coolies were often seen with the masks hanging around their necks instead of being over their mouths. Hence the high death rate of the sanitary staff can not be regarded as proof of the inefficiency of masks.

In Mukden the mask which was almost universally employed consisted of a pad of absorbent cotton about 16 by 12 centimeters and about 1.5 centimeters thick; this was wrapped in gauze, the ends of which were tied at the back of the head. (See Plate V, fig. I. B.) A many-tailed bandage (see Plate V, fig. I. A) composed of three layers of gauze with holes for the eyes was tied around the entire head and served to press the mask firmly against the face and to keep it snugly in place for hours at a time. When first put on, this mask was decidedly uncomfortable, but after a few minutes one became somewhat accustomed to it and could wear it for two or three hours at a time. There was, however, always an intense feeling of

[2] *Ibid.*, p. 242.

[3] *Ibid.*, p. 244.

relief on removing it. We shall designate this type of mask in the discussion to follow as the "Mukden mask." [4]

The following experiments were undertaken with the idea of determining whether this Mukden mask is, in fact, an efficient barrier against the passage of plague bacilli into the lungs and, also, whether or not other types of masks are more efficient.

At the International Plague Conference held in Mukden in April, 1911, Broquet, the French delegate, demonstrated a mask "copied from those used by doctors in the epidemic of the fourteenth century as shown in old books." [5] It consisted of a hood of light canvas or khaki cloth, covering the entire head and drawn in at the neck. In front was a window of mica. No experiments had been performed to test the efficacy of this mask. We shall refer to this type of mask hereafter as the "Broquet mask." It was not used during the recent epidemic of pneumonic plague in Manchuria with the exception of a few times by Broquet himself.

Our preliminary tests indicated that a hood of heavy Canton flannel with a nap was more effective in holding back *Bacillus prodigiosus* than hoods of lighter cloth such as the one demonstrated by Broquet. Instead of mica for the window, we used sheet celloidon such as one sees in the storm curtains of automobiles. The hood was made narrow at the neck so that it would spread out over the shoulders and could be drawn in and tied snugly around the neck. Comparative experiments were made with this mask and the Mukden mask; the subjects wearing the two masks were forced to breathe air containing *Bacillus prodigiosus* simultaneously for the same length of time.

Bacillus prodigiosus was selected for the experiments as being entirely harmless and easily recognizable on account of its pigment production. An ordinary throat atomizer was used for making the spray, but with the idea of getting smaller droplets the rubber bulb was removed and a stronger airblast was obtained by using an automobile pump.

Special precautions were taken to avoid accidental contamination with *B. prodigiosus* on removing the mask. (See Plate V, fig. 2.) The subject was clothed in an operating gown and, in the case of the Mukden mask, his head was covered with a cloth and the eyes protected by automobile goggles. The spraying was generally done in a small, single-roomed stable which

[4] We were informed that this mask was extensively used in Harbin before its introduction into Mukden.

[5] Report of the International Plague Conference, p. 303.

was boarded up on all sides to keep out the light and to avoid, to a certain extent, currents of air. The gowns, goggles, and head-cloths were removed after the subjects had left the stable and before they entered the laboratory building. One of the authors attended to the spraying and exposure of the subjects, the other endeavored to keep himself and his laboratory room free from *B. prodigiosus* and made the necessary plate-cultures in order to determine the result of the test. At first the saliva, taken before and after the spraying, was smeared over agar plates, but later it was found that small pieces of moistened cotton, placed in the nostrils and before the mouth (underneath the Mukden mask), rendered the test much more delicate.

Agar plates were exposed during the course of the experiment in order to obtain an indication of the *living* prodigiosus bacilli that were in the air around the mask at that time.

The following protocols, selected from a long series of such experiments, demonstrate the general mode of procedure and the results obtained.

PROTOCOL NO. 1. (EXPERIMENT NOS. 97 AND 98.)

Two laboratory boys[6] served as subjects. Control plates were made as follows: A quantity of saliva was expectorated into a plate containing solidified agar, distributed by means of a sterile cotton plug, and a small

[6] The first experiment was performed upon ourselves to demonstrate the harmlessness of the procedure. Then several of our colleagues and about 8 different laboratory boys served as subjects in these experiments. Yet, owing to the large number of experiments that were done, it was found necessary to use the same laboratory boys repeatedly as subjects. However, a period of at least a week was allowed to elapse before a boy was again called upon to serve, and then smears were made from nostrils and saliva to determine whether by any chance *Bacillus prodigiosus* was present. These tests proved to be in every case negative. In order to gain some idea of the length of time that *Bacillus prodigiosus* can persist in the mouth, one of us rinsed his mouth with a suspension of prodigiosus (one slant in 10 cubic centimeters of salt solution) and gargled some of the same suspension. Plates inoculated with his saliva at intervals gave the following results:

Saliva after three-fourths hour	Plate No. 1: Overgrown with prodigiosus.
Saliva after 3½ hours	Plate No. 1: Overgrown with prodigiosus. Plate No. 1: Overgrown with prodigiosus.
Saliva after 5½ hours	Plate No. 1: Overgrown with prodigiosus.
Saliva after 16 hours	Plate No. 1: 20 colonies of prodigiosus. Plate No. 2: 15 colonies of prodigiosus.
Saliva after 19½ hours	Plate No. 1: No colonies of prodigiosus. Plate No. 2: No colonies of prodigiosus.

Two meals were taken during the course of this experiment.

portion spread thinly over a second agar plate. Both plates were preserved for growth and examination. At the same time the nostrils were swabbed with a small pledget of sterile cotton moistened with salt solution and this rubbed over solidified agar. (In no case was *B. prodigiosus* obtained from the nostrils or saliva in these controls taken before spraying.)

The boys were clothed with operating gowns.

Boy No. 1 wore a Mukden mask consisting of two and one-half layers of Johnson and Johnson absorbent cotton. Thin layers of this cotton in Petri dishes were steamed in an Arnold sterilizer and then placed in the ice box so that water would condense upon the cotton and inside of the Petri dishes. A portion of the cotton thus moistened was placed in approximately the center of the mask between the layers of the cotton, so that when the mask was in place it lay before the mouth and nostrils. Small bits of the moist cotton were placed within the nostrils and a larger piece before the mouth and nostrils. This latter piece was held in place by the mask. Small pieces of dry absorbent cotton were placed on each side of the nose and then the Mukden mask was tied in place. Automobile goggles were worn over the eyes. The exposed portion of the head above the mask was covered with a cloth.

Boy No. 2 wore a Broquet mask of heavy Canton flannel cloth. This hood had been used in a number of previous experiments after each of which it had been disinfected in lysol solution and placed in the sun to dry. Small bits of the steamed moist cotton were placed loosely within the nostrils, and as in the preceding instance a larger piece of the same cotton was placed over the mouth and nostrils. This was held in place by a strip of gauze which was tied at the back of the head. A straw hat was placed on the boy's head, and the mask was then put on and tied in snugly around the neck. (See Plate V, fig. 2.)

The two boys, thus masked, were taken into a stable with the walls boarded up to keep out the light and to prevent currents of air. A suspension of prodigiosus bacilli in 0.5 per cent sodium chloride solution (1 agar slant in about 40 cubic centimeters) was sprayed by means of a throat atomizer connected with an automobile pump. The spray was directed alternately toward one mask and then the other for a period of three minutes. The boys were then brought back to the laboratory. But the gowns, goggles, and head-cloths were removed before they entered the laboratory building which was only a few meters away. This was done in order to prevent a possible contamination of the test culture plates with prodigiosus bacilli which might have become scattered in the air while the masks were being removed. (The gowns and cloths were sterilized in an autoclave at 120°C. before they were used in the next experiment.)

The subjects then proceeded to the door of the laboratory room where the masks were removed and cultures made as follows:

The cotton taken from before the mouth, that from the nostrils, and, in case of the Mukden mask, that from the interior of the mask were transferred by sterile forceps to separate Petri dishes containing solidified agar, and rubbed over the surface of the agar. Each mass of cotton was then transferred to a second Petri dish well wet with salt solution and rubbed over the second plate and left on the surface of the media.

The cotton was wet in order to afford conditions for growth to any *B. prodigiosus* which might otherwise have remained in the dry center of the cotton. (In a few cases the wet cotton mass alone, after twenty-four hours, showed the red color indicative of the growth of *B. prodigiosus*.) All plates were left in the dark at room temperature (25° to 30°C.), protected by glass jars.

The result of all the cultures, read two days later, was as follows:

Boy No. 1. Mukden mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Cotton before mouth after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Cotton within the mask after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*

Boy No. 2. Canton flannel Broquet mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent. Plate No. 1: Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*

A plate exposed to the air of the laboratory room, while the above plates were being prepared, showed no red colonies.

DISCUSSION OF PROTOCOL NO. 1.

This experiment shows that neither the Mukden mask nor the heavy Canton flannel Broquet mask is able to hold back completely prodigiosus bacilli when they are sprayed in large numbers continuously for a period of three minutes about the heads of the subjects. As this Broquet mask is the most efficient of all the masks with which we have experimented, it follows that none of our masks can withstand this test. The fact that the moist cotton from the center of the Mukden mask contained many prodigiosus bacilli shows that some of the prodigiosus bacilli passed directly through the mask; or, in other words, that the inefficiency of this mask is not due solely to the fact that the bacilli pass around the edges of the cotton pad or through the free spaces at the sides of the nose which were,

perhaps, only imperfectly plugged with cotton.[7] In this experiment the masks are subjected to a much more severe test than would occur in practice; nevertheless, it presents conclusive evidence, we believe, that these masks do not offer absolute protection against infection with pneumonic plague.

PROTOCOL NO. 2. (EXPERIMENTS NOS. 69 AND 70.)

February 3. A fresh culture of *B. prodigiosus* upon slanted agar was suspended in 0.5 per cent sodium chloride solution and about one-half of this suspension was sprayed through an atomizer by means of an automobile pump. The spray was directed toward all parts of a small single-roomed stable with the walls boarded up to keep out the light and, to a certain extent, the currents of air. Three minutes after the spraying had been discontinued, two subjects, one wearing our Canton flannel Broquet mask and the other a "Mukden mask" were taken into the room and allowed to remain for ten minutes. The temperature of the stable measured 28° 5 C. The weather was overcast and there had been a drizzling rain of short duration about one hour before the experiment began.

Number of living B. prodigiosus in the air.

	Time after spraying.	Number of prodigiosus colonies.
Subjects exposed.	½ to 3 minutes	Innumerable.
	3 to 6½ minutes	11,400
	6½ to 9 minutes	1,416
	9 to 12 minutes	472
	12 to 23 minutes	63

Subject No. 1. Canton flannel Broquet mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 1: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.

[7] In another experiment we obtained further evidence that bacteria may pass directly through the cotton pad of the Mukden mask. Layers of cotton as thick as the Mukden mask, sufficiently wide to cover the entire face and overlapping at the back of the head, were held in place by a many-tailed bandage, no openings in the cotton or bandage being made for the eyes. The remaining portion of the subject's head and his neck were then bandaged with layers of cotton of the same thickness and a suspension of prodigiosus bacilli was sprayed about his head for a period of seven minutes. The bacilli were recovered from the cotton immediately before his mouth and from his saliva.

Subject No. 2. Mukden mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Cotton before mouth after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 1: Prodigiosus *present.*
Cotton within the mask after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.

DISCUSSION OF PROTOCOL NO. 2.

Living prodigiosus bacilli were very numerous at the beginning of the test, but decreased very rapidly during the ten minutes that the subjects were exposed. This must be regarded also as a very severe test, though by no means so severe as the preceding one. The Broquet mask withstood the tests, while the Mukden mask failed to hold back all the prodigiosus bacilli. This experiment, therefore, demonstrates clearly the superiority of the Broquet mask over the Mukden mask.

PROTOCOL NO. 3. (EXPERIMENTS NOS. 67 AND 68.)

February 1, 1912. Spraying as the preceding experiment. The two masked subjects were taken into the stable six minutes after the spraying had been discontinued and allowed to remain ten minutes. Hot, sunshiny day. Temperature in the stable 29°C.

Number of living prodigiosus bacilli in the air.

	Time after spraying.	Number of prodigiosus colonies.
Subjects exposed.	1 to 3 minutes	6,000
	3 to 6 minutes	2,760
	6 to 9 minutes	280
	9 to 12 minutes	127
	12 to 15 minutes	29
	15 to 30 minutes	1

Subject No. 1. Mukden mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus *present.* (Cotton red and 32 colonies.)
Cotton within the mask after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.

Subject No. 2. Canton flannel Broquet mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.

DISCUSSION OF PROTOCOL NO. 3.

This test was an extremely light one. A Petri dish exposed during the first three minutes that the masked subjects were in the room developed only 280 prodigiosus colonies and another, during the last three minutes, only 29 colonies. In spite of the small number of living prodigiosus bacilli that were in the air, the Mukden mask failed to hold back all of them. We are inclined to believe that this test is even a less severe one than that to which the masks were subjected during the recent plague epidemic in Manchuria, as the coughing patients in the crowded wards must have been throwing out hundreds of fine droplets almost continuously and, on account of the low temperature, the plague bacilli in these droplets must have remained suspended in the air in a viable condition for a considerable period of time. Since we have found repeatedly in tests which were not severe that the Mukden mask allowed bacilli to pass, we are forced to the conclusion that the sense of security felt by those who wore this mask in the Manchurian epidemic was not justified.

PROTOCOL NO. 4.

This experiment was carried out in a cold-storage room measuring about 2.5 by 3 meters at a temperature of 12°C. A 24-hour agar-culture of prodigiosus was suspended in about 40 cubic centimeters of 0.5 per cent sodium chloride solution and filtered twice through cotton. A portion of this suspension was sprayed by means of a throat atomizer connected by rubber tubing with a two-cylinder force-pump such as is used in filling automobile tires. The spraying was continued for a period of two minutes, the spray being directed toward all portions of the room. The pump was then removed and the door of the cold room quickly closed. A period of two hours was allowed to elapse, and then the three masked boys were hurried into the room and the door was closed behind them. They remained ten minutes in the room. During this time each held in his hand an open Petri dish containing solidified agar and closed it immediately after leaving the cold room.

Boy No. 1 wore a Mukden mask, boy No. 2 our Canton flannel Broquet mask. The usual measures against accidental contamination with *B. prodigiosus* were adopted. Boy No. 3 wore a mask of wet gauze. Strips of

gauze were boiled and while still warm were squeezed out and applied loosely over the lower portion of the face from the eyes to below the chin. The gauze was not in layers but was placed irregularly as in surgical dressings which are intended to absorb pus. A many-tailed bandage with holes for the eyes, such as is used with the Mukden mask, pressed the moist gauze firmly against the face and held it snugly in place. This mask was about five or six centimeters thick over the mouth and became thinner toward the edges. Goggles were worn by this boy also and the top of his head was covered with a cloth reaching down to the mask.

Boy No. 1. Mukden mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Prodigiosus absent.
Cotton within mask after exposure	Plate No. 1: Prodigiosus present. Plate No. 2: Prodigiosus present.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus present. Plate No. 2: Prodigiosus present.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus present. Plate No. 2: Prodigiosus present.
Plate held by boy during exposure	4,420 prodigiosus colonies.

Boy No. 2. Broquet mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Plate held by boy during exposure	4,000 prodigiosus colonies.

Boy No. 3. Mask of wet gauze.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus present. Plate No. 2: Prodigiosus present.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus present. Plate No. 2: Prodigiosus present.
Plate held by boy during exposure	4,485 prodigiosus colonies.

DISCUSSION OF PROTOCOL NO. 4.

In spite of the long interval (two hours) which elapsed between the spraying and the exposure of the subjects, this test must be regarded as a very severe one, for the plates show that numerous living prodigiosus bacilli still remained suspended in

the air at the time of the exposure. Furthermore, the number of living bacilli in the air in the cold room remains practically constant during the ten minutes of the test, while, as we have seen, in the warm stable there is a rapid decrease. This experiment shows again the superiority of our Broquet mask over the Mukden mask. It also proves that prodigiosus bacilli may pass directly through the cotton pad of the Mukden mask, for a piece of moist cotton placed near the center of the pad contained prodigiosus bacilli after the test. The mask of wet gauze also failed to hold back all the bacilli and is hence inferior to our Broquet mask. The experiment does not afford any evidence as to the relative efficiency of the Mukden mask and the mask of moist gauze.

PROTOCOL NO. 5.

March 1, 1912. The mouth of one of us was rinsed with sterile salt solution and then about 10 cubic centimeters of saliva were collected in a sterile test tube. One slant of a fresh prodigiosus culture was suspended in this saliva. The resulting suspension was thoroughly shaken and then taken a little at a time into the mouth and made into a spray by being blown between the lips. The spraying was done in a cold storage room at 9°C. The room was then kept closed for one hour, when the three masked subjects were quickly taken in and the door closed behind them. They remained inside ten minutes, each subject holding during that time an open Petri dish of solidified agar.

The masks were removed and cultures made as in the preceding experiment.

Number of living prodigiosus bacilli in the air.

	Number of prodigiosus colonies.
Plate held by subject No. 1	2,340
Plate held by subject No. 2	2,405
Plate held by subject No. 3	3,120

Subject No. 1. Mukden mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Cotton before mouth after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Cotton within the mask after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Saliva taken after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.

Subject No. 2. Canton flannel Broquet mask.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Saliva taken after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.

Subject No. 3. Mask of wet gauze.

Saliva taken before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils before exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton from nostrils after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.
Cotton before mouth after exposure	Plate No. 1: Prodigiosus *present.* Plate No. 2: Prodigiosus *present.*
Saliva taken after exposure	Plate No. 1: Prodigiosus absent. Plate No. 2: Prodigiosus absent.

DISCUSSION OF PROTOCOL NO. 5.

This experiment was designed to approximate more nearly to the conditions that occurred in Manchuria. It seemed possible that the viscid sputum of pneumonic plague might form larger droplets than the salt solution of our experiments and on that account be unable to pass through the masks. Preliminary tests were made by taking prodigiosus bacilli into the mouth and then holding Petri dishes containing solidified agar immediately before the mouth while talking or coughing. It was found that under these conditions prodigiosus bacilli were emitted in too small numbers and too inconstantly for the method to be satisfactory in testing our masks. Swabbing the vocal cords with the bacilli might have given satisfactory results, but this was not tried. Instead of this, it was decided to blow saliva containing prodigiosus bacilli between the lips thus converting it into a spray. The droplets of saliva produced in this way apparently passed through the masks as readily as the salt solution droplets from the atomizer. This experiment furnishes strong evidence that droplets of sputum from pneumonic-plague patients may be able to pass through the Mukden mask.

General discussion.—The protocols which have been cited could be supplemented by numerous others[5] giving similar results.

While these experiments furnish evidence that fine droplets of sputum of patients suffering from pneumonic plague may pass through the mask that was so widely used in Manchuria, yet they do not at all indicate that this mask was entirely without value. Obviously, the mask would hold back gross visible particles of sputum which are sometimes thrown out in coughing. Moreover in our experiments, when prodigiosus bacilli were recovered from the nostrils, it is probable that in the same test without the mask far greater numbers would have entered; in other words, it seems probable that great numbers of bacteria, that otherwise would have entered the nose and mouth, remain on the surface of the mask and in its substance.

Hence we believe that masks should be worn by those attending pneumonic-plague patients, but that they should not be regarded as affording absolute protection against infection; bearing this in mind, even when masked, one should remain in the near vicinity of the patient only so long as is necessary for the work in question.

CONCLUSIONS.

(1) The "Mukden mask" in general use during the epidemic of pneumonic plague in Manchuria, during the winter of 1910 to 1911, does not prevent the passage into the mouth and nostrils of *B. prodigiosus* when contained in small droplets sprayed

[5] The Mukden mask was used in 42 tests and was found to hold back the prodigiosus bacilli in only 6 of these and to allow them to pass in 36 instances. Of the 6 tests in which the bacilli failed to penetrate the mask, three were preliminary experiments to determine whether a satisfactory spray was produced in talking or coughing after rinsing the mouth with a suspension of prodigiosus bacilli; plates exposed during the experiment showed less than 20 colonies each and the method was therefore abandoned. In two others of these 6 tests the exposed plates showed only 15 and 200 colonies respectively. Finally, in the last of these 6 tests, the subject drew the cotton from before his mouth and nose into his mouth where it became saturated with saliva and plates were not made from the cotton within the nostrils.

In some of the tests in which the prodigiosus bacilli passed through the Mukden mask, the exposed plates contained only a few colonies, indicating that the test was much less severe than those in the protocols recorded above.

Our Canton flannel Broquet mask was employed in 17 different experiments. It held back all the prodigiosus bacilli in 10 of these and allowed some of them to pass in 7.

around the mask. This mask consists of a pad of absorbent cotton held over the mouth and nose by a many-tailed gauze bandage.

(2) A hood of heavy Canton flannel cloth, covering the entire head and tied in snugly at the neck, withstands much severer tests than does the Mukden mask. It does not, however, offer an absolute barrier to the passage of prodigiosus bacilli into the mouth and nostrils of the subject. This mask, with a window in front, is not more inconvenient nor more uncomfortable than the Mukden mask.

(3) It is shown that the inefficiency of the Mukden mask is not due solely to the fact that the mask fails to conform to the configuration of the face but that the bacteria may pass directly through the mask; for a piece of moist cotton placed in the center of the mask was found after the test to contain prodigiosus bacilli.

(4) It is believed that, although masks hold back many bacteria that would otherwise pass into the mouth and nostrils, nevertheless their use during the recent epidemic of pneumonic plague in Manchuria lent a *false* sense of security which may have led to the taking of unnecessary risks. We believe that these experiments fully justify the conclusion that masks such as were used in that epidemic do not offer an absolute protection against pneumonic plague.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

ILLUSTRATIONS.

PLATE I.

Pneumonic plague hospital, Mukden.
FIG. 1. Side view.
2. Rear view.

PLATE II.

FIG. 1. American laboratory within courtyard of plague hospital, Mukden.
2. Room in which necropsies were performed in Mukden.

PLATE III.

FIG. 1. Ward with attendants in plague hospital, Mukden.
2. Some of the nurses and attendants outside of plague ward.

PLATE IV.

Uniform adopted for protection from infection when in contact with pneumonic-plague cases.

PLATE V.

Masks for protection against pneumonic plague.
FIG. 1. The Mukden mask.
A. The many-tailed bandage to hold the pad securely in place.
B. The cotton pad wrapped in gauze.
2. Two subjects wearing the modified Broquet mask and the Mukden mask, respectively, ready for exposure to the sprayed bacilli.

PLATE VI.

The tarbagan (*Arctomys bobac* Schreb.). (Photograph by Dr. Wu.)

PLATE VII.

FIG. 1. Lung of guinea pig which died of advanced plague infection after being exposed to air in which plague bacilli were suspended by means of spraying.
2. Lung of monkey which died of pneumonic-plague infection from inhalation; lobular pneumonia.
3. Lung of monkey which died of pneumonic-plague infection from inhalation, showing progression of lesions; lobular and lobar pneumonia.

PLATE VIII.

Human lung in pneumonic plague; marked lobar pneumonia, showing deep hyperæmia of bronchi.

PLATE IX.

Human lung in pneumonic plague, showing more well-marked areas of lobular pneumonia and pleural exudate.

PLATE X.

Human lung, pneumonic plague, showing gray hepatization and fibrinous pleurisy.

PLATE XI.

Human throat, larynx, and trachea in pneumonic plague. Marked hyperæmia of the larynx and trachea; the tonsils not swollen; marked hyperplasia of an incised lymphatic gland to the right of the trachea and of a small more hæmorrhagic gland at the base of the trachea.

PLATE XII.

FIG. 1. Lung of dog with pneumonic plague.
2. Liver of tarbagan (*Arctomys bobac* Schreb.), showing chronic plague infection.

PLATE XIII.

Microscopical section of human lung, showing particularly congestion of the alveoli filled with plague bacilli. (Drawn from magnification of 150 diameters.)

PLATE XIV.

Microscopical section of human lung, showing particularly alveoli filled with plague bacilli. (Drawn from magnification of 780 diameters.)

PLATE XV.

Microscopical section of human lung in advanced stage of pneumonia, showing bacilli in great masses about blood vessels. (Drawn from magnification of 780 diameters.)

PLATE XVI.

Microscopical section of human lung in stage of hepatization with absence of fibrin. Section stained for fibrin by Weigert's method. (Drawn from magnification of 330 diameters.)

PLATE XVII.

Microscopical section of human lung in pneumonic plague, showing character of alveolar exudate. (Drawn from magnification of 330 diameters.)

PLATE XVIII.

Microscopical section of human tonsil, pneumonic plague, showing congestion. (Drawn from magnification of 150 diameters.)

Fig. 1. Side view.

Fig. 2. Rear view.

PLATE I. PNEUMONIC-PLAGUE HOSPITAL, MUKDEN.

Fig. 1. American laboratory within courtyard of plague hospital, Mukden.

Fig. 2. Room in which necropsies were performed in Mukden.

PLATE II.

Fig. 1. Ward with attendants in plague hospital, Mukden.

Fig. 2. Some of the nurses and attendants outside of plague ward.

PLATE III.

PLATE IV. UNIFORM ADOPTED FOR PROTECTION FROM INFECTION WHEN IN CONTACT WITH PNEUMONIC-PLAGUE CASES.

Fig. 1. The Mukden mask. A. The many-tailed bandage to hold the pad securely in place. B. The cotton pad wrapped in gauze.

Fig. 2. Two subjects wearing the modified Broquet mask and the Mukden mask, respectively, ready for exposure to the sprayed bacilli.

PLATE V. MASKS FOR PROTECTION AGAINST PNEUMONIC PLAGUE.

PLATE VI. The TARBAGAN (*Arctomys bobac* Schreb.).

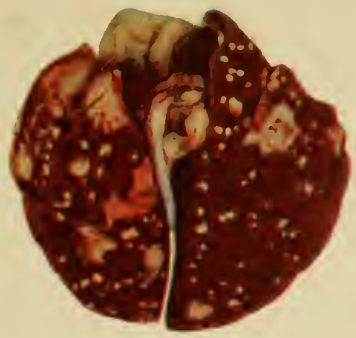


Fig. 1. Lung of guinea pig which died of advanced plague infection, after being exposed to air in which plague baoilli were suspended by means of spraying.

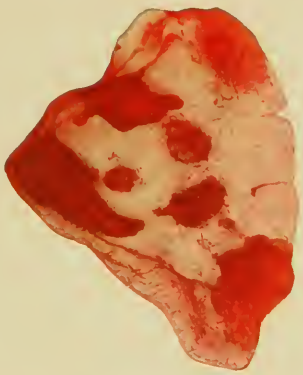


Fig. 2. Lung of monkey which died of pneumonic-plague infection from inhalation; lobular pneumonia.

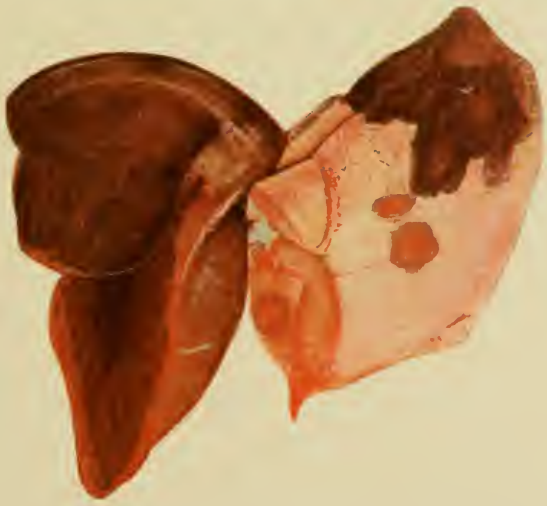


Fig. 3. Lung of monkey which died of pneumonic-plague infection from inhalation, showing progression of lesions; lobular and lobar pneumonia.

PLATE VII.

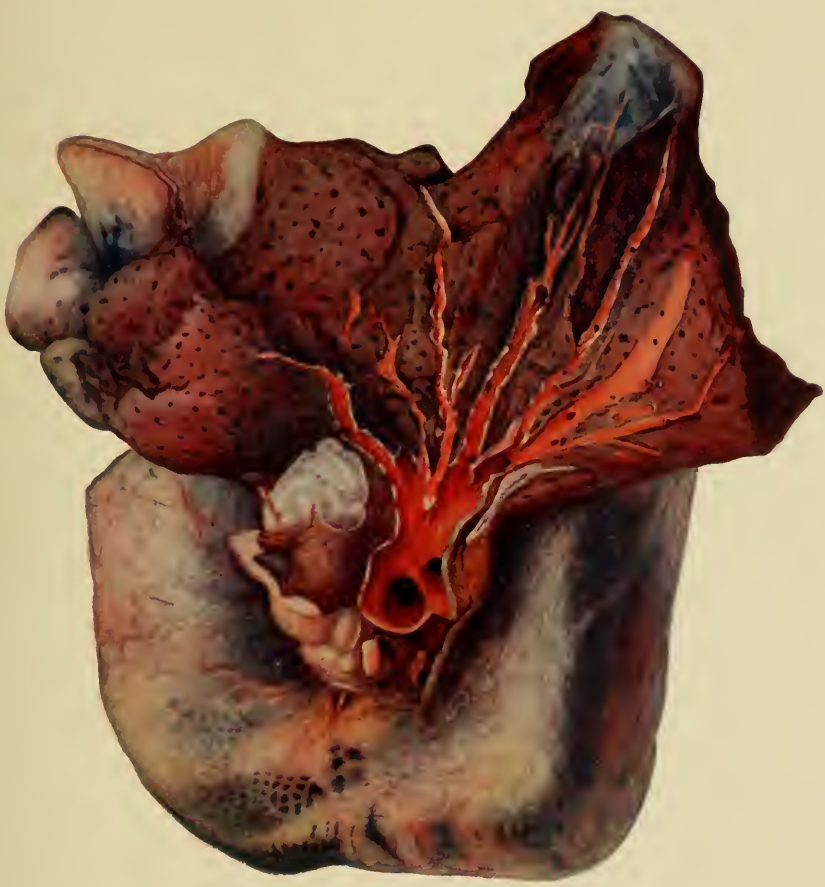


PLATE VIII

PLATE I. LUNG IN PNEUMONIC PLAGUE. LOBAR PNEUMONIA: SHOWING DEEP HYPERÆMIA OF BRONCHI.

Plate I of the Report of the International Plague conference is reproduced here as Plate VIII.

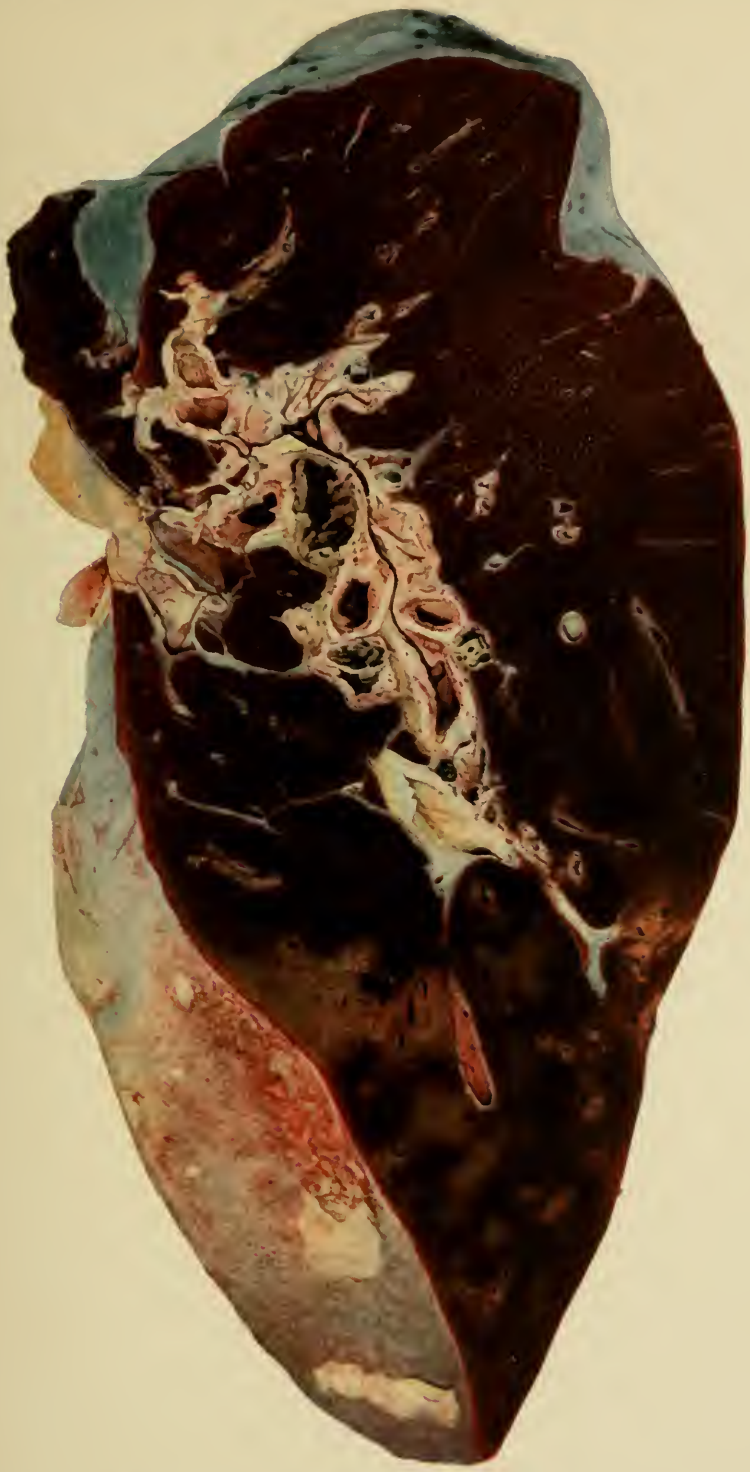


PLATE IX. HUMAN LUNG IN PNEUMONIC PLAGUE, SHOWING MORE WELL-MARKED AREAS OF LOBULAR PNEUMONIA AND PLEURAL EXUDATE.

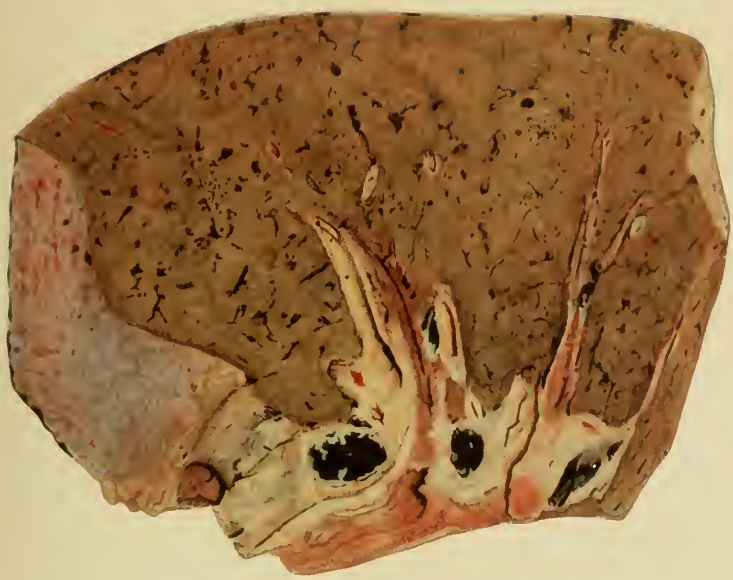


PLATE X. HUMAN LUNG, PNEUMONIC PLAGUE, SHOWING GRAY HEPATIZATION AND FIBRINOUS PLEURISY.

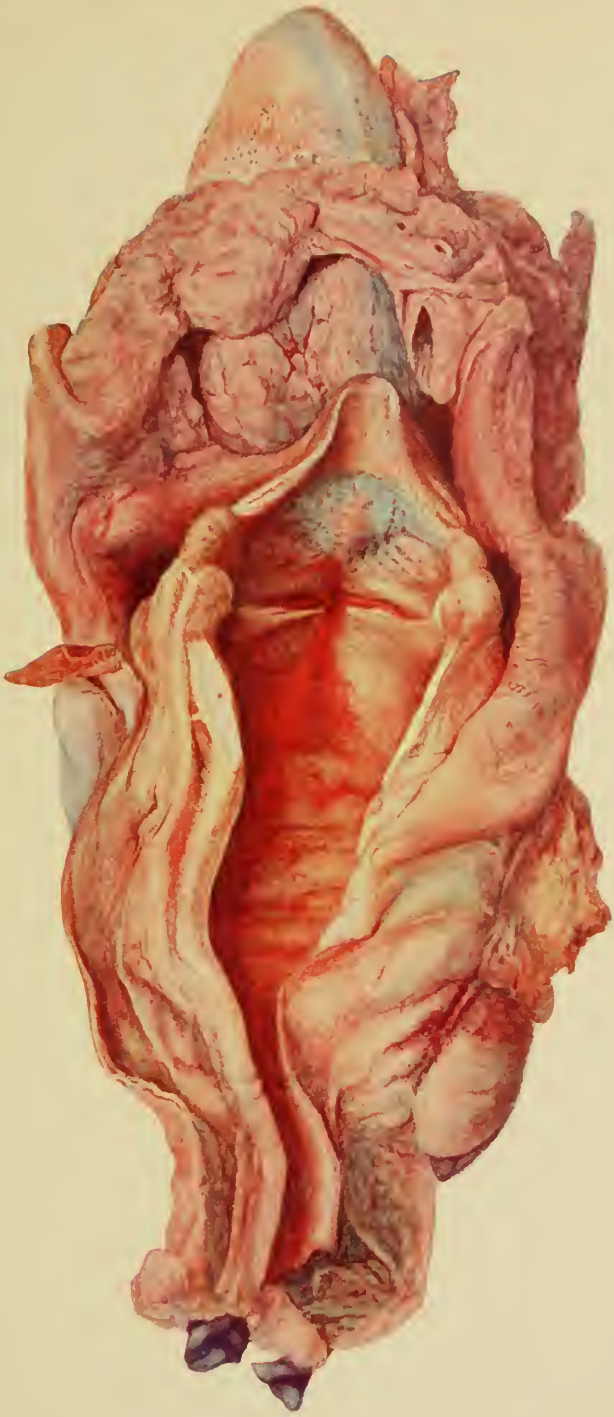


PLATE XI.

PLATE II. THROAT, LARYNX, AND TRACHEA IN PNEUMONIC PLAGUE. MARKED HYPERÆMIA OF THE LARYNX AND TRACHEA; TONSIL NOT SWOLLEN. MARKED HYPERPLASIA OF AN INCISED LYMPHATIC GLAND TO THE RIGHT OF THE TRACHEA, AND OF A SMALL MORE HÆMORRHAGIC LYMPHATIC GLAND AT THE BASE OF THE TRACHEA.

Plate II of the Report of the International Plague Conference is reproduced here as Plate XI.

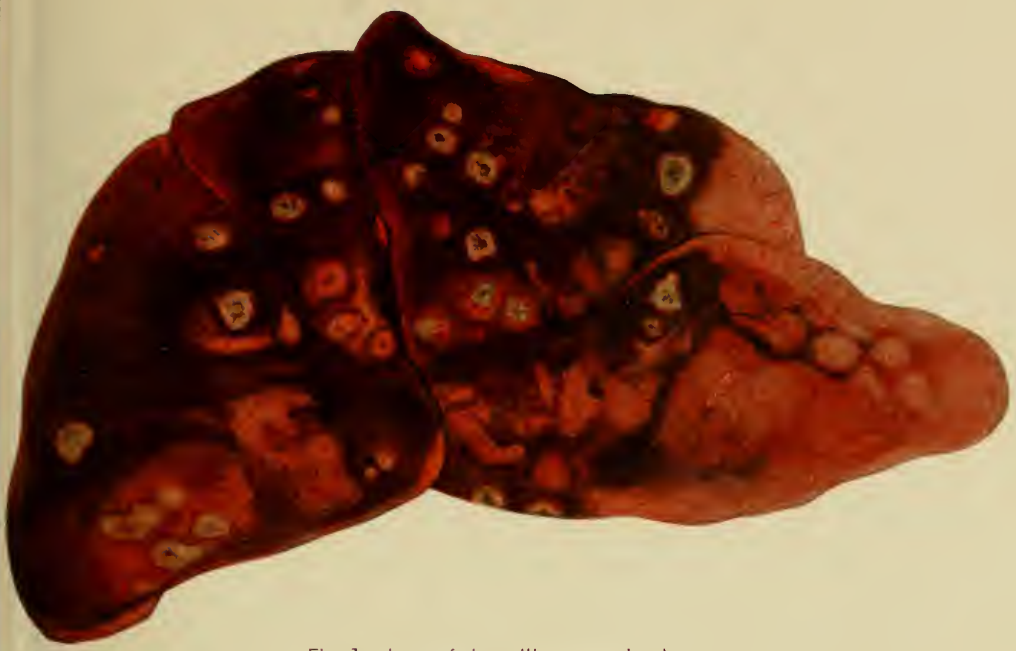


Fig. 1. Lung of dog with pneumonic plague.

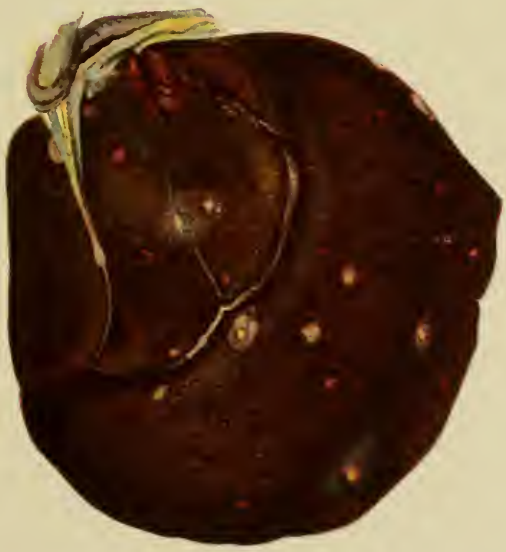


Fig. 2. Liver of tarbagan (*Arctomys bobac* Schreb.), showing chronic plague infection.

PLATE XII.

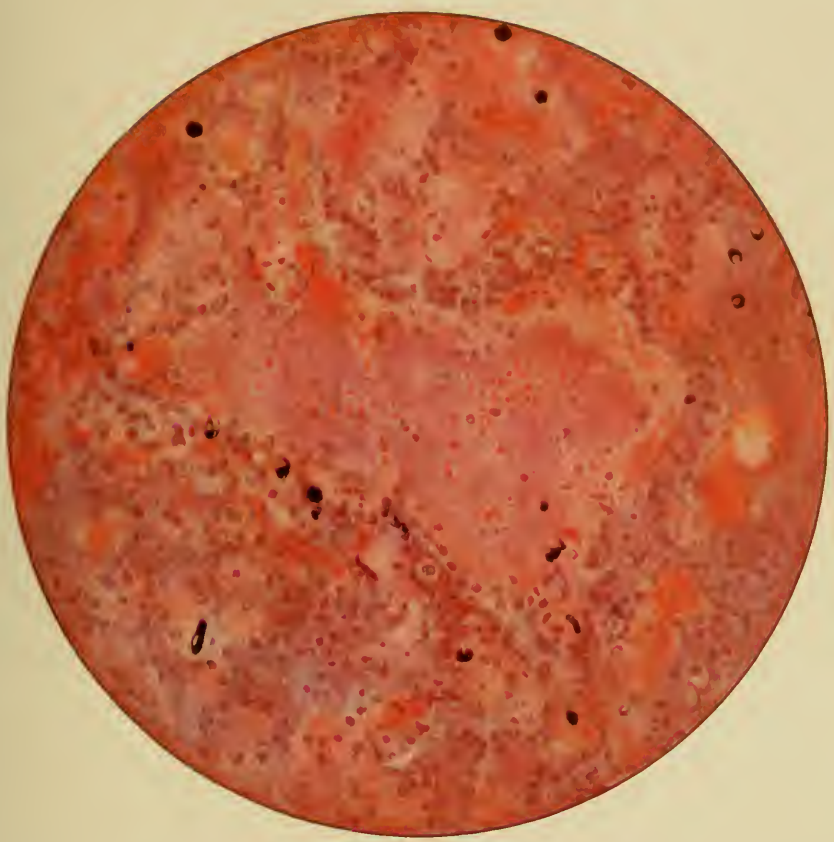


PLATE XIII. MICROSCOPICAL SECTION OF HUMAN LUNG, SHOWING PARTICULARLY CONGESTION OF THE ALVEOLI FILLED WITH PLAGUE BACILLI.

(Drawn from magnification of 150 diameters.)

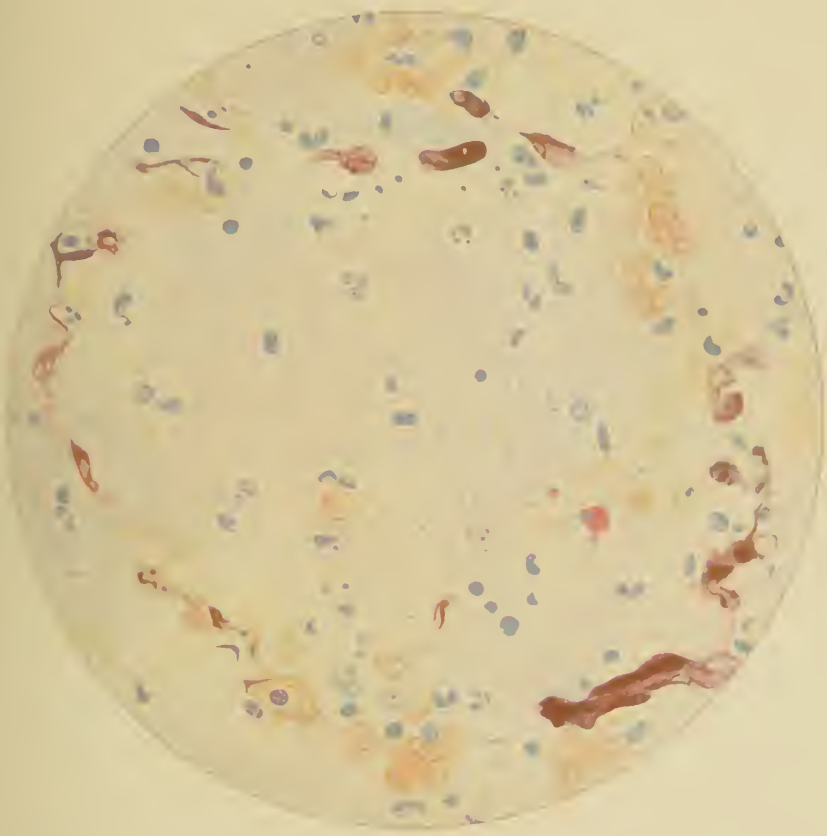


PLATE XIV. MICROSCOPICAL SECTION OF HUMAN LUNG, SHOWING PARTICULARLY ALVEOLI FILLED WITH PLAGUE BACILLI.

(Drawn from magnification of 780 diameters.)

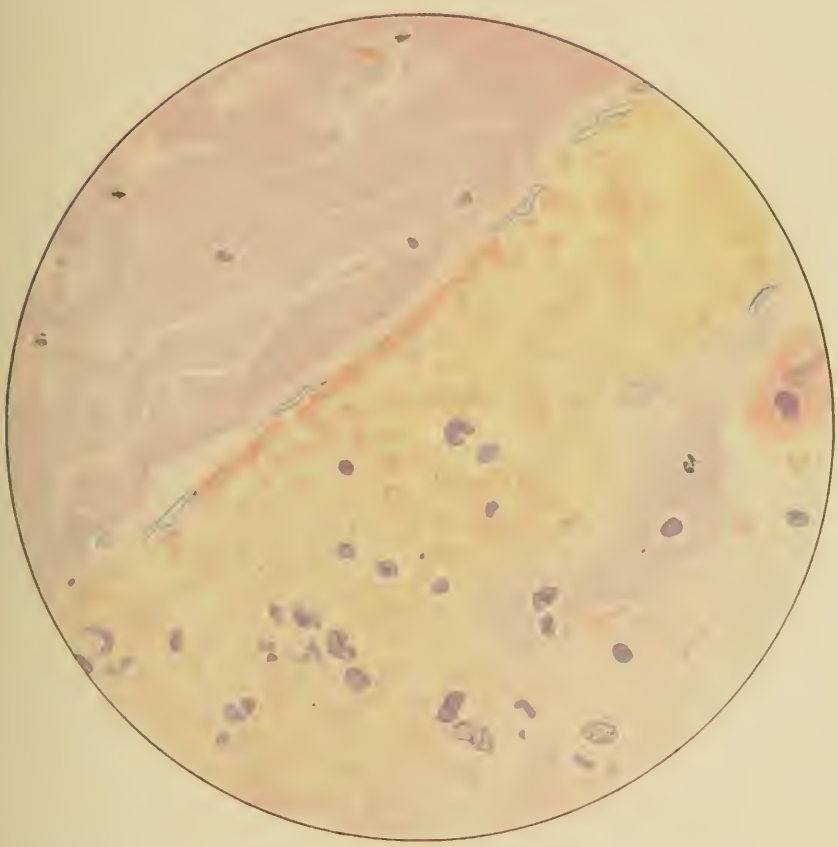


PLATE XV. MICROSCOPICAL SECTION OF HUMAN LUNG IN ADVANCED STAGE OF PNEUMONIA, SHOWING BACILLI IN GREAT MASSES ABOUT BLOOD VESSELS.

(Drawn from magnification of 780 diameters.)

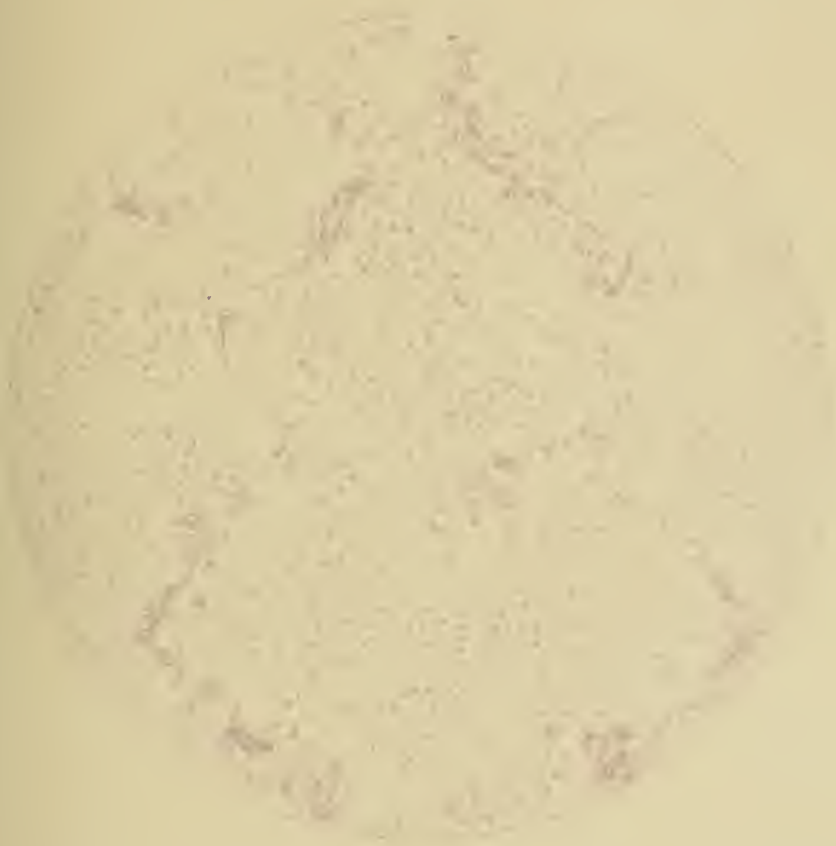


PLATE XVI. MICROSCOPICAL SECTION OF HUMAN LUNG IN STAGE OF HEPATIZATION WITH ABSENCE OF FIBRIN. SECTION STAINED FOR FIBRIN BY WEIGERT'S METHOD.

(Drawn from magnification of 330 diameters.)

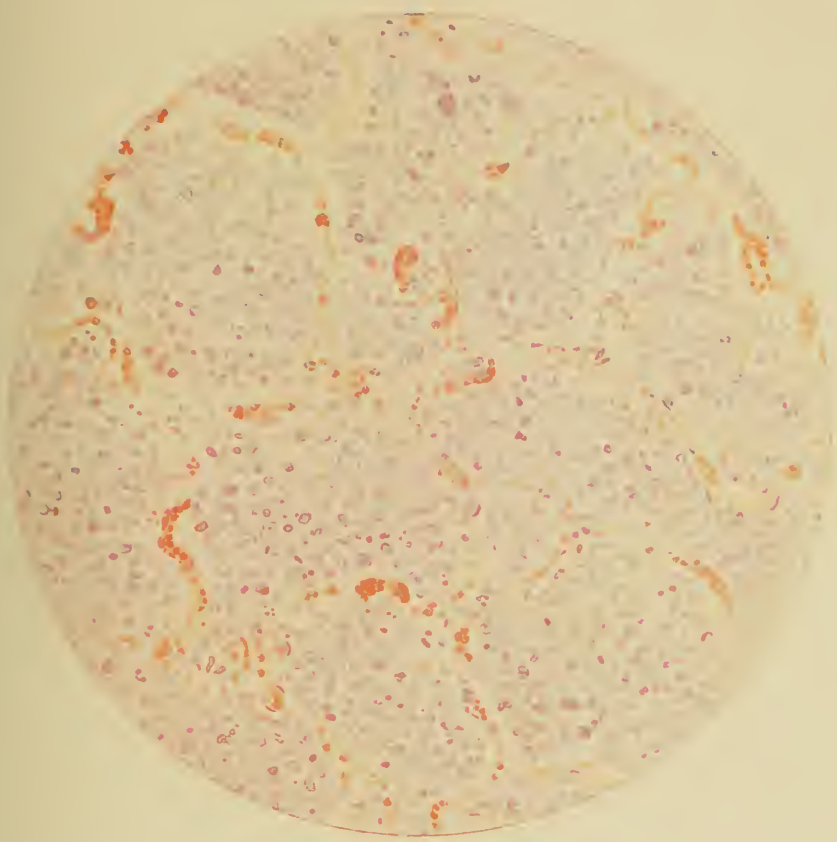


PLATE XVII. MICROSCOPICAL SECTION OF HUMAN LUNG IN PNEUMONIC PLAGUE, SHOWING CHARACTER OF ALVEOLAR EXUDATE.

(Drawn from magnification of 330 diameters.)

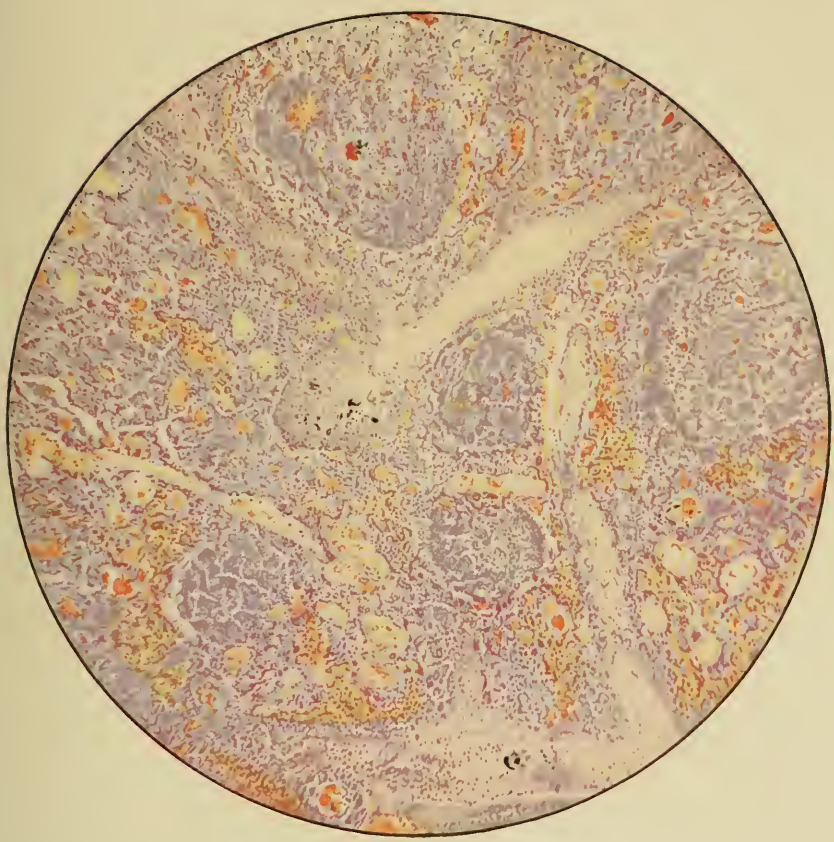


PLATE XVIII. MICROSCOPICAL SECTION OF HUMAN TONSIL, PNEUMONIC PLAGUE, SHOWING CONGESTION.

(Drawn from magnification of 150 diameters.)

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

THE SUBANUNS OF SINDANGAN BAY.

By EMERSON B. CHRISTIE.

121 pages, 1 map, 29 plates.

Order No. 410. Paper, $1.25 United States currency, postpaid.

Sindangan Bay is situated on the northern coast of Zamboanga Peninsula. The Subanuns of this region were studied by Mr. Christie during two periods of five and six weeks, respectively.

The following is an abstract from the contents of Mr. Christie's report on the Subanuns: Habitat and history; relations with the Moros; material culture; houses; industries; trade; agriculture; family life; social customs; administration of justice; religion; the medicine man; ceremonies; tales; word-lists; physical measurements.

The 29 plates illustrate the Subanuns at work and at play; their industries, houses, altars, and implements; and the people themselves.

THE HISTORY OF SULU.

By NAJEEB M. SALEEBY.

275 pages, 4 maps, 2 diagrams.

Order No. 406. Paper, $0.75 United States currency, postpaid.

In the preparation of his manuscript for The History of Sulu Doctor Saleeby spent much time and effort in gaining access to documents in the possession of the Sultan of Sulu. It is fortunate that these records have now been translated and preserved in permanent form. This book is a history of the Moros in the Philippines from the earliest times to the American occupation.

STUDIES IN MORO HISTORY, LAW, AND RELIGION.

By NAJEEB M. SALEEBY.

107 pages, 16 plates, 5 diagrams.

Order No. 405. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

This volume deals with the earliest written records of the Moros in Mindanao. Doctor Saleeby was fortunately able to obtain exact copies of carefully preserved early records written in the Magindanao dialect with Arabic characters. The author presents translations of these as well as 16 half-tone illustrations of certain pages from the originals. The names of the rulers of Magindanao are recorded in five folding diagrams.

NEGRITOS OF ZAMBALES.

By WILLIAM ALLAN REED.

83 pages, 62 plates.

Order No. 402. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

The introductory chapter deals with the general distribution of Negritos and with the distribution of the Philippine branch of the race. The succeeding chapters deal with the various industries, amusements, and social relations of these little men.

Plates from photographs, the greater part of which was taken for this publication, show ornaments, houses, men making fire with bamboo, bows and arrows, dances, and various types of the people themselves.

CONTENTS.

STUDIES ON PNEUMONIC PLAGUE AND PLAGUE IMMUNIZATION.

The "Philippine Journal of Science" is issued as follows:	U. S. currency.
Section A. Chemical and Geological Sciences and the Industries	$2.00
Section B. The Philippine Journal of Tropical Medicine	3.00
Section C. Botany	2.00
Section D. General Biology, Ethnology and Anthropology (Section D began with Volume V)	2.00
Entire Journal, Volume II, III, IV, or V	5.00
Entire Journal, beginning with Volume VI	7.00
Single numbers	.50
Volume I, 1906 (not divided into sections)	10.00
Supplement to Volume I (botany)	3.50
Volume I (without supplement)	6.50

Each section is separately paged and indexed.

Publications sent in exchange for the Philippine Journal of Science should be addressed: Library, Bureau of Science, Manila, P. I.

Subscriptions may be sent to the BUSINESS MANAGER, Philippine Journal of Science, Bureau of Science, Manila, P. I., or to any of the agents listed below:

AGENTS.

The Macmillan Company, 64–66 Fifth Avenue, New York City, U. S. A.
Wm. Wesley & Son, 28 Essex Street, Strand, London, W. C., England.
Martinus Nijhoff, Nobelstraat 18, The Hague, Holland.
Mayer & Müller, Prinz Louis Ferdinandstrasse 2, Berlin, N.W., Germany.
Kelley & Walsh, Limited, 32 Raffles Place, Singapore, Straits Settlements.
A. M. & J. Ferguson, 19 Baillie Street, Colombo, Ceylon.
Thacker, Spink & Co., P. O. Box 54, Calcutta, India.

Entered at the post-office at Manila, P. I., as second-class matter.

VOL. VII, SEC. B, No. 4 AUGUST, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

SECTION B

THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

RICHARD P. STRONG, PH. B., M. D.
EDITOR

MANILA
BUREAU OF PRINTING
1912

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

REPORT OF THE INTERNATIONAL PLAGUE CONFERENCE.

Held at Mukden, April, 1911, under the auspices of the Chinese Government.

Edited by ERICH MARTINI, G. F. PETRIE, ARTHUR STANLEY, AND RICHARD P. STRONG.

483 pages, 18 plates (2 colored, 4 half-tones, 12 charts and maps).

Order No. 416. Cloth, $3.50; paper, $2.50 United States currency, postpaid.

The proceedings of this International Conference and information gained therefrom, together with the results of certain bacteriological investigations, constitute the present report.

Nothing hitherto has been published which gives such a complete and comprehensive account of the entire subject of pneumonic plague.

Delegates from America (United States of), Austria-Hungary, France, Germany, Great Britain, Italy, Japan, Mexico, the Netherlands, Russia, and China attended the Conference.

The Bureau of Science of the Government of the Philippine Islands has been appointed sole agent for the distribution of the printed proceedings of the International Plague Conference.

THE SUGAR INDUSTRY IN THE ISLAND OF NEGROS.

By HERBERT S. WALKER.

145 pages, 10 plates, 1 map.

Order No. 412. Paper, $1.25 United States currency, postpaid.

Considered from the viewpoint of practical utility, Mr. Walker's Sugar Industry in the Island of Negros is one of the most important papers published by the Bureau of Science. This volume is a real contribution to the subject; it is not a mere compilation, for the author was in the field and understands the conditions of which he writes. The following is a brief synopsis of the contents:

Tables of soil analyses, both chemical and physical; analyses of the cane, juice and bagasse; estimates based on actual information as to the costs of production and of cultivation; and estimates of the cost and location of possible central factories. The island is considered by sugar-producing districts; the area of cultivation and the production per hectare are given, and the possibility for future expansion discussed.

The plates illustrate various phases of sugar industry from the cultivation of the field to the transportation of sugar in native sailboats.

A MANUAL OF PHILIPPINE SILK CULTURE.

By CHARLES S. BANKS.

53 pages, 20 plates.

Order No. 413. Paper, $0.75 United States currency, postpaid.

The silk industry is particularly adapted to be undertaken by persons with small capital, and like the making of hats in the Philippine Islands it should thrive with a little encouragement.

In A Manual of Philippine Silk Culture we have presented the results of several years' actual work with silk-producing larvæ together with a description of the new Philippine race. Half-tone plates illustrate in natural size silkworms in different stages of development, pupæ, adult moths, samples of cloth made from eri silk, hand reel, and silk house. Other plates illustrate the various appliances used in raising silkworms and in spinning silk; hand and power reels are illustrated; working drawings are given for a silk house and for a hand reel.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. THE PHILIPPINE JOURNAL OF
TROPICAL MEDICINE

VOL. VII AUGUST, 1912 NO. 4

THE ETIOLOGY OF BERIBERI.

By RICHARD P. STRONG and B. C. CROWELL.
(From the Biological Laboratory, Bureau of Science, Manila, P. I.)

The etiology of beriberi is a problem about which there has been very extensive and prolonged controversy. The theories advanced in regard to the cause of the disease have been numerous and of widely different characters. Many of them have been based upon little or no accurate experimental investigation. Notwithstanding the large number of very valuable observations that have appeared in the literature on this subject during the past few years, at the present time there is no theory of the cause of beriberi that has been entirely accepted. The reason for this becomes more apparent when we consider the recent publications upon the subject. While very extensive feeding experiments by numerous investigators have been performed upon fowls, regarding the production of polyneuritis gallinarum (Eijkman), and while a few similar experiments have been employed, even sometimes successfully, by several investigators in relation to the production of a "beriberi-like" disease in other animals, nevertheless, there has been, regarding the etiology of beriberi, not a single experiment upon man which, from a scientific standpoint, we can regard in any way as a crucial test, with the exception of that one performed by Fraser and Stanton[1] in

[1] Studies from Institute for Medical Research. Federated Malay States (1909), No. 10; *Lancet* (1909), 1, 451.

1909. At the close of their publication regarding this experiment, these authors state:

> The general results [of these experiments] lend support to the view that the disease beriberi as it occurs in this Peninsula has, if not its origin in, at least, an intimate relationship with the consumption of white rice and justify further research along these lines.

We have referred to the fact that the theories regarding the etiology of beriberi have been numerous. However, it is not our intention to consider them in detail in this publication. They have been discussed in numerous text-books and, among other authors, particularly by Herzog of this laboratory in 1906,[2] and more recently by Castellani[3] and by Schaumann.[4] However, we wish to consider briefly the question of whether beriberi is an infectious disease, owing its origin to some living specific microörganism, either bacterial or protozoal, or its toxin, and conveyed directly or indirectly from man to man, or whether it is one due to disturbances in metabolism caused by an abnormal diet. Among those who have had a wide experience with beriberi and who have favored the theory that the disease is an infectious one and not one due to deficient or scanty nutrition may be mentioned Manson,[5] Scheube,[6] Balz,[7] Jeanselme,[8] le Dantec,[9] Marchoux,[10] Daniels,[11] Wright,[12] Castellani,[13] and Shibayama,[14] and the arguments which some of these writers deduce against the theory of a dietetic causation are very convincing. Castellani,[15] writing in 1910 after a consideration of Fraser and Stanton's experiments, states:

[2] *This Journal* (1906), 1, 709.

[3] Castellani and Chalmers, Manual of Tropical Medicine. London (1910), 888.

[4] *Beiheft z. Arch. f. Schiffs- u. Trop.-Hyg.* (1910), 14, 329.

[5] Tropical Diseases. London (1907), 367; Allbutt's System of Medicine (1907), 2, Pt. II, 619.

[6] Die Krankheiten der warmen Länder. Jena (1903), 265.

[7] Mense's Handbuch der Tropenkrankheiten (1905), 146.

[8] Le béribéri. Paris (1907), 1; *Bull. Soc. path. exotique* (1910), 3, 8.

[9] *Ibid., Bull. Soc. path. exotique* (1910), 63, 118, 122.

[10] *Ibid.*, 116.

[11] Studies from Institute for Medical Research. Federated Malay States (1906), 4, No. 8, Pt. I, 91.

[12] *Ibid.* (1902), 2, No. 2, 58.

[13] *Loc. cit.*

[14] *This Journal, Sec. B* (1910), 5, 123.

[15] Castellani and Chalmers, Manual of Tropical Medicine. London (1910), 884.

To summarize from the evidence, it appears more likely that a parasite will be found to be the spreader of the disease, which makes it more probable that the actual cause will be found to be a protozoon than that it is due to diet, which, however, may be a predisposing cause, especially if the nutritive value of the food is low, or the proportions wrong.

Shibayama [16] also holds a somewhat similar view:

It is therefore not unreasonable to assume that the microörganisms of beriberi are only present in the Orient and, given a predisposing cause, are capable of causing the disease, whereas in the West beriberi does not appear, owing to the absence of the infecting organisms, although the same favorable predisposing cause may be present.

Marchoux [17] (also writing in 1910) believes that a diet of white rice furnishes in the intestine a favorable culture-medium for the development of the specific organism of beriberi and that the addition of rice-bran to the diet without doubt renders the condition in the intestine unfavorable for the development of this organism.

However, none of these authors has brought forward any definite proof that beriberi is caused by a specific microörganism and, although numerous other investigators have described either various species of bacteria or of protozoa as the cause of the disease, yet to-day not one of these claims has been substantiated from a scientific standpoint. Obviously, however, the fact that the specific microörganism for the disease has not been discovered is not a final argument against its infectious nature, for the causative organism in many diseases of an undoubted infectious nature has been sought for as diligently and in a manner equally as unsuccessful as in the case of beriberi. The result of the experiments of de Haan and Grijns [18] failing to demonstrate the presence of antibodies in the blood serum or various organisms of beriberi patients or of fowls suffering with polyneuritis, as well as that of the experiments of Shiga and Kusama,[19] who failed to obtain the reaction of deflection of the complement in the serum of beriberi cases, also does not exclude definitely the possibility of the disease being an infectious one.

However, if by scientifically controlled and accurate experiments we can produce the disease and exclude the influence of a living specific microörganism, the infectious theory of its origin

[16] *Loc. cit.*
[17] *Loc. cit.*
[18] *Genees. Tyds. v. Ned. Ind.* (1909), 49.
[19] *Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* (1911), 15, 61.

can be regarded as tenable no longer. Recently, few investigators[20] have pursued researches relating to a search for a specific organism for beriberi, but, on the other hand, the theory that the disease owes its origin to disturbances in nutrition has been widely discussed. However, as mentioned, the great majority of these recent publications relate to experiments upon the production of polyneuritis gallinarum and not to the production of beriberi in man.

In regard to the relation of polyneuritis gallinarum to beriberi, it seems advisable to consider the views of a number of investigators upon this subject. Shibayama[21] cautions against regarding polyneuritis of fowls as being identical with human beriberi, and Eijkman[22] states:

> Regarding the question of the relationship between polyneuritis gallinarum and beriberi, I have always expressed myself very reservedly. I have not claimed their identity in an etiological sense, but I also could not absolutely deny this, and am of the same opinion at the present time. In my first publication (1889) I have mentioned besides the many points of agreement in the two, also some points of difference.

Schaumann [23] believes:

> Not that both diseases are identical but that there seem to exist many more reasons for assuming that both are intimately related to each other than to presume the contrary, chiefly by taking into consideration that the same cause must not necessarily have the same results in different organisms.

Shiga and Kusama[24] state:

> It would be too much to say that the polyneuritis of animals and beriberi are identical without further proof. Many prominent authorities, both clinicians and pathologists, are of the opinion that in the diagnosis of human beriberi two chief symptoms, namely the sensory and motor paralyses of the lower legs and the dilatation and hypertrophy of the heart, must be considered.[25]

Fraser, in December, 1911,[26] states:

> On account of the prominence given the experiments on animals, it is possible to lose sight of the fact that we, as medical men, are concerned with the etiology of a disease which affects men, and is known as beriberi. * * * Experiments on fowls have proved to be of an inestimable value

[20] See Bréaudat, *Bull. Soc. path. exotique* (1910), 3, 13, 65, 123, 128, 317; le Dantec, *ibid.*, 62, 118, 122; Mathis and Leger, *ibid.*, 352; and Kohlbrügge, K. Akademie van Wetenschappen te Amsterdam (1911), 904.

[21] *Loc. cit.*

[22] *Arch. f. Schiffs- u. Trop.-Hyg.* (1911), 15, 702.

[23] *Trans. Soc. Trop. Med. & Hyg.* (1911), 5, 89.

[24] *Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* (1911), 15, 65.

[25] As Shiga only found dilatation of the heart in one monkey, his subsequent conclusions seem hardly justified.

[26] *Trans. Soc. Trop. Med. & Hyg.* (1911), 5, 81.

in working out the etiology of beriberi; the reaction in fowls is quite as delicate as, and comparable with, a reaction *in vitro*, but there is no necessity whatsoever to argue for or against the identity of polyneuritis in fowls and beriberi in man.

On the other hand, Chamberlain and Vedder [27] and Tsuzuki [28] believe that polyneuritis gallinarum and beriberi are essentially the same disease. Obviously, however, this latter view seems hardly justifiable until confirmed by further experiments on human beings.

We believe that, while experiments on fowls have been of very great benefit in elucidating many problems relating to the etiology and cure of beriberi, nevertheless, without similar experiments or observations on man, the results obtained with the former would not be applicable to man. The experiments on fowls have certainly in some instances furnished a justification for adopting a similar method of procedure in man in relation to the study and care of beriberi, and therein perhaps lies their greatest value. The results of the experiments on other animals, including monkeys (Eijkman,[29] Fraser and Stanton,[30] Schaumann,[31] Aron,[32] Shiga and Kusama,[33] Wright,[34] Durham,[35] and others), have been hitherto too uncertain to warrant our drawing conclusions from them in relation to beriberi in man. Monkeys as well as fowls sometimes suffer with polyneuritis from various causes.

Since, before we can arrive at a definite decision as to the infectious or noninfectious nature of the disease beriberi, we must have observations upon man in relation to this question, let us consider the previous literature upon the subject with the idea of ascertaining what experimental evidence there previously has been presented in which a reasonable supposition for a cause of the disease exists and in which the action of a specific organism conveyed directly or indirectly from man to man as the etiological factor has been rigidly excluded.

[27] *This Journal, Sec. B* (1911), 6, 395.
[28] *Bull. Soc. path. exotique* (1911), 4, 588.
[29] *Virchow's Arch.* (1897), 148, 523.
[30] Studies from Institute for Medical Research. Federated Malay States (1911), No. 12, 28.
[31] *Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* (1910), 14, 544.
[32] *This Journal, Sec. B* (1910), 5, 95.
[33] *Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* (1911), 15, 67.
[34] Studies from Institute for Medical Research. Federated Malay States (1902), 2, No. 2, 63.
[35] *Journ. Hyg.* (1904), 4, 129.

VIEWS OF SOME PREVIOUS INVESTIGATORS.[36]

The idea that beriberi is a disease which may have a dietetic causation is a very old one. Van Leent, as early as 1867,[37] writes:

> The principal cause of beriberi is recognized as being a diet too uniform, insufficient, and of bad quality. The body, deprived of indispensable elements for the maintenance of the normal composition of the blood and consequently of its nutrition, becomes impoverished little by little.

Later, in 1880,[38] van Leent regards the cause of beriberi as due to too small a proportion of albuminous substances or of fat in the diet.

The Anglo-Indian physicians at an early period pointed to an insufficient diet or a diet not corresponding to the needs of the body, such as the exclusive or preponderant use of rice and of dried fish as a cause of the malady, and many observers in the Dutch East Indies and Japan assigned such a cause the first place in the etiology.[39]

A similar view was held by Maget and Wernich[40] who studied the disease in Japan. The latter wrote:

> Rice, as the exclusive food of the people, is answerable for beriberi in a quite special way. Not, however, as some have thought, because it is used in a decomposed state, but because it is used in such quantities that the power of assimilation is gradually lost for other kinds of food; and even the large quantity of rice is unable to render the nutrition and blood-making adequate; although the Japanese diet contains albuminous elements in the form of fish and bean-cheese, these are not sufficient.

Takaki[41] believed that beriberi is caused by the disproportion of nitrogenous and nonnitrogenous elements (nitrogen and carbon in food); that is, the amount of the nitrogenous was insufficient and that of the nonnitrogenous excessive. Up to 1883 the cases in the navy in Japan averaged over one-fourth of its strength and in that year there were 1,236 cases of beriberi among 5,349 men. In 1884 the diet was changed, a larger proportion of nitrogenous food being given, and in 1885 there were

[36] In this consideration of the previous investigations of other authors only those relating to the occurrence of beriberi in the Tropics have been reviewed and not those, with one exception, relating to ship beriberi.

[37] *Arch. d. Med. Nav.* (1867), 241.

[38] *Genees. Tijd. v. Ned. Ind.* (1880), 9, 295.

[39] Hirsch's Handbuch der historisch-geographischen Pathologie (1883), 2, 414.

[40] Geographisch-medizinische Studien. Berlin (1878), 193.

[41] *Lancet* (1906), 1, 1371, 1451, 1520.

only 41 cases, in 1886 only 3. By the beginning of 1891, under the improved diet, beriberi was entirely eradicated and the incidence of other diseases greatly decreased. Other hygienic measures were also introduced into the navy during these years.

Vorderman,[42] in a study based on Eijkman's researches observed that fully hulled and incompletely hulled rice as a food influenced the occurrence of beriberi among the prisoners in the Dutch East Indies in quite a different way. He states that of 96,530 prisoners who were fed chiefly with incompletely hulled rice (that is, in which not more than 25 per cent of the pericarp was removed from the grain) only 9, that is 0.009 per cent, sickened with beriberi, while of 150,226 prisoners fed chiefly with fully hulled rice (that is, in which only 25 per cent of the pericarp remained with the grain) 420, that is 2.079 per cent, suffered from beriberi. The conclusion reached was that a connection existed between the prevalence of beriberi and the consumption of hulled rice.

In the year 1901 Rœlfsema[43] observed an epidemic of beriberi among the coolies at the coaling station at Sabang, Sumatra. He could not observe any amelioration in the condition of the patients when he gave them meat and other extra articles of food, but he did observe that the epidemic ended as soon as he prescribed *katjang idjo.*

Hulshoff-Pol[44] repeated these experiments in the Insane Asylum at Buitenzorg. During the period from August 1 to April 30, 1902, the patients from 12 pavilions in the asylum received the following in addition to the ordinary diet: In 3 pavilions, 150 grams of *katjang idjo;* in 3 pavilions, 300 grams of fresh greens; and in 6 pavilions, ordinary diet. The pavilions were disinfected once a week with carbolic soap, 3 per cent, in order to kill any insects which might be of importance in the dissemination of beriberi. The following results were obtained: Among 70 insane who ate *katjang idjo,* none developed beriberi; among the 86 who were given fresh greens, 16 cases; and among the 78 who lived in the disinfected pavilions, 33 contracted the disease. There were 58 control patients of whom 19 contracted beriberi.

Kiewiet de Jonge[45] repeated Hulshoff-Pol's experiments on 384 patients in the Insane Asylum at Buitenzorg. *Katjang idjo* was given to 182 of these, but not to the remaining 202. The results were as follows:

[42] Cited by Schaumann, *Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* (1910), 14, 344. See also, Eijkman, *Arch. f. Schiffs- u. Trop.-Hyg.* (1911), 15, 699.

[43] Quoted by de Haan, *This Journal, Sec. B* (1910), 5, 69.

[44] Cited by de Haan, *loc. cit.*

[45] *Genees. Tyds. v. Ned. Ind.* (1909), 49.

As to the curative action of katjang idjo.

	With *katjang idjo* (per cent).	Without *katjang idjo* (per cent).
Suffered from beriberi and remained unchanged	15.0	23.4
Improved	75.0	13.3
Became worse	10.0	63.3
Died	2.5	30.0

Braddon,[46] from his observations from 1901 to 1906 relating to beriberi, became fully convinced:

That the disease was not in any sense an infection but a form of food poisoning of which the cause lay in the nature of the grain. That in places and in communities where rice-eaters and non-rice-eaters lived side by side, sharing in common the chances of supposable infection, beri-beri attacked invariably only rice-eaters, never the non-rice-eaters. That among rice-eaters, otherwise equally exposed to infection, beri-beri again attacked those only who ate certain sorts of rice, or rather rice in a certain condition. Those who ate fresh rice (as prepared by the Malay *i. e.*, hand pounded daily for their own use) and those who ate rice prepared by the parboiling process (as customarily used by Tamils, cured rice) never got beri-beri. It attacked those only whose staple diet was the common commercial white rice of the shops, the so-called Rangoon or Siam rice—sorts which, in contradistinction to the other varieties, were designated "non cured." That the severity of the disease and its extent (the number of attacked) in communities was directly proportional to the quantities of the rice consumed. Its progress, whether as a malady of the individual, or as an epidemic in communities becoming greater when the rice was increased, diminished when this was lessened, and ceasing altogether when the noxious rice was withdrawn, without change of any other circumstance.

He believed that the rice husk contained a special fungus which is able after decortication to affect the seed saprophytically and to produce a poison therein. He collected very extensive statistical evidence regarding his claims and insisted upon his arguments with great energy. Although Braddon's ideas were vigorously opposed by many authorities on beriberi, some of whom, after examining his evidences, claimed that the hypothesis that diet can cause the disease has no facts to support it, nevertheless, he maintained the courage of his convictions and eventually the government was persuaded to investigate the question. Official permission was granted to conduct an inquiry, and Doctor Braddon having found a place where the conditions were considered favorable, a research was planned and carried out with Doctor Fraser.[47] The result of this study has been

[46] The Etiology of Beri-beri. Federated Malay States Medical Archives (1901); Cure and Prevention of Beri-beri. London (1907); The Discovery of the Cause of Beri-beri. London (1911).

[47] *Trans. Soc. Trop. Med. & Hyg.* (1911), 5, 81.

reported by Fraser and Stanton,[48] and will be considered later in this paper.

Fletcher in 1907[49] states:

During the year 1905 an epidemic of beri-beri broke out in the Kuala Lumpur Lunatic Asylum. Commencing in February, it reached its height in July and August, declining somewhat towards the end of December. Out of 219 lunatics treated in the asylum during the year 94 persons were affected, of whom 27 succumbed to the disease. The chief constituent of the rations supplied to the inmates of the asylum was uncured (Siamese) rice, and in view of the fact pointed out by Dr. Braddon that beri-beri occurs chiefly amongst communities with whom such rice is the staple article of diet it was decided, with the sanction of the Government, to place half the lunatics on cured (Indian) rice. The Government readily gave its consent and the experiment was commenced on Dec. 5th, 1905. Except for the difference in the rice the two parties—those on cured and those on uncured rice—received the same kind and the same amount of rations. Excepting the rice the food-stuffs for all patients were prepared together in the same kitchen and cooked in the same cooking pots.

The lunatics are housed in two exactly similar buildings on opposite sides of a quadrangle surrounded by a high wall. On Dec. 5th all the lunatics at that time in the hospital were drawn up in the dining shed and numbered off from the left. The odd numbers were subsequently domiciled in the ward on the east side of the courtyard and no alteration was made in their diet, they were still supplied with the same uncured rice (Siamese) as in 1905. The even numbers were quartered in the ward on the west of the quadrangle and received the same rations as the occupants of the other ward, with the exception that they were supplied with cured (Indian) rice instead of the uncured Siamese variety. The following is the ordinary diet scale of the lunatic asylum: fresh meat, 4 ounces four times a week; fresh fish, 5⅓ ounces two times a week; salt fish, 5⅓ ounces once a week; vegetables, 8 ounces daily; curry stuffs, 1⅓ ounces daily; and cocoanut oil, ⅔ of an ounce daily. Uncooked rice: Siam, 28 ounces to be supplied as per sample for uncured rice ward; Bengal, 28 ounces to be supplied as per sample for cured rice ward. At the commencement of the experiment all patients showing unmistakable symptoms of beri-beri were removed to the district hospital, which is two miles distant from the asylum. On Dec. 5th there were 59 lunatics in the asylum; of these 29 were put on cured rice and 30 on Siamese rice. The next patient admitted to the asylum was admitted to the Bengal rice ward, and the one admitted after him to the uncured rice ward, the next to the cured, and so on alternately to the end of the year.

The result up to December 31 1906 (i. e., one year and 26 days) was that 34 out of 120 persons fed on uncured rice suffered from beri-beri and 18 died, whilst among 123 patients dieted on cured rice there were no deaths from beri-beri and only two cases, both of whom were suffering from the disease on their admission to the asylum.

[48] *Lancet* (1909), 1, 451; Studies from Institute for Medical Research. Federated Malay States (1909), No. 10.

[49] *Lancet* (1907), 1, 1776.

In a subsequent paper,[50] he records the results during the year 1907 when 136 patients were treated in the "uncured" rice ward. Of these patients 28 suffered from beriberi, 4 of whom were suffering from the disease on their admission, while in 24 the disease developed whilst they were in the asylum. During the same year, 131 patients received a diet containing "cured" rice; 4 of them were admitted actually suffering from beriberi, but none of these 131 patients developed the disease in the asylum. Fletcher concludes that the cause of beriberi is to be sought for in the diet, and the result of his experiments tends to show that white polished rice, although of the best quality, is the cause of beriberi, acting either by some poison which it contains or by a starvation due to some defect in the nutritive value of such rice.

Fales,[51] from a study of an outbreak of an epidemic of beri-beri in Bilibid prison, in Manila, came to the conclusion that the lack of fresh vegetables conduced powerfully to both beri-beri and scurvy.

In November, 1901, there were two cases of the disease, and no deaths, in the gaol. The food was then changed to a ration consisting of 97.17 grammes of proteids, 17.24 grammes of fats, 491.04 grammes of carbohydrates and 26.52 grammes of salts. In this diet there were 85.05 grammes of potatoes and 453.60 grammes of rice. Put into other figures, this diet consisted of: Nitrogen, 172.1 grammes; carbon, 4,166.5 grammes; hydrogen, 61.9 grammes; sulphur, 13.2 grammes; salts, 140.2 grammes—the proportion of nitrogen to carbon being as 1 to 24.2, whereas, calculating the weight of Filipinos at 125 pounds, it was estimated that proteids ought, according to Voigt's diet, to have been at least 94 grammes, fats 45 grammes, and carbohydrates 400 grammes; or, according to Moleshott's diet, nitrogen, 256 grammes; carbon, 3,789 grammes; hydrogen, 143 grammes; sulphur, 23 grammes; salts, 172 grammes—*i. e.*, N : C :: 1 : 0.15.

The epidemic of beri-beri now began: December, 1901, 52 cases and 2 deaths; January, 1902, 169 and 12; February, 1,087 and 16; March, 576 and 15; April, 327 and 15; May, 310 and 19; June, 451 and 17; July, 233 and 33; August, 571 and 24; September, 522 and 31.

On October 20 the diet was again changed, and this time proteids were 101.71 grammes; fats, 19.37 grammes; carbohydrates, 395.73 grammes; salts, 29.13 grammes; including 119.07 grammes of potatoes and 255.15 grammes of rice. Nitrogen was 209.8 grammes; carbon, 3,816.2 grammes; hydrogen, 70.4 grammes; sulphur, 17.2 grammes; and salts, 185.8 grammes—N : C :: 1 : 13.4.

In October there were 579 cases and 34 deaths; November, 476 and 8; December, 89 and 3; half January, 1903, 4 cases and no deaths.

Along with the beri-beri there was an epidemic of scurvy, and Fales was of the opinion that both diseases were led up to by a deficiency of vegetables, the essential principle of which he believed to be potassium carbonate, of which rice contains only 0.01 grain per ounce, while potatoes

[50] *Journ. Trop. Med.* (1909), 12, 127.

[51] Castellani and Chalmers, Manual of Tropical Medicine. London (1910), 890. See also, *Journ. Am. Med. Assoc.* (1907), 48, 778.

contain 1.875 grains. Hence, according to Fales, the disappearance of the disease when a sufficiency of vegetables, especially of potatoes, was given. But he says this deficiency is only a predisposing cause, which enables the micro-organism, whatever it is, which is the true cause of the disease, to flourish and produce the symptoms.

Ellis,[52] in 1903, was convinced that the consumption of moldy, microbic, or otherwise diseased rice is not a cause of beriberi and that his experiments completely disproved any connection between beriberi and food. Later, in 1909,[53] he performed experiments in the Singapore Lunatic Asylum in feeding the inmates cured and uncured rice. He concludes that since only cured rice has been employed in the asylum, there has been no recurrence of the disease for over a year, although formerly there were many outbreaks of it.

Fraser and Stanton,[54] as has already been mentioned, carried out important experiments with reference to Braddon's ideas regarding the causation of beriberi. On account of the great importance of their investigations, we shall quote freely from their report, as follows:

The investigation hereinafter described was undertaken primarily to determine if, when other factors were excluded or controlled people fed on white rice did develop Beri-Beri and if people under exactly similar conditions but fed on parboiled rice did not develop the disease. It was hoped also that opportunity would be forthcoming for the investigation of other aspects of the question.

At the outset it is necessary to state that the disease under investigation is that form of multiple peripheral neuritis, known as Beri-Beri, which occurs endemically in this peninsula and the neighbouring islands. As much confusion has been caused by assigning this name to classes of cases differing widely in their clinical manifestations it is desirable to make it clear that we seek only for an explanation of this disease as met with here.

For the purpose of the inquiry it was necessary to observe two parties of men under similar conditions as to environment, etc., and whose food supply was definitely known. In view of the suggestion [made by numerous observers] that the disease may be bacterial or protozoal in origin it was desirable that the places chosen should have been hitherto uninhabited or that no case of Beri-Beri should have occurred there for some time previously; further the places should be in an isolated district sufficiently remote from towns or villages to exclude as far as possible the entrance of a supposed infection. Such a situation would also have the advantage, on account of the absence of shops, that the men under observation could not readily obtain food other than that supplied to them. It is obvious that the conditions required for such an investigation could not be secured

[52] *Brit. Med. Journ.* (1903), 2, 1268.
[53] *Ibid.* (1909), 2, 935.
[54] *Loc. cit.*

in a public institution as in all such in these States Beri-Beri is known to be endemic.

Various places were visited with a view to securing satisfactory conditions, and it was finally decided to carry on observations with regard to some three hundred Javanese indentured labourers employed in the work of road construction in a remote part of the Jelebu district in the State of Negri Sembilan * * * the places in which the labourers were at this time located * * * [the fifty-first mile and the fifty-eighth mile from Seremban] were sufficiently remote from the nearest village or town for the purpose; Malay settlements in the district were few in number and small in size. In connection with these latter it should be remembered that abundant evidence exists to show that Malays in such situations do not suffer from Beri-Beri.

Under the terms of contract the rice issued to these laborers was supplied by the employer. It may be added that the Javanese prefer white rice, which is the kind consumed by them in their own country.

In the early months of 1906 Beri-Beri occurred among them, and in May, June and July of that year it was a serious source of invaliding and mortality. From August 2nd, 1906, the employer, adopting the suggestion of Dr. Braddon, issued only parboiled rice instead of white rice [hitherto issued]; thenceforward it is stated, and this statement is confirmed by the hospital records, no case of Beri-Beri occurred.

Here then the conditions seemed to be in every way suitable for an inquiry into the part played by rice in the causation of Beri-Beri, because these labourers without exception still desired to return to a white rice diet and at this time the evidence of a connection between the consumption of white rice and Beri-Beri was by no means convincing either to the general body of medical and scientific workers or to ourselves. The importance of reaching some conclusion regarding the origin of the disease cannot be over-estimated as the number of its victims in this Peninsula alone runs into many thousands annually.

Throughout these States no labourers other than Tamils will consume parboiled rice unless compelled to do so and while there was any doubt as to the harmful influence of white rice no effective measures could be taken for the suppression of Beri-Beri.

By acceding to the wishes of the group of labourers comprised in this investigation opportunity would be afforded for a thorough testing of the position of dietary factors as causative agents. The labourers were therefore given the option of returning to a white rice diet after it had been fully explained to them that by so doing they ran the risk of contracting Beri-Beri. Without exception they chose the white rice but as for the purpose of comparison two parties were required, half the number only were allowed this diet. It was hoped also that by continuous observation of a large party of men on a parboiled rice diet it might be determined whether, apart from its disagreeable musty odour, any grounds existed for the objections made to the consumption of this rice.

[At the time the investigation was commenced, April, 1907] The 300 labourers were divided into two parties of approximately equal numbers and were housed some miles apart. Before beginning the experiment an examination was made of each person and the presence of cases of existing or recent Beri-Beri was thereby excluded.

To one party white rice (No. 2 Siam) was issued as the staple article of diet, and to the other party parboiled rice. In about three months cases of Beri-Beri began to occur among the members of the party on white rice. When a certain number of cases had been noted white rice was discontinued and thereafter no cases occurred. No sign of the disease appeared among the control party on parboiled rice.

The conditions were then reversed. The party hitherto on parboiled rice were given white rice and after a somewhat longer interval than in the first instance, Beri-Beri broke out in this group also. This outbreak ceased on discontinuing the issue of white rice. Again no sign of the disease appeared among the control party on parboiled rice. By the transfer of individuals suffering from Beri-Beri and of whole groups in which the disease was occurring it was found possible to test the influence of place considered as a nidus of infection and also to test the possibility that the disease was communicable from one individual to another.

The average daily ration was as follows—

Rice	21.3	oz.	603	grammes.
Dried salt fish	4.25	"	120	"
Onions	1.75	"	50	"
Potatoes	1.75	"	50	"
Coconut oil	0.85	"	24	"
Coconut	1.50	"	42	"
Tea	0.12	"	3.4	"
Salt	0.1	"	2.8	"

The symptoms and subsequent histories of the cases which developed beriberi during the course of the investigation are not given in Fraser and Stanton's publication and merely the dates are stated on which the patients developed the disease, though Fraser and Stanton write with regard to party No. 1-B:

It is proper to mention here that in determining whether a given case was to be admitted as a case of Beri-Beri the most rigid exclusion was practised. Only such cases as presented unequivocal signs of the disease were admitted. In every instance the diagnosis was based on the opinion of at least two medical men, in most instances on that of four. Where any doubt was cast upon the accuracy of the diagnosis such case was rejected. The result therefore is that, apart from the cases here recorded, there were many others which, in the opinion of the writers as well as of those associated with them in this inquiry, were really mild or obscure cases of the disease. The difficulties in this respect will be appreciated by those who have had to deal with the disease clinically. No such doubtful case was at any time observed among the people on parboiled rice and the inclusion of cases of this type occurring in the white rice parties in no way strengthens the case for an infectious origin of the disease.

The conclusions arrived at as a result of their inquiry were stated as follows:

Twenty cases of Beri-Beri occurred among 220 people on white rice. No case occurred among 273 people on parboiled rice and under similar conditions to those which obtained in the white rice parties at the time Beri-Beri was prevalent among them.

Since all cases presenting doubtful signs of the disease were excluded we are of opinion that there were many other cases which in the ordinary routine of clinical practice would have been regarded as Beri-Beri. Such cases only occurred among people who consumed white rice. * * *

No case of Beri-Beri occurred in any coolie who had been on white rice for a less period than 87 days.

Systematic examinations were made of the blood and urine of patients suffering from Beri-Beri. Various methods of examination were employed but in no instance were any organisms found, except those well known as the causative agents of other disease.

In the course of the inquiry patients in various stages of Beri-Beri were at times in contact with parties of men on parboiled rice. The results of observations made on such occasions furnished evidence that the disease is not a directly communicable one.

Removal of patients suffering from beri-beri from one place to another did not influence the progress of the disease and removal of entire parties from the place where the disease had occurred did not influence the progress of the outbreak so long as they continued on white rice. These experiments suggest, although they do not prove, that place *per se* or considered as a nidus of infection has no influence upon the development of Beri-Beri.

In three instances in which definite outbreaks of Beri-Beri occurred among parties on white rice, substitution of parboiled rice was followed by a cessation of the outbreak. * * *

No evidence was obtained to show that any article of food other than white rice was a possible source of a causative agent of the disease.

Ankylostomes and other nematode worms were not found in a larger proportion of patients suffering from Beri-Beri than in the general population under observation.

The general results lend support to the view that the disease Beri-Beri as it occurs in this Peninsula, has, if not its origin in, at least an intimate relationship with the consumption of white rice and justify further research along these lines.

Among the many investigators who have brought arguments, based upon experiments, against the rice causation of beriberi may here be mentioned Wright, Durham, Travers, Daniels, and very recently Montel.

Hamilton Wright,[55] after eleven months' study of the disease in the jail at Kuala Lumpur, states that proof has been obtained that beriberi is independent of diet considered as diet; that the jail itself is a focus in which the virus of beriberi is generated; that evidence has been produced that confirms the view that beriberi is broadly speaking an infectious disease. He further states:

The diet of all prisoners was as physiologically correct as that provided in the Japanese Navy after 1884, and to which is ascribed the disappearance of beri-beri from its personnel by several Japanese authorities, TAKAKI

[55] Studies from Institute for Medical Research. Federated Malay States (1902), 2, No. 2, 56.

more particularly. In spite of this physiologically correct diet it may be seen (in Tables 21 and 29) that 49 cases originated and 123 re-developed signs of paresis or recontracted the disease during its continuance at the gaol, and that after the regular scales of diet were reverted to there was no increase but rather a decline in the number of cases of beri-beri.

TABLE No. 18.—*Diet scale between May 8, 1901, and January 1, 1902.*

Rice	21	ozs.	daily	to	all	Prisoners.
Buffalo beef	6	"	"	"	"	Malays.
Do. alternating with pork	6	"	"	"	"	Chinese.
Mutton	6	"	"	"	"	Tamils.
Two duck's eggs			"	"	"	Bengalis. and Sikhs.
Vegetables (pumpkin, peas, cabbage, etc.)	7	"	"	"	"	Prisoners.
Towgay or sprouting beans	2	"	"	"	"	"
Coconut oil	1	"	"	"	"	"
Curry Stuff	1	"	"	"	"	"
Salt	½	"	"	"	"	"

Durham [56] also states:

In the Pudu Jail, patients in the jail hospital were recovering whilst about the cells or work-places their mates were being invalided day by day. They ate of the same rice which was all cooked together.

Durham concluded that the dietetic or physiological or the unsound food theories all appear to be insufficient in accordance with the attending circumstances to have accounted for the spread of beriberi. However, he found from a study of the urine [57] that the metabolism in beriberi is seriously diminished.

Travers [58] writes that from the years 1892 to 1894 no cases of beriberi had originated in the Kuala Lumpur jail:

The prisoners were then transferred to a new gaol about two miles away, and in this institution beri-beri broke out in 1895. About 100 prisoners were then sent back to the old gaol, the food with which they were supplied being in every respect similar to that consumed by the prisoners at the new gaol. For the first three months the food was actually cooked in the new gaol and carried to the gaol twice daily. No cases of beri-beri occurred among the prisoners during the nine months spent by them at the old gaol, whereas no less than 323 cases occurred in the new gaol during the same period. The result of this experiment was taken to prove conclusively that, in at any rate this instance, there was no con-

[56] *Journ. Hyg.* (1904), 4, 112.
[57] *Brit. Med. Journ.* (1904), 1, 480.
[58] *Journ. Trop. Med.* (1904), 7, 285.

nection between the rice eaten by the prisoners and the beri-beri from which they suffered.

Some years having elapsed since the date of the above experiment, I thought it advisable to, if possible, confirm the results then arrived at by a somewhat more extensive observation carried out under conditions which would exclude all possibility of error. The institutions selected for observation were the Pudoh Gaol, the Tai Wah Institution and the Leper Asylum.

The Tai Wah Institution is set apart for the care of persons suffering from incurable disease, or who are unable to support themselves. On October 31st, 1902, there were fifty-one patients in the wards, all of Chinese nationality. These Chinamen were, almost without exception, formerly employed as coolies, and were drawn from the same class as the inhabitants of the Pudoh Gaol. Of the fifty-one patients, forty-three, or 84.5 per cent, had been continuously in the hospital for over seven months.

The Leper Asylum is, as its name implies, exclusively set apart for the treatment of lepers. On October 21st, 1902, there were 131 patients in the wards, of which 129 were Chinese and two Tamils. One hundred and eighteen, or 90 per cent, of the inmates had been continuously in the Asylum for more than seven months.

The two hospitals referred to and the Pudoh Gaol are supplied with Rangoon rice by the same Chinese contractor; it is purchased from a merchant in Penang, it is taken delivery of at the Kuala Lumpur Railway Station and is removed to a store in the town. This store is light, clean and well ventilated. The rice is kept on a platform raised from the ground, and is distributed to the various hospitals as required. At no time is more than three weeks' supply kept in the store, and the bags of rice are taken out and sent to the various institutions without selection of any kind.

In the Pudoh Gaol, the Tai Wah Institution and the Leper Asylum we have three institutions, the inhabitants of which are of the same nationality, and the Rangoon rice consumed by them is supplied from the same source, by the same contractor. It would be reasonable to suppose that if the disastrous outbreaks of beri-beri in one of them—the Pudoh Gaol—were caused by a toxin conveyed by Rangoon rice, the patients in the other two—the Tai Wah Institution and the Leper Asylum—should suffer from beri-beri in the same way as the inmates of the prison. This, however, is not the case, and no outbreak of beri-beri has at any time occurred in either the Tai Wah Institution or the Leper Asylum.

From January 1st to October 31st, 1902, 291 fresh cases of beri-beri occurred among the prisoners in the Pudoh Gaol, whereas not a single case of beri-beri occurred among the patients at the Tai Wah Institution or Leper Asylum. *This, I think, disposes of the theory of the connection of beri-beri with the consumption of rice.*[50] * * *

The Pudoh Gaol has now, after having been scourged by beri-beri for nearly seven years, been free from the disease for seven months. Although there is still some doubt as to the actual cause of the outbreak, it is hoped that our experience of the disease among the prisoners may not have been entirely valueless, and that some hitherto obscure points may have been elucidated by the various observations carried out.

[50] Italics are mine. R. P. S.

Shibayama[60] reports that:

In 1908, 1,195 cases of beriberi developed in the Blinjoe, one of the mining districts. Mine No. 3 was especially unfortunate, for 166 out of 410 workmen contracted the disease, and mine No. 4 developed 118 cases among 390. No. 5 had 400 workmen, and 97 of these were ill with beriberi; on the other hand, the remaining mines showed but few cases. For two years the workmen had received unpolished, fresh rice, not only in mines Nos. 3, 4, and 5, but also in No. 11, in which latter 49 out of 300 workmen contracted the disease; on the other hand, the laborers in the remainder always had polished and old rice. It may further be stated, according to Hulshoff-Pol, that the workmen in all the mines received 150 grams *kadjang idjo* beans, together with dried fish and fresh vegetables, daily. The result of our observations, therefore, was as follows:

1. Even if the workmen in the mines receive 150 grams of *kadjang idjo* regularly every day, nevertheless beriberi occurs among them.

2. Even if the laborers are given a diet of fresh, unpolished rice, nevertheless they develop more cases of beriberi than those in the other mines, where they receive polished and older Java rice.

I therefore could not find the assumption to be confirmed that unpolished rice, which has the same composition as parboiled rice, could prevent beriberi. * * *

All my observations lead me to the conclusion that uniform, but little changing, monotonous diet predisposes to the disease. The condition of nourishment of the Chinese in two of the mines of Banka was fairly good, the total quantity of the chief constituents of diet, namely, protein, fat and carbohydrates, was sufficient, but the diet was always one-sided and not varied throughout the year. This is also true of the general epidemic of beriberi aboard the steamship referred to above, and in the fishing villages the one-sided diet was the only point to be observed.

However, the one-sided or monotonous diet is only the predisposing cause of beriberi; the true cause must be sought in other directions. * * *

Montel,[61] at the meeting of the Far Eastern Association of Tropical Medicine held during the present year, reports the occurrence of an epidemic of beriberi near Saigon which could not be entirely explained by the so-called rice origin of the disease. He calls attention to an instance in a monastery and a convent where the conditions were more or less the same and yet in one beriberi frequently occurred while in the other outbreaks of the disease were never known. The monastery and convent were located in the same area of the town and were only separated by a small stream. In the monastery rice was consumed a few days after it was hulled and no case of beriberi occurred. In the convent much the same rice was used, but large quantities were hulled at a time and stored, and in this institution beriberi outbreaks were quite common.

[60] *This Journal, Sec. B* (1910), 5, 124.
[61] *Med. Rec.* (1912), 81, 630.

At the same meeting Davis[62] presented a paper which lent evidence favoring the infectious theory of the disease. The prisoners in the Shanghai Jail at one time suffered severely from beriberi which diminished, it is true, with a change in diet but again reached a high figure when the improved sanitary conditions due to a coincident occupancy of a new jail had in time deteriorated. When steps were taken to overcome infestation with vermin, the incidence of the disease again diminished markedly.

To enter into a discussion of the literature regarding epidemics of beriberi among people who never eat rice would lead us too far astray in our argument in relation to the etiology of tropical beriberi.

However, in this communication attention may be called to the investigations of Axel Holst[63] in relation to the occurrence of beriberi on Norwegian ships. This author points out that the frequency of beriberi, under these conditions, coincides with certain alterations in the food during long voyages, and he reports the production of polyneuritis gallinarum in fowls by feeding tinned meats, which have been boiled for one-half an hour at a temperature of 110° C., and even sometimes by feeding salt meat, somewhat tainted, boiled for one hour at 100° C.

It is not our intention to criticize here the conclusions reached by these investigators from their experiments which we have quoted, but merely to call attention to the fact that considerable evidence has been presented by various authors against the idea that the continuous consumption of white rice as a staple article of diet is the cause of beriberi. In fact, in a number of other outbreaks of beriberi which have occurred recently, the evidence submitted has been entirely opposed to the idea of the rice causation of beriberi. However, it must be admitted that in regard to the cause of these outbreaks the evidence is no more complete or convincing than is that given in the articles already referred to and therefore it will not be quoted here. A number of physicians in Manila and elsewhere, who have had a wide experience with beriberi, still decidedly oppose the idea that the disease is due to the prolonged consumption of polished rice as the staple article of diet.

From the consideration of the literature on this subject, as outlined in this article, it will be clearly seen that no experiments

[62] Quoted by *Journ. Am. Med. Assoc.* (1912), 58, 1859.

[63] *Journ. Hyg.* (1907), 7, 619; *Trans. Soc. Trop. Med. & Hyg.* (1911), 5, 71.

in which an infectious agent as the cause of the disease has been excluded in any way as near as rigid a manner as in those of Fraser and Stanton have been performed. However, the contributions of Ellis,[64] Highet,[65] Chamberlain,[66] and particularly of Heiser[67] are all very valuable from an epidemiological standpoint and lend considerable additional support to the view that beriberi is caused by the prolonged use of polished rice as a staple article of diet.

Castellani,[68] in considering the experiments of Fraser and Stanton states:

> The isolated position in which the gangs were working almost excluded any possibility of infection from place or from persons, but not quite from the latter.

As Fraser and Stanton both point out in their later publication,[69] the whole Malay Peninsula has long been known as an endemic focus of beriberi, and the mortality rates from this disease have been enormous there for several decades.

Wright[70] also remarks there is no better place than the Malay Peninsula in which to investigate this disease.

Fraser and Stanton in their article also write:

> At this time, evidence of a communication between the consumption of white rice and beri-beri was by no means convincing either to the great body of medical and scientific workers or to ourselves,

and at the conclusion of their article, detailing their experiments on human beings, they state that their experiments appear to justify further research along these lines.

At the meeting of the Far Eastern Association of Tropical Medicine in 1910 a resolution was passed calling the attention of the various governments concerned to the fact that sufficient evidence has now been produced in support of the view that beriberi is associated with the continuous consumption of white (polished) rice as a staple article of diet. There was considerable opposition to the passage of this resolution in this form on the ground that it was not sufficiently conservative from a scien-

[64] *Loc. cit.*

[65] *This Journal, Sec. B* (1910), 5, 73.

[66] *This Journal, Sec. B* (1911), 6, 133.

[67] *This Journal, Sec. B* (1911), 6, 229; *Annual Rep. P. I. Bur. Hlth.* (1910); *Journ. Am. Med. Assoc.* (1911), 56, 1237.

[68] Castellani and Chalmers, Manual of Tropical Medicine (1910), 890.

[69] Studies from Institute for Medical Research. Federated Malay States (1911), No. 12, 1.

[70] *Loc. cit.*

tific standpoint in relation to our present knowledge at the time. In fact, its passage was only secured at a final business meeting after the association had adjourned from Manila to Baguio, the summer capital of the Philippines, and at which meeting only a portion of the members of the association were present. Near the close of the year, 1910, the question of passing a law placing a tax upon all imported polished rice was considered by the Government of these Islands, but, owing to the fact that there was still considerable difference of opinion expressed regarding the definite etiology of the disease in relation to rice alone, the question was temporarily postponed. It was then decided by one of us to carry out as careful a test of this question as was possible.

In the year 1910 the etiology of beriberi was still to such an extent an open question that the Société de Pathologie Exotique through its president, M. Roux, director of the Pasteur Institute, appointed a committee[71] to investigate the subject and to collect information in the countries where beriberi existed.

The researches which will be here recorded were planned during the year 1910 and commenced at the beginning of the year 1911; but, owing to the hurried departure of one of us to Manchuria, it was necessary to discontinue them and to postpone them until the beginning of the present year.

CONDITIONS UNDER WHICH THE EXPERIMENTS WERE PERFORMED.

The object of our study was to determine definitely, if possible, whether beriberi, as it occurs in the Philippine Islands, is an infectious disease or whether it is one which has its origin in disturbances in metabolism, brought about by the prolonged use of polished rice as a staple article of diet. The experiments were carried out in Bilibid Prison in which institution the hygienic conditions may be said to be almost ideal. The area inside the prison walls comprises 3.43 hectares (8.5 acres); the average number of inmates is 3,000, but the subjects upon which our experiments were performed were entirely isolated, and no case of beriberi had been known to occur among them since their confinement. Individuals who have been sentenced to im-

[71] This committee was composed of MM. Bréaudat, le Dantec, Jeanselme, Kermorgant, Marchoux, and Pottevin and its report did not reach us until after our experiments were commenced. The important researches which have been performed by various investigators upon the subject are recorded in this excellent report and the theory of the dietetic origin of the disease endorsed. See *Bull. Soc. path. exotique* (1911) (Nov. and Dec.), 4, 575, 656.

prisonment on entering the institution undergo a quarantine of five days, and, if found to be suffering from any disease, are subsequently kept in the prison hospital and are not permitted to return to the general prison centers until well. The discipline of the prison is very strict.[72]

The nature of the experiments having been outlined and the Government having given its sanction to the same, a number of prisoners, under sentence of death, were selected and the nature of the proposed experiments carefully explained to them in their own dialect. They were told that the experiments were for the purpose of testing the comparative value of different kinds of rice as a food; the articles of food comprising the diet that would be given to them were enumerated, and they were also told that perhaps they might contract beriberi. The proposition was stated to them clearly. In addition, they were to be allowed an abundance of cigarettes of any kind that they wished, and also cigars if they desired them. Volunteers were then asked for. Twenty-nine of the number volunteered. The remaining ones did not care to undertake the experiment. Each of the volunteers then signed a statement, written in his own dialect, stating that he undertook the experiment entirely voluntarily and that he would agree to continue with the experiment until it was completed. This having been accomplished, the volunteers were divided into 4 groups. Three of the groups were placed in a bartolina or small inner prison on one side of the institution, known as the *presidio* side. The fourth group was placed in a bartolina on the other side of the prison known as the *carcel* side. The two bartolinas are a considerable distance (72 yards) apart. There are three high stone walls between them, one measuring about 4.8 meters in height, and two 3.6 meters in height; there is no approach to either except through the entrance to the prison, and this is situated a considerable distance from each. The location of the bartolinas may be seen upon reference to the plan. (See Plate I, A and B.) The bartolinas are alike in structure. They are surrounded by stone walls, 3.6 meters in height; there is but a single entrance through a high iron gate and but one key to the gate, and this was in the possession of an American guard. No one could enter or leave the bartolina without this American guard being present. Other

[72] We wish to express particularly our thanks to Colonel Dorrington, director of the Prison, Inspector Rabb, Doctor Smith, Mr. Henshaw, and Mr. Milbrodt for many courtesies and much assistance during the course of the experiments.

guards continually watched the gate. Toward one end of the quadrangle formed by the walls of the bartolinas a stone cell house is situated, consisting of five rooms (see Plate II), each with a separate entrance. The walls of the five cells are of stone, the floors of cement. Ventilation is obtained through iron-barred windows and through the roof, and in the day time through the doorway. In each prison cell, besides the beds, constructed of an iron frame covered with canvas, was a porcelain flush water-closet with running water and a large receptacle kept locked containing distilled water for drinking purposes. (See Plate III.) A shower bath was situated in the courtyard. The rooms were always kept scrupulously clean and the hygienic arrangements were excellent. Each group of the subjects of the experiments was assigned to one of these rooms of the cell house and was locked in it at night. In the morning each prison cell was unlocked and during the day all the subjects of the experiments in one bartolina were allowed to mingle freely with one another, except at meal times. During the meal time the different groups ate in separate rooms under the observation of one of us or occasionally under the observation of the American guard, so that it was quite impossible for any interchange of food between the different groups to occur. At the close of the meal each man turned in his pail containing the amount of food uneaten and a record of the amount was entered in the notes. None of the prisoners was allowed to retain any of the uneaten food except in one or two instances noted under the histories of each individual case. The conditions of the isolation of the men as is obvious were such as to preclude the possibility of any other food reaching them in any way or at any time. Groups I, II, and III were confined in Bartolina A and Group IV in Bartolina B.

THE DIET EMPLOYED IN THE EXPERIMENTS.

The food used was weighed for each meal and cooked outside of the prison in a special kitchen by a special cook, in a clean manner, and under very careful supervision. After cooking it was divided into equal parts according to the number to be fed. At first it was divided by weight, but it soon became possible to estimate sufficiently accurately the division into equal parts. Each man's food was put into a special dinner pail marked with his number and so served to him. A record was taken at the close of each meal of the amount eaten by each man; it was

estimated in fractions of the amount served and expressed in grams. The rice was served hot; it was, of course, always freshly cooked for each meal as were all the articles of the diet. The meals served were as follows:

TABLE I.—*Diets employed.*

Breakfast.
Bread about 100 grams.
Coffee about 500 cubic centimeters.
Sugar about 15 grams.

	Grams.
Dinner I.	
Rice	300
Bacon	50
Dinner II.	
Rice	300
Onions	100
Lard	15
Dinner III.	
Rice	300
Bananas	100
Sugar	25
Dinner IV.	
Rice	200
Bread	150
Bacon	30
Dinner V.	
Rice	100
Bread	150
Starch	50
Sugar	25
Lard	20

	Grams.
Supper I.	
Rice	350
Onions	150
Lard	20
Supper II.	
Rice	300
Bacon	50
Supper III.	
Rice	300
Bananas	150
Sugar	75
Supper IV.	
Bread	200
Rice	100
Starch	50
Sugar	25
Lard	20

It soon became evident that it was impossible to serve dinner No. V and supper No. IV in an acceptable form to the subject of the experiment and, therefore, these were eliminated. The other diets were alternated.

On the ninety-seventh day of the experiment with Groups I, II, and III and on the eighty-first day with Group IV, 100 grams of potatoes and 30 grams of dried codfish were added to the diet and these articles were served at intervals with 300 grams of rice in rotation with the other meals. The following table gives the percentage of phosphorus pentoxide and of the nitrogen in the articles of diet employed throughout the experiment.

TABLE II.—*Composition of foods used in the experiment.*

Kind of food.	P_2O_5.	N.
	Per cent.	*Per cent.*
Bacon	0.21	0.7
Onions	0.7	1.8
Codfish (dried)	2.9	10.58
White rice (la blanco)	0.37	1.25
Red rice (pinawa)	0.69	1.16
Starch	trace	0.18
Rice polishings (darác)	4.47	1.8
Sugar	trace	2.11
Potatoes	0.23	0.31
Alcoholic extract of rice polishings	0.025	0.365

NATURE OF THE RICE EMPLOYED.

All the subjects of the experiment received exactly the same diet, except in regard to the kind of rice. As the experiment was originally planned, it was proposed to feed three groups as follows:

I. White rice + rice polishings.
II. White rice + alcoholic extract of rice polishings.
III. White rice alone.

However, after a few days it was found impossible to persuade any of the individuals to eat further the rice mixed with the polishings or to prepare the polishings so that they would be eaten. Although they were not informed what they were being served to eat, they detected at once that the polishings were mixed with the rice. They were persuaded to eat some of it for a few days, then they persistently refused to partake of it, even though they began to suffer from marked hunger, insisting that it caused gastric disturbances and soreness in the pharynx. The polishings were, of course, uncooked and were mixed with the rice after it was cooked in order that there might be no opportunity for the criticism that the protective substances in the polishings had been destroyed by heat. As there was no object in continuing the experiment if the members of this group (No. I) did not eat the rice, we placed them upon red (*pinawa*) rice.[73]

The white polished rice employed throughout our experiments was especially milled and polished for us by Messrs. Smith, Bell, & Co., Ltd. of Manila at their new mills, and the samples contained 0.37 per cent of phosphorus pentoxide. The rice

[73] Throughout this article the term "white rice" will be used to indicate the highly polished rice and the term "red rice" the unpolished rice.

polishings employed at first mixed with the rice and also for the purpose of making the alcoholic extract that was used throughout the experiment were also especially prepared by this firm and were free from grain weevils. The commercial polishings for sale in the markets always contain weevils in great abundance, and it is very difficult or impossible to separate them from the polishings.

PREPARATION OF THE EXTRACT OF RICE POLISHINGS EMPLOYED.

The extract of the polishings was prepared by Mr. Hocson of the physiological laboratory of the College of Medicine and Surgery to whom we wish to express our thanks. The extract was always freshly prepared every third day and used before any deterioration could have occurred. The method of preparation employed, which was essentially that of Chamberlain and Vedder,[74] was as follows:

> Five kilograms of rice polishings (*darác*) were extracted with 14,000 cubic centimeters of 95-per-cent alcohol by three successive macerations of twenty-four hours each, using for the first day 6,000 cubic centimeters and for the second and third 4,000 cubic centimeters respectively. After each day of maceration the liquid was strained, pressed, filtered, and the filtrate transferred to a porcelain dish to facilitate the evaporation of the alcohol of which there was a large amount present, a portion of the alcohol was evaporated more rapidly by means of an electric fan and the fat separated from the extract. The extract was then concentrated to 125 cubic centimeters in vacuum at 60°C., and the residue obtained was made up in volume to 625 cubic centimeters with distilled water and filtered.

EXPERIMENT.

We shall now proceed to consider the experiments in detail. The nature of the rice received by each individual is stated at the beginning of the summary of his history during the experiment. In general, it may be mentioned that the groups were fed for the greater part of the time occupied by the experiments as follows:

Group I. White rice + extract of rice polishings + special diet.
Group II. White rice + special diet.
Group III. Red rice + special diet.
Group IV. White rice + special diet.

For about the first thirteen days Group I were fed white rice mixed with the rice polishings, as we had not sufficient extract on hand to begin the experiment with this group; and Group III for the first seventeen days were fed white rice mixed with

[74] *This Journal, Sec. B* (1911), 6, 254; (1912), 7, 40.

rice polishings, red rice being then substituted, for the reasons already stated.

The experiments were continued for as long a period as practicable. When a prisoner insisted upon being returned to the regular prison ration or his condition became such that such a change of diet seemed advisable, the experiment in his case was discontinued.

Several attempts were made to secure skiagrams of the hearts of the individuals, but the electric instalment in the prison was such that satisfactory X-ray photographs for publication could not be secured. For the same reason the testing of the electrical reactions of the patients, which was attempted during the experiment, was unsatisfactory, and we could not secure a satisfactory, suitable, and portable electric apparatus for this purpose in Manila. As these prisoners were all under sentence of death, they could not be taken outside of the prison for any purpose. The prisoners are referred to by numbers. With the history of each case is given a curve of the weight during the experiment and there is placed after the last case in each group a table showing the amount of food consumed each day. All of the prisoners were healthy at the time of the beginning of the experiment and had been under observation for some weeks. None of them gave a history of having suffered with beriberi previously. A summary of the important features of the history of each individual who partook of the diet will now be considered.

SUMMARY OF THE RECORDS OF THE CASES OF GROUP I.

CASE NO. 1 (GROUP I).

Diet: White rice + rice polishings[75] for 13 days followed by white rice + extract of polishings for 95 days, together with the special diet common to all the groups.	Total period of experiment, 108 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: The examination showed an apparently healthy individual; percussion and auscultation of the chest revealed no abnormality of the lungs; the examination of the heart showed no increase in the area of cardiac dulness beyond the normal limits; the point of

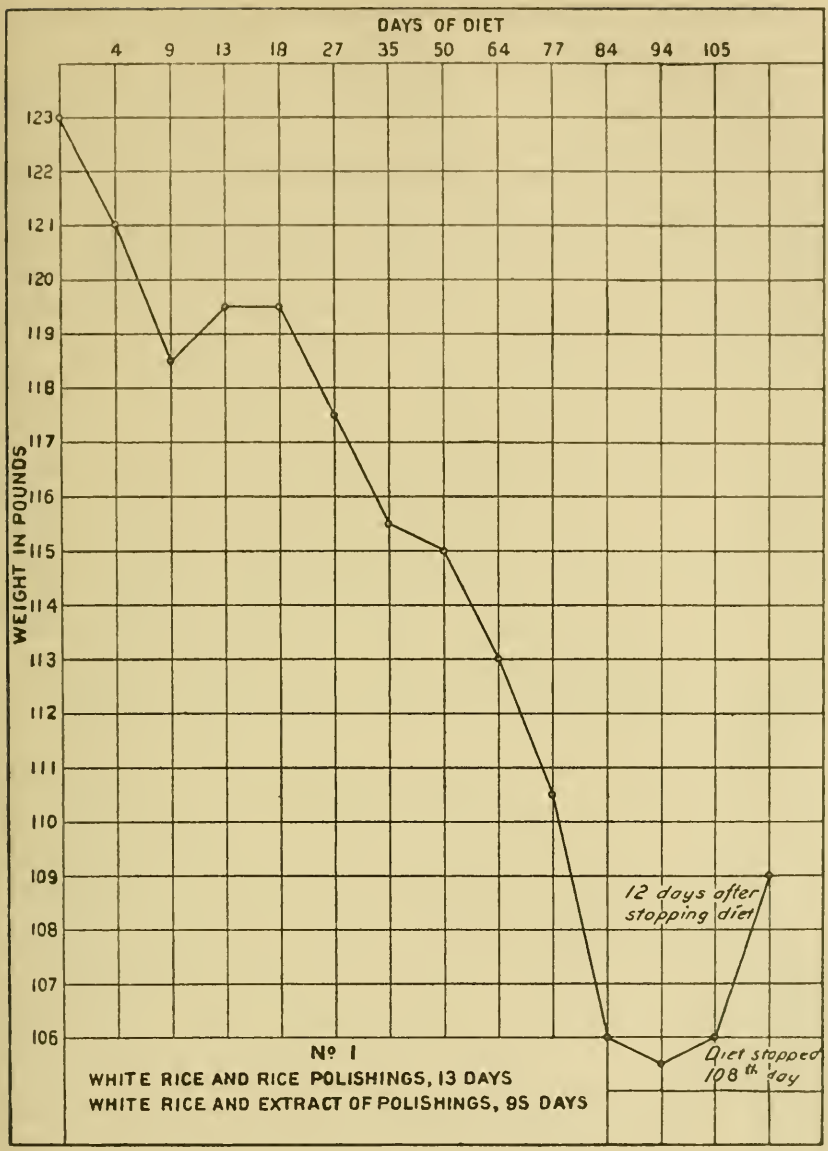
[75] The cases in Group I were fed rice polishings for 13 days as a sufficient amount of the fresh extract of polishings was not prepared at that time with which to begin the experiment satisfactorily.

maximum impulse was invisible; it was palpable 5.5 centimeters to the left of the median line and 3 centimeters below the nipple line; the heart sounds were clear at the apex and base; there was no visible epigastric pulsation; the pulse was 82, and the systolic blood pressure 124 millimeters of mercury [76] (Faught); the area of liver dulness was not increased; the spleen was not palpable; the knee jerks were active.

The subject soon objected to the taste and odor of the rice mixed with the polishings and lost in weight. As soon as a sufficient amount of fresh extract of polishings was prepared, this was substituted for the polishings themselves. However, while after a time he ate more, he continued to lose in weight. (See accompanying chart.) Reference to the table placed after the last case of the group on p. 308 will show the amount and kind of food consumed each day. The earlier notes in regard to the case are otherwise unimportant. On the eighty-first day of diet, the knee jerks were found to be very active. He complained slightly of cloudiness of vision. On the eighty-fifth day of diet he remained in bed and complained of pain in the abdomen and neck. The knee jerks were still very active. The voice was husky. The pulse, when standing, was 160, and epigastric pulsation was present. The point of maximum impulse was still invisible. The heart sounds were clear. There was very slight œdema of the legs and slight pain in the calves of the legs. Pain was elicited on pressure. The skin was moist and cool, but he stated that he felt hot. No distinct areas of anæsthesia of the skin were discovered. There was no fever. On the eighty-seventh day the patient was still in bed. The voice was very weak and husky, at times whispering, and he complained of numbness of the fingers and tenderness of the calves of the legs. The knee jerks were active. On the ninetieth day of diet he seemed better. On the ninety-fifth day the knee jerks were active, the voice was still very weak and harsh. There was no cough, no sore throat, nor other evidences of a laryngitis, and no pain in the throat. Owing to the many complaints received from this prisoner undergoing the experiment regarding his diet, and to his loss in weight, and that of a number of the other prisoners comprising this group, the prison authorities felt that it was necessary to give them additional articles of food. Therefore, dried codfish and potatoes were added to the diet. On the ninety-eighth day the voice seemed a little stronger.

[76] Hereafter in the paper, the symbol Hg will be used for mercury.

The pulse was 104, and the knee jerks very active. On the ninety-ninth day the note made was as follows: Pulse, 100; slight visible epigastric pulsation; no visible throbbing over cardiac area; the point of maximum impulse is visible and palpable just within the nipple line; the heart sounds are clear; the hoarseness is still present, but the voice is no longer whispering; the œdema has disappeared considerably and is no longer distinct; there is no pain nor tenderness of the legs; the knee jerks are active. Beginning on the one hundred third day, 20 cubic centimeters of the extract of polishings were given daily in water in addition to the usual amount of 40 cubic centimeters mixed with the rice. Owing to the general dissatisfaction among the individuals undergoing the experiment regarding the continuance of the diet, the prison officials felt that these prisoners should be allowed to return to the regular prison ration. It, therefore, became necessary to discontinue the experiment on the one hundred eighth day. The note made on the case on this day reads: Subject fairly well nourished; pulse 84, regular and of good volume; respirations normal; moderate epigastric pulsation; point of maximum impulse visible 6 centimeters to the left of the median line and 3 centimeters below the nipple line; no visible pulsation over the rest of the cardiac area; area of cardiac dulness not apparently increased beyond the normal limits; the heart sounds are clear; the conjunctivæ are of fairly good color; he complains of no pain in the calves of the legs, and there is no tenderness on pressure; there is no œdema of the legs, and the knee jerks are very active; the voice is still somewhat husky, but there is no pain in the throat. He says he feels well, but on closer questioning says that he was much stronger before he began the diet. The urine contains no albumin and no casts. The patient was placed on the regular prison ration (see Table III) and in twelve days had gained 4 pounds. His voice gradually became normal, and he has since been well. A diagnosis of beriberi was not made in this case. Nevertheless the symptoms were suggestive of this disease. While it is a well-known fact that all cases of beriberi do not show loss of knee jerks, nevertheless, in an experiment of this nature, a definite diagnosis of beriberi was not made unless the knee jerks had disappeared in addition to the occurrence of other symptoms of this disease. It is impossible to state definitely what would have occurred had the original diet been persisted in for a longer period of time.



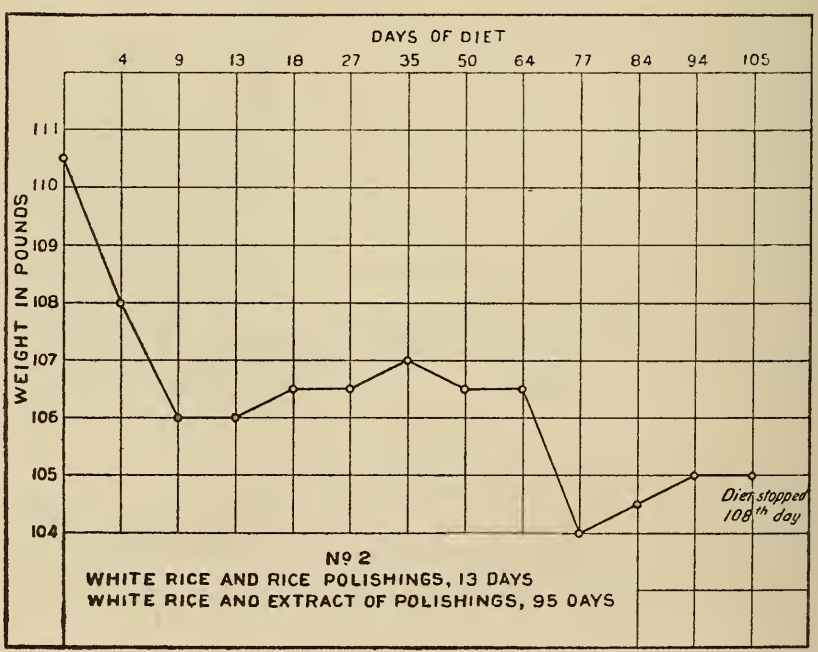
CASE NO. 2 (GROUP I).

Diet: White rice + rice polishings for 13 days followed by white rice + extract of polishings for 95 days, together with the special diet common to all the groups. } Total period of experiment, 108 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes on the case: Individual fairly well nourished; the examination of the lungs reveals nothing abnormal; the examination of the heart shows the area of cardiac dulness is not increased beyond the normal limits; the point of maximum impulse is not distinctly visible, but is palpable 6.5 centimeters from the midsternal line and 0.75 centimeter below the nipple line; the heart sounds are clear at the apex and base; there is no visible epigastric pulsation; the pulse is 108, and the systolic blood pressure 128 millimeters Hg (Faught); the spleen and liver are apparently not enlarged; the knee jerks are active.

The patient lost 2.04 kilograms (4.5 pounds) during the first two weeks of the experiment. After the substitution of the extract of polishings for the polishings themselves mixed with the rice, his weight remained about stationary, until about the sixty-fourth day of the experiment, when he again lost slightly in weight. His condition remained fairly good, however, and the notes made in regard to him during this time were otherwise unimportant. The knee jerks remained active. On the eighty-fifth day of diet the systolic blood pressure was 90 millimeters Hg. On the ninety-ninth day the following note was made: The heart sounds are rapid but clear; pulse, 114; no visible throbbing over cardiac area. There is no œdema of the legs and no



complaint of pain. The knee jerks are active. The condition of the patient continued about the same. On the one hundred eighth day of diet when it became necessary to discontinue the experiment, owing to the reasons already stated under the previous case, the following note was made: Subject rather sparely nourished; pulse, 104 and of fair volume; quite moderate epigastric pulsation; no visible throbbing over cardiac area; apex beat not distinctly visible and indistinctly palpable. Area of cardiac dulness not increased. The heart sounds are clear. The tongue is clean and the conjunctivæ of good color. There is no pain nor tenderness of the legs and no œdema of the legs. The knee jerks are active. He says he feels weaker than at the beginning of the experiment. The urine contained no albumin nor casts.

CASE NO. 3 (GROUP I).

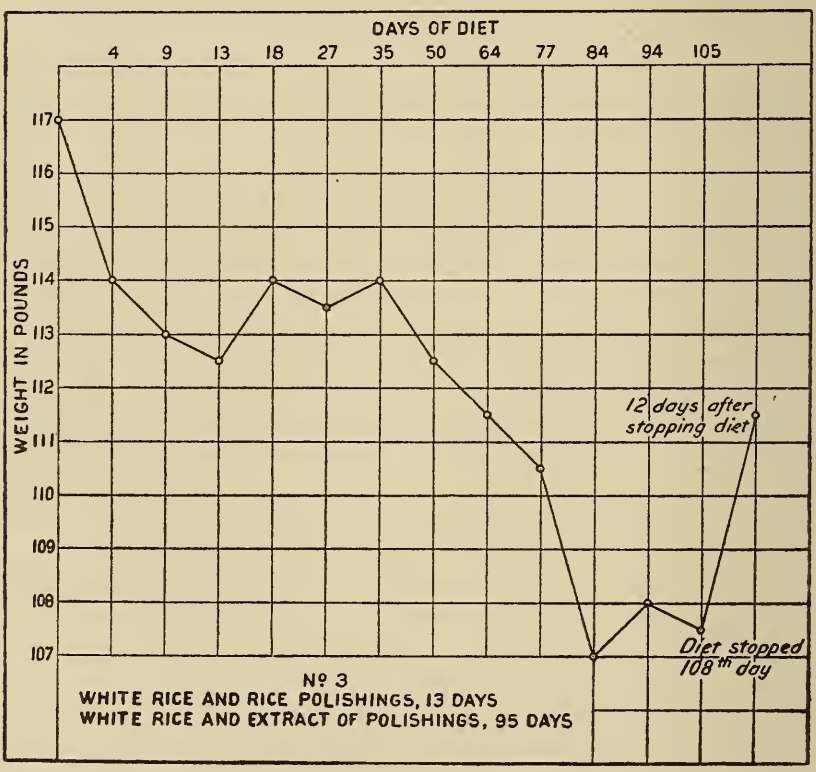
Diet: White rice + rice polishings for 13 days followed by white rice + extract of polishings for 95 days, together with the special diet common to all the groups. } Total period of experiment, 108 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: The subject is fairly well nourished; percussion and auscultation of the lungs reveals nothing abnormal; on examination of the heart, the area of cardiac dulness is not increased; the point of maximum impulse is invisible, but is palpable 7 centimeters to the left of the median line and 1.5 centimeters below the nipple. The pulse is 84, and the systolic blood pressure 110 millimeters Hg (Faught). There was no epigastric pulsation. The liver and spleen were not enlarged. The knee jerks were active.

The patient lost steadily in weight, but the notes of his condition during the earlier part of the experiment are otherwise unimportant. By the eighty-first day he had lost 4.5 kilograms (10 pounds). On this day he remained in bed, complained of being sick, and refused to eat. His temperature was normal (37° C.), pulse 112, respiration 28. He complained of headache and pain in his stomach and stated that he had vomited twice during the night. There was slight visible epigastric pulsation, but no throbbing visible over the cardiac area. On the eighty-second day at noon the pulse was 78. He was eating but little. He complained of severe headache. At 4 o'clock in the afternoon he was still sick, pulse 109. He complained of pain in his stomach and of pulsation in his abdomen. On the eighty-third day at noon he seemed weak, his pulse was

88. At 4 o'clock in the afternoon, pulse 80. He complained of headache and of pains in the calves of his legs. On the eighty-fourth day his pulse was 100, respirations 24. He complained of marked pain in the calves of his legs and of tenderness on pressure. The knee jerks were active. Epigastric pulsation was visible. There was no throbbing over the cardiac area. The examination of the heart showed no definite changes. On the eighty-fifth day at noon the note made was as follows: He complains chiefly of pain in the calves of the legs. Pulse, 96; visible epigastric pulsation still present; the knee jerks are very active; the systolic blood pressure is 95 millimeters. Eighty-seventh day, still complains of pain in the abdomen, calves of legs, and head. By the ninety-fifth day the voice had became husky. On the ninety-seventh day he developed marked conjunctivitis. Dried codfish and potatoes were added to the diet on this day. On the ninety-ninth day the note shows that the huskiness of the voice continued. The heart sounds remained clear; there was no throbbing over the cardiac area and no



œdema of the legs; the pulse was 88; the knee jerks were active; the conjunctivitis was treated. On the one hundred fifth day the condition of the eyes was improving. For the reasons already stated under case No. 1, it became necessary to discontinue the experiment. On the one hundred eighth day the note made was as follows: The nutrition is fair; pulse 94 and of good volume; moderate epigastric pulsation; point of maximum impulse not distinctly visible nor palpable; no increase in the area of cardiac dulness; first heart sound somewhat prolonged at apex; no distinct murmur; the pain and tenderness in the legs has disappeared; there is no œdema of the legs; the knee jerks are active; the voice is still somewhat harsh, and the conjunctivitis marked; he says he feels weaker than before the experiment; he has lost 4.5 kilograms (10 pounds) during the experiment; the urine is normal. Twelve days after being placed upon the regular prison ration he had gained 1.8 kilograms (4 pounds); his voice gradually resumed its normal tone. Possibly this prisoner also had already symptoms of beriberi.

CASE NO. 4 (GROUP I).

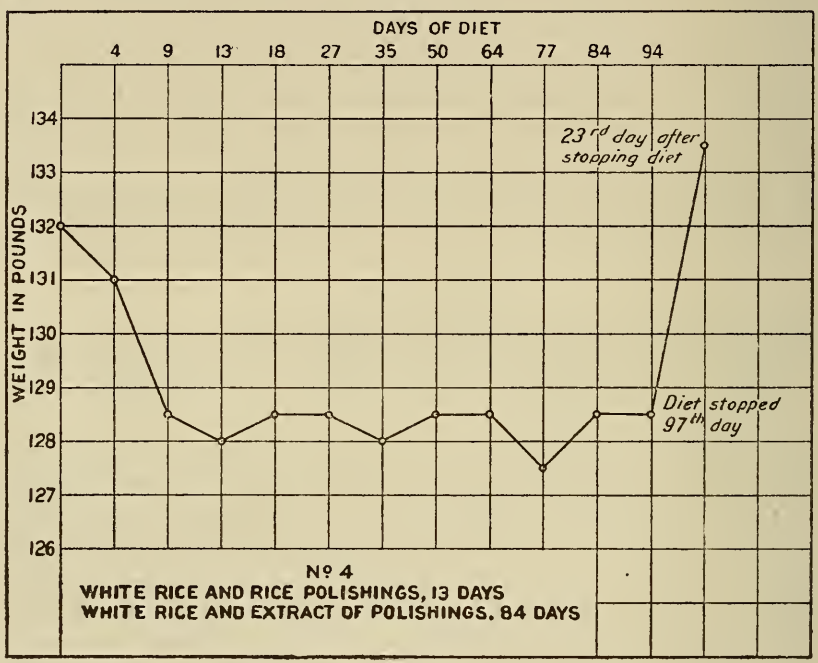
Diet: White rice + rice polishings for 13 days followed by white rice + extract of polishings for 84 days, together with the special diet common to all the groups.	Total period of experiment, 97 days.[77]

Following is a summary of the notes of the case: Well-nourished man; expansion of chest good; auscultation and percussion of lungs normal; examination of heart shows no increase in area of dulness beyond the normal; point of maximum impulse invisible and just recognizable on palpation, 8 centimeters to left of median line and exactly in the nipple line; the heart sounds are clear at both apex and base; there is no special accentuation of either second sound at the base, though the second aortic seems sharper in the second interspace; there is no epigastric pulsation; the pulse is 80, and the systolic blood pressure 140 millimeters.

The prisoner lost a few pounds in weight during the first two weeks of the experiment, as did the other members of the group. The earlier notes are unimportant regarding his condition. The knee jerks remained active. He gained 2.2 kilograms (5

[77] This prisoner refused to continue the diet after ninety-seven days and was returned to the regular prison ration at the request of the prison authorities.

pounds) in twenty-three days following the change of diet from polishings mixed with the rice to alcoholic extract of polishings. On the eighty-fifth day of diet the systolic blood pressure was 100 millimeters Hg. A few small erosions developed about the corners of the lips during the experiment which healed promptly under local applications of a 5 per cent solution of silver nitrate. He refused to continue the diet on the ninety-seventh day of the experiment and was returned to the regular prison ration on that day. At this time his condition appeared good and his knee jerks were active.



CASE NO. 5 (GROUP I).

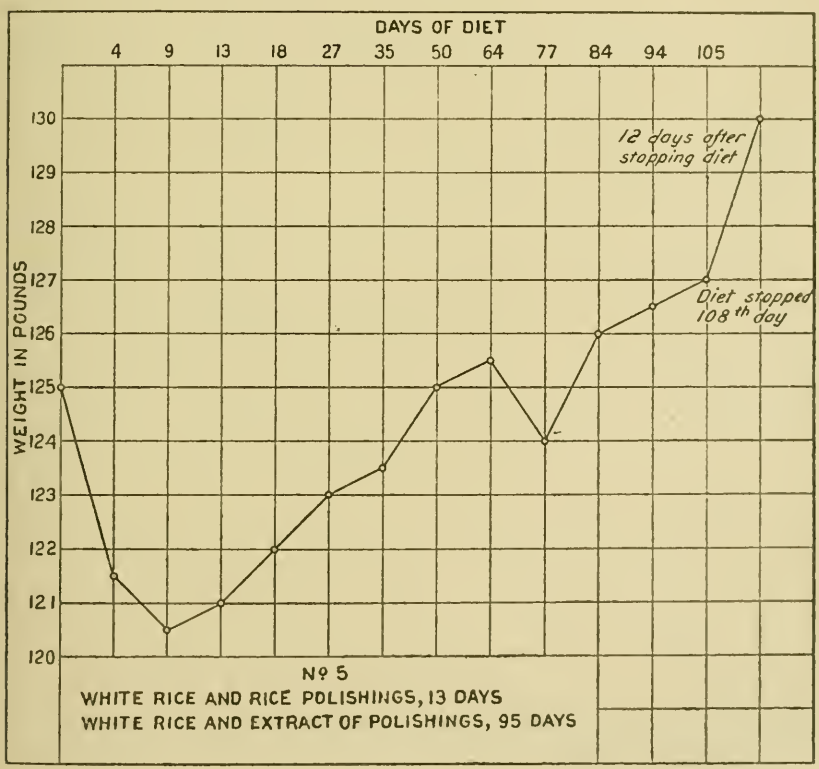
Diet: White rice + rice polishings for 13 days followed by white rice + extract of polishings for 95 days, together with the special diet common to all the groups. } Total period of experiment, 108 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: He states that he is 67 years old; his knee jerks are absent; examination of the lungs shows moderate emphysema; the examination of the heart shows that the area of cardiac dulness does not extend to the right of sternum, while on the left it extends 2.5 centi-

meters outside of nipple line. The point of maximum impulse is invisible; it is indistinctly palpable 8 centimeters to the left of median line and 3.5 centimeters below the nipple line; there is no epigastric pulsation; the pulse is 104 and the systolic blood pressure 144 millimeters Hg; the heart sounds are clear but somewhat enfeebled; the liver and spleen are not enlarged.

The patient lost about 1.8 kilograms (4 pounds) in weight while upon the rice mixed with the polishing, but, upon being placed on the rice with the extract, he began to gain in weight and continued to do so up to the time of the end of the experiment. The earlier notes regarding him are unimportant. On the eighty-fifth day the systolic blood pressure was 120 millimeters Hg. On the ninety-ninth day the note made was as follows: Pulse slow and regular, rather weak; no throbbing over cardiac area; no epigastric pulsation; heart sounds clear; no œdema of the legs; knee jerks absent; his condition remained about the same. At the end of the experiment on the one hundred eighth day, the note read as follows: Point of maximum



impulse not visible nor distinctly palpable; heart sounds feeble but clear; second aortic sound accentuated at the base; no œdema of the legs, and no tenderness of the calves; says he feels weaker than before taking the diet, but he weighs 0.9 kilogram (2 pounds) more than before the experiment. The urine contained no albumin nor casts. Twelve days after his return to the regular prison ration he had gained 1.3 kilograms (3 pounds) more.

CASE NO. 6 (GROUP I).

Diet: White rice + rice polishings for 13 days followed by white rice + extract of polishings for 95 days, together with the special diet common to all the groups. } Total period of experiment, 108 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Examination shows a well-developed and well-nourished man; percussion and auscultation of the lungs reveals nothing abnormal; examination of the heart shows the point of maximum impulse not distinctly visible; just palpable 6 centimeters to the left of the median line and 3 centimeters below the nipple line; there is no increase in the area of cardiac dulness; the heart sounds are clear; there is no epigastric pulsation; the pulse is 80, and the systolic blood pressure 114 millimeters Hg; the liver and spleen are not enlarged; the knee jerks are active.

He lost 4.08 kilograms (9 pounds) in weight during the time he was fed on rice mixed with the polishings, but when the extract of polishings was added to the rice instead of the polishings, he regained about 0.9 kilogram (2 pounds). The earlier notes in regard to him are otherwise unimportant. The knee jerks remained active. On the eighty-fifth day the systolic blood pressure was 95 millimeters. On the ninety-ninth day epigastric pulsation was visible, but there was no throbbing over the cardiac area; the point of maximum impulse was not visible, but was just palpable within the nipple line; the heart sounds were clear, and the pulse slow and regular; there was no œdema of the legs; the knee jerks were active. The prisoner made no complaints except of small erosions on the edge of the lips and on the tongue. On the one hundred fifth day there was no particular change in his condition. The erosions about the mouth had improved by application of a 5-per-cent solution of silver nitrate. On the one hundred eighth day the note made was as follows: Fairly well nourished; pulse 100, and of good volume; some epigastric

pulsation; no throbbing over the cardiac area; point of maximum impulse not visible nor distinctly palpable; heart sounds clear; no pain nor tenderness of the legs; no œdema of legs; the knee jerks are active; he says he feels about the same as before he began the diet; the urine contained no albumin nor casts. He was placed on the regular prison ration, but thirteen days later he had not gained in weight.

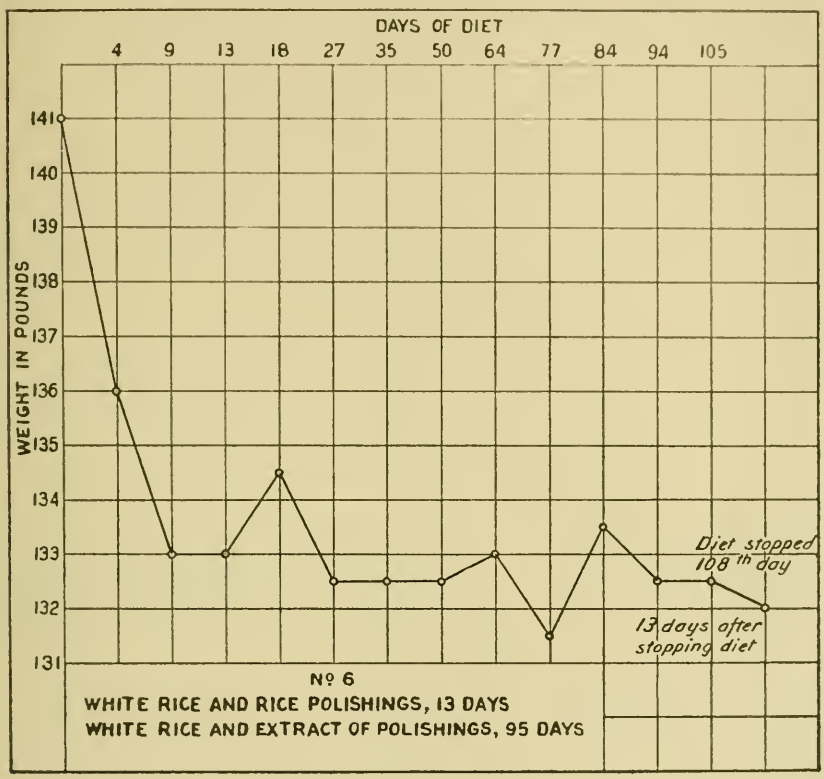


TABLE III.—*Record of rations consumed by prisoners of Group I.*[a]

Prisoner number.	Kind of rice.	Duration of experiment.
4	White rice + rice polishings, 13 days; and white rice + extract of rice polishings, 84 days.	97 days, January 17 to April 22.
2, 1, 6, 5, 3	White rice + rice polishings, 13 days; and white rice + extract of rice polishings, 95 days.	108 days, January 17 to May 3.

[a] Breakfast was uniform throughout the experiments and consisted of bread, about 100 grams; coffee, about 500 cubic centimeters; and sugar, about 15 grams. See Table I, page 293.

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 1.						
Rice	150	150	150	150	150	150
Bacon	50	50	50	50	50	50
Day 2.						
Onions	50	50	50	50	50	50
Lard	10	10	10	10	10	10
Rice	300	300	300	300	300	300
Sugar	0	75	0	75	25	25
Bananas	150	150	150	150	150	150
Day 3.						
Bread	100	100	100	150	100	100
Rice	100	100	100	100	100	100
Starch	0	0	0	15	0	25
Sugar	0	0	0	10	0	15
Lard	0	0	0	5	0	10
Rice	150	150	150	150	150	150
Bacon	0	0	0	0	0	0
Day 4.						
Rice	25	25	25	25	25	25
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	25	25	25	25	25	25
Sugar	75	75	75	75	75	75
Bananas	150	150	150	150	150	150
Day 5.						
Bread	150	150	150	150	150	150
Rice	25	25	25	25	25	25
Bacon	30	30	30	30	30	30
Bread	200	200	200	200	200	200
Rice	50	50	50	50	50	50
Starch	50	50	50	50	50	50
Sugar	25	25	25	25	25	25
Lard	20	20	20	20	20	20
Day 6.						
Rice	0	0	0	0	0	0
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	0	0	0	0	0	0
Bacon	50	50	50	50	50	50
Day 7.						
Rice	0	0	0	0	0	0
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Bread	200	200	200	200	200	200
Rice	0	0	0	0	0	0
Starch	0	0	0	0	0	0
Sugar	0	0	0	0	0	0
Lard	0	0	0	0	0	0

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 8.						
Rice	0	0	0	0	0	0
Bacon	50	50	50	50	50	50
Rice	0	0	0	0	0	0
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 9.						
Bread	150	150	150	150	150	150
Rice	0	0	0	0	0	0
Bacon	30	30	30	30	30	30
Rice	0	0	0	0	0	0
Sugar	0	0	0	0	0	0
Bananas	150	150	150	150	150	150
Day 10.						
Rice	0	0	0	0	0	0
Bacon	50	50	50	50	50	50
Bread	200	200	200	200	200	200
Rice	0	50	0	50	0	0
Starch	0	25	0	25	0	0
Sugar	0	10	0	10	0	0
Lard	0	5	0	5	0	0
Day 11.						
Rice	0	0	0	0	0	0
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	0	0	0	0	0	0
Bacon	50	50	50	50	50	50
Day 12.						
Bread	150	150	150	150	150	150
Rice	0	0	0	0	0	0
Bacon	30	30	30	30	30	30
Rice	0	0	0	0	0	0
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 13.						
Bread	150	150	150	150	150	150
Rice	0	0	0	25	0	0
Starch	20	20	20	20	20	20
Sugar	10	10	10	10	10	10
Lard	10	10	10	10	10	10
Rice	0	0	0	0	0	0
Sugar	75	75	75	75	75	75
Bananas	150	150	150	150	150	150
Day 14.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	350
Rice	350	350	350	350	250	50

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 14—Ctd.						
Onions	150	150	150	150	125	75
Lard	20	20	20	20	20	20
Day 15.						
Bread	150	75	150	150	150	75
Rice	100	50	100	100	100	50
Starch	50	25	50	50	50	25
Sugar	25	10	25	25	25	10
Lard	20	10	20	20	20	10
Bread	150	75	100	100	100	150
Rice	200	200	200	200	200	200
Bacon	50	50	50	50	50	50
Day 16.						
Rice	300	300	300	300	300	300
Sugar	25	25	25	25	25	25
Bananas	100	100	100	100	100	100
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 17.						
Bread	50	50	75	140	150	150
Rice	200	200	100	65	0	0
Bacon	30	30	30	30	30	30
Rice	300	300	300	300	300	300
Sugar	40	40	40	40	40	40
Bananas	150	150	150	150	150	150
Day 18.						
Rice	300	300	300	300	225	300
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Bread	100	100	100	175	200	200
Rice	100	100	100	100	100	100
Starch	25	25	0	25	0	0
Sugar	10	10	0	10	0	0
Lard	10	10	0	10	0	0
Day 19.						
Rice	300	300	300	200	225	200
Bacon	50	50	50	50	50	50
Rice	300	300	300	300	300	300
Sugar	65	40	50	75	75	75
Bananas	150	150	150	150	150	150
Day 20.						
Rice	300	300	300	265	225	200
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Bread	65	150	135	150	200	200

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 20—Ctd.						
Rice	100	35	50	50	75	50
Starch	50	75	25	25	40	25
Sugar	25	10	10	10	10	10
Lard	20	10	10	10	10	10
Day 21.						
Rice	300	300	265	300	300	300
Bananas	100	100	100	100	100	100
Sugar	15	15	25	25	25	25
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 22.						
Rice	200	200	200	200	200	200
Bacon	30	30	30	30	30	30
Bread	150	135	100	100	75	0
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 23.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	300	300	300	300	300
Sugar	75	75	75	75	75	75
Bananas	150	150	150	150	150	150
Day 24.						
Bread	150	150	150	150	150	150
Rice	0	30	0	30	0	0
Starch	0	15	0	15	0	0
Sugar	0	10	0	10	0	0
Lard	0	5	0	5	0	0
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 25.						
Rice	200	200	200	200	200	200
Bread	150	0	100	75	135	150
Bacon	30	30	30	30	30	30
Dinner	No record kept.					
Day 26.						
Rice	300	300	150	265	300	300
Bananas	100	100	100	100	100	100
Sugar	0	0	0	10	0	0
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 27.						
Rice	300	300	300	300	300	265
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Bread	200	200	200	200	200	200
Rice	30	30	30	30	30	30
Starch	20	20	20	20	20	20
Sugar	10	10	10	10	10	10
Lard	5	5	5	5	5	5
Day 28.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	0	0	100	75	0	75
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 29.						
Bread	150	150	150	150	150	150
Rice	0	0	0	0	0	0
Starch	0	0	0	0	0	0
Sugar	25	25	25	25	25	25
Rice	350	115	175	305	350	175
Onions	150	150	150	150	150	150
Lard	20	20	10	20	20	20
Day 30.						
Rice	200	200	200	175	200	200
Bread	150	150	150	75	150	150
Bacon	30	30	30	30	30	30
Rice	300	300	300	265	300	150
Bread	0	0	0	0	150	150
Bacon	50	50	50	50	50	50
Day 31.						
Rice	300	300	200	300	300	265
Bananas	150	150	150	150	150	150
Rice	300	300	300	225	300	300
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Day 32.						
Rice	200	200	200	200	200	300
Bread	150	150	75	110	140	75
Bacon	30	30	30	30	30	30
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 33.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 33—Ctd.						
Rice, Onions, Lard	No record kept.					
Day 34.						
Rice	200	200	200	200	100	0
Bread	150	25	75	100	150	150
Bacon	30	30	30	30	30	30
Rice	300	300	100	300	300	150
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 35.						
Rice	200	300	300	270	270	270
Bananas	100	100	100	100	100	100
Sugar	10	0	0	0	0	0
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 36.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice, Bananas, Sugar	No record kept.					
Day 37.						
Rice	200	200	200	200	200	200
Bread	150	50	110	110	150	150
Bacon	30	30	30	30	30	30
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 38.						
Rice	300	300	200	300	100	100
Bananas	100	100	100	100	100	100
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 39.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	350	350	175	350	350	350
Onions	150	0	0	150	150	150
Lard	20	0	0	20	20	20

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 40.						
Rice	200	200	200	200	200	165
Bread	100	135	150	100	150	150
Bacon	30	30	30	30	30	30
Rice	0	300	225	300	300	100
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 41.						
Rice	300	300	300	240	300	300
Bananas	100	100	100	100	100	100
Rice	350	350	350	305	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 42.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	300	265	300	300	300
Bananas	150	150	100	150	150	150
Day 43.						
Rice	200	200	200	200	200	200
Bread	50	100	0	100	150	50
Bacon	30	30	30	30	30	30
Rice	350	350	350	350	350	350
Onions[a]	150	150	150	150	150	150
Day 44.						
Rice	300	300	300	300	300	300
Onions	100	100	100	100	100	100
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Day 45.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 46.						
Rice	200	200	200	200	200	100
Bread	0	25	0	25	50	0
Bacon	30	30	30	30	30	30
Rice	300	300	150	300	300	300
Bananas	150	150	150	150	150	150
Sugar	0	25	0	0	25	0
Day 47.						
Rice	150	265	150	300	300	240
Bananas	100	100	100	100	100	100

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 47—Ctd.						
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 48.						
Rice	0	265	265	240	300	0
Bacon	50	50	50	50	50	50
Rice	0	270	100	100	300	0
Bananas	50	150	100	50	150	150
Day 49.						
Rice	175	180	100	170	100	100
Bread	110	140	0	110	140	75
Bacon	30	30	30	30	30	30
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 50.						
Rice	300	300	225	300	270	265
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	270	200	100	300	300	100
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 51.						
Rice	0	240	0	0	60	0
Bananas	0	100	0	50	100	100
Sugar	25	25	25	25	25	25
Rice	0	0	0	0	300	0
Bacon	50	50	50	50	50	50
Day 52.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	350	350	230	350	350	175
Onions	150	150	75	150	150	75
Lard	20	20	10	20	20	10
Day 53.						
Rice	200	200	200	200	200	200
Bread	0	75	75	150	50	75
Bacon	30	30	30	30	30	30
Rice	0	0	0	0	0	0
Bananas	150	150	150	150	150	150
Day 54.						
Rice	0	0	0	0	100	0
Bananas	50	100	100	100	100	100
Sugar	0	25	0	0	25	0

[a] Raw onions with vinegar.

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 54—Ctd.						
Rice	0	0	0	0	175	115
Onions	150	150	0	150	150	0
Lard	20	20	0	20	20	0
Day 55.						
Rice	225	300	240	300	225	240
Bacon	50	50	50	50	50	50
Rice	300	300	0	300	300	300
Bananas	50	150	50	50	50	50
Day 56.						
Rice	200	0	175	165	200	200
Bread	0	0	75	110	150	150
Bacon	30	30	30	30	30	30
Rice	350	350	350	350	350	350
Onions	50	20	150	150	0	150
Lard	10	5	20	20	0	20
Day 57.						
Rice	300	300	300	300	300	300
Onions	100	30	100	100	100	100
Lard	15	5	15	15	15	15
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Day 58.						
Rice	75	0	150	100	150	0
Bananas	50	100	0	100	100	100
Rice	300	240	300	300	300	300
Bacon	50	50	50	50	50	50
Day 59.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	350	350	350	350	350	350
Onions	75	75	75	75	75	75
Lard	10	10	10	10	10	10
Day 60.						
Rice	300	300	300	300	75	0
Bread	0	0	0	0	150	150
Bacon	30	30	30	30	30	30
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Day 61.						
Rice	300	270	150	275	265	225
Bananas	100	100	100	100	100	100
Sugar	25	0	0	0	25	0
Rice	350	115	115	350	350	265
Onions	150	0	150	150	150	150
Lard	20	0	20	20	20	20

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 62.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	0	265	300	265	60
Bananas	150	150	150	150	100	50
Day 63.						
Rice	200	200	200	200	200	200
Bread	0	0	0	0	100	0
Bacon	30	30	30	30	30	30
Rice	350	350	350	350	350	350
Onions	150	0	0	150	150	150
Lard	20	0	0	20	20	20
Day 64.						
Rice	300	300	265	300	300	300
Onions	0	0	0	0	0	0
Lard	0	0	0	0	0	0
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Day 65.						
Rice	300	300	265	300	300	300
Bananas	50	100	100	100	100	100
Sugar	0	25	0	25	0	0
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 66.						
Rice	300	300	240	300	300	300
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	300	75	150	300	150	200
Bananas	150	150	150	150	150	150
Sugar	75	0	0	50	0	0
Day 67.						
Rice	200	200	200	200	200	200
Bread	150	0	0	75	150	75
Bacon	30	30	30	30	30	30
Rice	350	230	350	350	350	175
Onions	150	0	0	150	150	75
Lard	20	0	0	20	20	10
Day 68.						
Rice	300	300	30	300	300	300
Bananas	150	150	150	150	150	150
Sugar	t[a]	t	0	0	t	0
Rice	350	0	0	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20

[a] Very small amount.

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 69.						
Rice	300	300	300	265	300	300
Bacon	50	50	50	50	50	50
Rice	300	0	150	75	300	240
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 70.						
Rice	300	300	300	300	300	300
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	300	300	150	300	240	200
Bacon	50	50	50	50	50	50
Day 71.						
Rice	200	200	200	200	200	200
Bread	0	0	0	0	0	0
Bacon	30	30	30	30	30	30
Rice	30	30	30	30	150	30
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 72.						
Rice	300	265	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	305	350	115	350	225	265
Onions	50	50	20	0	150	50
Lard	10	10	5	0	20	10
Day 73.						
Rice Bananas Sugar Rice Onions Lard	No record kept.					
Day 74.						
Rice	200	200	200	200	200	200
Bread	0	0	0	0	0	0
Bacon	30	30	30	30	30	30
Rice	300	150	0	300	240	200
Bananas	150	150	150	150	150	150
Sugar	75	0	0	75	75	40
Day 75.						
Rice	0	0	0	0	0	0
Bananas	100	100	100	100	100	100
Sugar	10	0	0	0	0	10
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 76.						
Rice	300	265	150	265	150	200
Onions	100	0	30	100	100	100
Lard	15	0	5	15	15	15
Rice	300	200	100	300	270	75
Bacon	50	50	50	50	50	50
Day 77.						
Rice	0	0	0	0	150	150
Bananas	50	100	50	100	100	100
Sugar	25	0	10	20	0	0
Rice	300	0	0	300	300	150
Bacon	50	50	50	50	50	50
Day 78.						
Rice	200	200	200	200	200	200
Bread	0	0	0	0	0	0
Bacon	30	30	30	30	30	30
Rice	350	350	305	350	350	350
Onions	t	t	t	t	150	150
Lard	t	t	t	t	20	20
Day 79.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	0	0	0	0	0	0
Bananas	150	t	0	t	0	150
Sugar	75	t	0	t	0	75
Day 80.						
Rice	300	0	0	300	265	300
Onions	100	0	0	0	50	0
Lard	15	0	0	0	10	0
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 81.						
Rice	300	300	300	200	300	225
Bananas	120	120	50	50	120	100
Sugar	10	10	10	25	25	25
Rice	90	90	35	35	350	Sick
Onions	40	120	0	20	0	Sick
Lard	5	15	0	5	0	Sick
Day 82.						
Rice	200	160	50	200	200	200
Bread	0	0	120	0	120	0
Bacon	30	30	30	30	30	30
Rice	265	40	40	265	40	40
Bacon	50	50	0	50	50	0

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 83.						
Rice	300	40	0	150	300	100
Onions	100	0	0	50	100	0
Lard	15	0	0	10	15	0
Rice	75	40	0	225	200	150
Bananas	150	150	150	150	150	150
Day 84.						
Rice	300	200	300	300	300	240
Bacon	50	50	50	50	50	50
Rice	115	230	t	230	175	175
Onions	150	75	0	40	40	75
Lard	20	10	0	5	5	10
Day 85.						
Rice	300	270	265	300	300	150
Bananas	100	100	100	100	100	100
Sugar	t	t	0	0	0	0
Rice	150	265	150	300	265	225
Bacon	50	50	50	50	50	50
Day 86.						
Rice	200	200	150	200	200	200
Bread	0	0	0	0	0	0
Bacon	30	30	30	30	30	30
Rice	350	280	0	265	90	90
Onions	75	75	0	75	0	0
Lard	10	10	0	10	0	0
Day 87.						
Rice	300	150	75	300	300	300
Bacon	50	50	25	50	50	50
Rice	0	0	40	40	80	40
Bananas	150	150	150	150	150	150
Sugar	75	0	10	75	25	30
Day 88.						
Rice	300	300	60	300	150	300
Onions	25	50	0	0	0	50
Lard	5	10	0	0	0	10
Rice	300	40	225	300	300	270
Bacon	50	50	50	50	50	50
Day 89.						
Rice	300	300	0	150	200	150
Bananas	0	100	50	0	100	100
Sugar	0	0	0	25	10	10
Rice	35	0	0	t	175	120
Onions	0	0	0	0	0	0
Day 90.						
Rice	200	160	135	200	200	200
Bread	0	0	0	0	0	0

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 90—Ctd.						
Bacon	30	30	30	30	30	30
Rice	300	t	40	225	225	200
Bacon	50	50	50	50	50	50
Day 91.						
Rice	300	150	150	300	300	300
Onions	0	50	100	0	100	50
Lard	0	10	15	0	15	10
Rice	0	0	0	240	150	0
Bananas	0	100	50	0	100	50
Sugar	0	t	t	0	0	t
Day 92.						
Rice	300	225	150	300	300	300
Bacon	50	50	50	50	50	50
Rice	350	175	t	225	225	225
Onions	0	20	0	20	150	20
Lard	0	5	0	5	20	5
Day 93.						
Rice	300	300	300	300	300	300
Bananas	100	100	100	100	100	100
Sugar	25	25	25	25	25	25
Rice	300	200	75	300	300	300
Bacon	50	50	50	50	50	50
Day 94.						
Rice	0	0	0	0	35	0
Bread	150	150	0	75	150	150
Bacon	30	15	30	30	30	30
Rice	350	350	(?)	350	350	350
Onions	0	0	(?)	0	150	150
Lard	0	0	(?)	0	20	20
Day 95.						
Rice	300	300	(?)	300	300	240
Bacon	0	0	(?)	0	0	0
Rice	240	300	(?)	300	225	265
Bananas	150	150	(?)	150	150	150
Sugar	75	20	(?)	0	0	30
Day 96.						
Rice	300	300	(?)	240	200	225
Onions	0	0	(?)	0	0	0
Rice	225	240	(?)	150	225	150
Bacon	50	50	(?)	50	50	50
Day 97.						
Rice	0	0	(?)	0	0	0
Bananas	100	50	(?)	100	100	0
Sugar	0	0	(?)	0	0	0
Rice	300	300	150	300	225	300
Fish	30	30	30	30	30	30

TABLE III.—*Record of rations consumed by prisoners of Group I*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 98.						
Rice	(a)	0	150	250	265	250
Fish	30	30	30	30	30	
Rice	300	200	300	300	225	
Potatoes	100	150	150	150	150	
Bacon	50	25	50	50	50	
Day 99.						
Rice	200	200	150	t	0	
Potatoes	75	75	150	150	0	
Bacon	15	15	30	30	0	
Rice	300	240	300	240	250	
Fish	30	30	30	30	30	
Day 100.						
Rice	265	240	300	300	150	
Bananas	100	100	100	100	100	
Rice	50	75	0	175	135	
Bread	75	150	150	150	0	
Bacon	30	30	30	30	30	
Day 101.						
Rice	300	300	300	300	300	
Fish	25	25	25	25	25	
Potatoes	100	100	100	100	100	
Rice	350	175	350	350	265	
Onions	0	0	0	0	0	
Day 102.						
Rice	300	300	300	300	300	
Fish	40	40	40	40	40	
Rice	225	225	265	300	300	
Potatoes	100	100	100	100	0	
Bacon	30	30	30	30	0	
Day 103.						
Rice	300	300	300	300	150	
Potatoes	100	100	100	100	100	

Diet.	Amount, in grams, consumed by prisoner number—					
	4	2	1	6	5	3
Day 103—Ctd.						
Fish	30	30	30	30	30	
Starch	10	10	10	10	10	
Lard	15	15	15	15	15	
Rice	40	40	225	225	150	
Bacon	50	50	50	50	50	
Day 104.						
Rice	200	265	300	200	200	
Potatoes	100	100	100	50	100	
Bacon	30	30	30	15	30	
Rice	300	225	265	300	150	
Bananas	150	150	150	150	150	
Day 105.						
Rice	240	265	250	300	300	
Fish	30	30	30	30	15	
Rice	225	100	150	265	265	
Potatoes	100	100	100	50	100	
Bacon	30	30	30	15	30	
Day 106.						
Rice	300	300	265	240	240	
Potatoes	100	100	100	100	100	
Fish	30	30	30	30	30	
Rice	100	100	100	300	75	
Bananas	150	50	150	150	150	
Sugar	0	75	0	75	0	
Day 107.						
Rice	225	200	100	225	150	
Bacon	50	50	0	50	50	
Rice, Potatoes, Fish	No record kept.					
Day 108.	End of experiment.					

[a] Diet discontinued.

GROUP II.

CASE NO. 7 (GROUP II).

Diet: White rice for 97 days followed by red rice for 20 days, together with the special diet common to all the groups. } Total period of experiment, 117 days.

Dried codfish and potatoes were added to the diet on the 97th day.

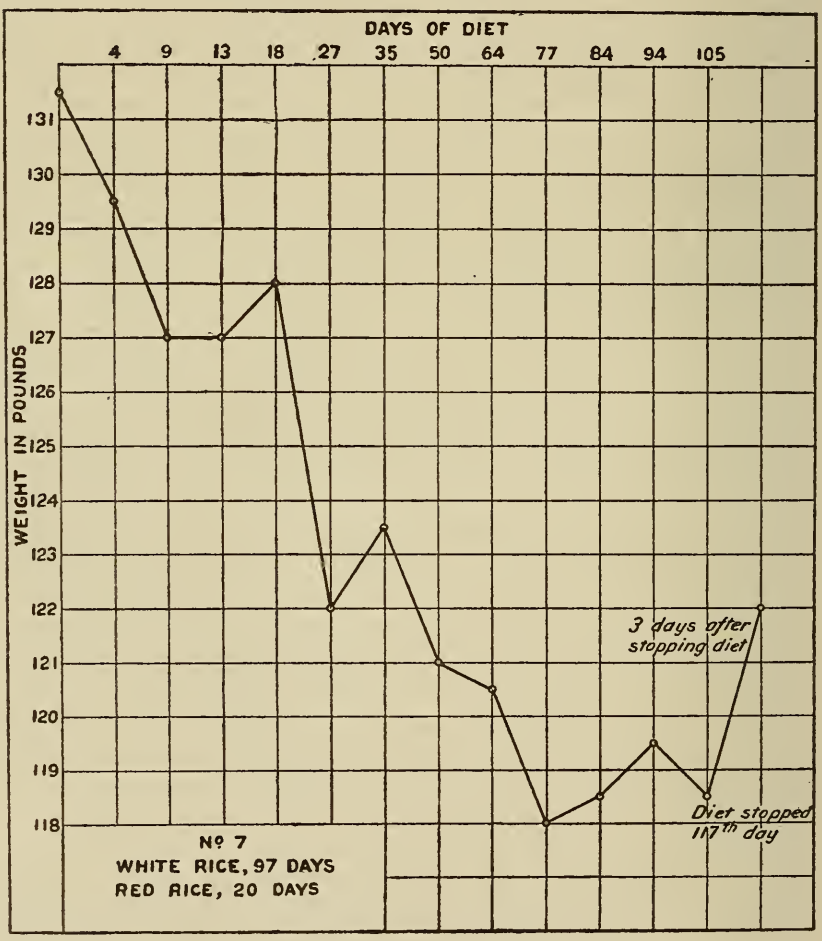
Following is a summary of the notes of the case: Fairly well-nourished man; has been wearing iron prison shackles on his

legs for several months; his knee jerks are absent; states that he has never had beriberi; age about 35 years; the examination of the lungs shows on percussion, anteriorly, general diminished resonance on both sides, more marked on the right side; no special areas of dulness; the respiratory sounds are slightly enfeebled over the right upper lobe of the lung anteriorly; evidently there is an old thickening of the pleura; on auscultation no râles are heard; there is no tubular modification of the breath sounds. The examination of the heart shows no increase in the area of dulness; the point of maximum impulse is not visible; very indistinctly palpable, 7.5 centimeters to the left of the median line and 2.8 centimeters below the nipple line; on auscultation, the first sound at the apex is slightly prolonged, but there is no distinct murmur; neither second sound is accentuated; there is no epigastric pulsation; the pulse is 96, and the systolic blood pressure 102 millimeters Hg; the liver flatness extends from the lower border of the fifth rib; the liver is not palpable below the costal margin; the spleen is not palpable.

Although he ate fairly well at first, he lost rapidly in weight, and after one month weighed 4.5 kilograms (10 pounds) less than when the experiment was begun. On the thirtieth day of the diet, the note made was as follows: Tongue swollen and reddened; slight erosions on the corners of the mouth; hordeolum on left lower eyelid; pulse 104, rather weak; temperature 99, respirations 18; complains of sore throat, and the voice is hoarse; there is no tenderness of the calf muscles, and no œdema of the legs; there is impaired sensation to touch and pain over the skin about the ankles. On the thirty-fourth day the following note was made. Complains of sore mouth and throat; gastric pain and soreness of the calves of the legs; the pain in the calves of the legs has persisted for two days. He is somewhat constipated. A mouth wash of tincture of myrrh and of boric acid, for hourly use, and fluid extract of cascara sagrada, for nightly use, were prescribed. The sores on the corners of the mouth and on the lips were touched with a solution of silver nitrate. The patient grew gradually weaker. A marked catarrhal conjunctivitis developed, which was treated locally. On the fifty-fourth day he was taken to the prison hospital with a temperature of 38°.6. The same diet was taken to him at the hospital, and he was not supposed to eat anything else, but we can not be absolutely sure that during the time which he spent in the hospital he did not sometimes eat other food. It seemed possible that his slight rise of temperature which continued for about two and

one-half days might have been due to old pulmonary trouble. However, there were no râles present in the lungs, and the sputum was negative for tubercle bacilli. On the fifty-seventh day he returned from the prison hospital. However, he continued to lose in weight. On the seventy-fourth day he was found lying in bed, complaining of weakness and of soreness "all over the body," and of a sense of tightness about the neck. He stated that when he moved his hands and legs they seemed stiff. He ate nothing at noon. The pulse was 130; the interval between the heart sounds was evenly spaced (pendulum spacing). There was no accentuation or reduplication of the second sounds at the base, and no murmurs were present. There was visible pulsation of the vessels of the neck. The point of maximum impulse was not distinctly visible nor palpable. The respirations were increased in number. At 4 p. m. he still would not eat. The pulse was slower and occasionally missed a beat. On the seventy-fifth day the following note was made: The pulse is 110; the heart sounds have the same equal spacing. On the seventy-seventh day, the patient feels much better, is up, and eating. Seventy-eighth day: Continues to feel much better, no change in heart sounds. Continues to lose in weight. Eighty-first day: He has recovered from all subjective symptoms and states that he feels well. On the eighty-fifth day the systolic blood pressure was 90 millimeters Hg. On the eighty-eighth day the note was made as follows: 12 m. in bed again; pulse 104; respirations 40; complains of feeling hot, and of tingling and pains in the fingers and toes, and of headache; 4 p. m. pulse 96, respirations 24; complains of pain all over the body, and will not eat. Eighty-ninth day, condition of patient much the same. Ninetieth day, pulse 100. Complains of headache, weakness, no appetite, and pains from the knees to the toes and from the elbows to the fingers. No areas of distinct anæsthesia found. During the whole time of the experiment the knee jerks were absent. On the ninety-first day the note was made that a severe catarrhal conjunctivitis had developed for which treatment was given. Pulse 100, respirations 18. Marked pain in the fingers and toes. Ninety-fifth day, has been in bed two days, complaining of pains throughout the body; pulse 120. There is no distinct increase in the area of cardiac dulness. The heart sounds are evenly spaced. Owing to the complaints of this prisoner, it became necessary to change his diet, and on the ninety-seventh day red rice was substituted for white rice, and dried codfish and potatoes were added to the diet. On the ninety-ninth day the note was made: There is no throbbing over

the cardiac area; the heart sounds are rapid and evenly spaced; no murmur; he complains of no pain. On the one hundred fifth day his condition was much the same. On the one hundred seventeenth day the diet was discontinued. On the one hundred nineteenth day the following note was made: Patient still complains of pains in his fingers and toes; there is no tenderness in the calves of the legs, but he complains of some pain in the chest; apparently nothing in the lungs to account for this pain; pulse 100; no præcordial nor epigastric pulsation; point of maximum impulse invisible; both heart sounds are clear at the apex and base; area of cardiac dulness not increased; there is no œdema of the legs; the knee jerks have been absent throughout the course of the experiment; the examination of the urine shows



no albumin and no casts. He says he feels better than he did before the last change was made in his diet, but weaker than he did before he began the experiment. He had lost 6.1 kilograms (13.5 pounds) during the time he was on the diet. Although this patient had some of the important symptoms of beriberi, a definite diagnosis of the disease was not made. Three days after the change to the regular prison ration he had gained 1.5 kilograms (3.5 pounds).

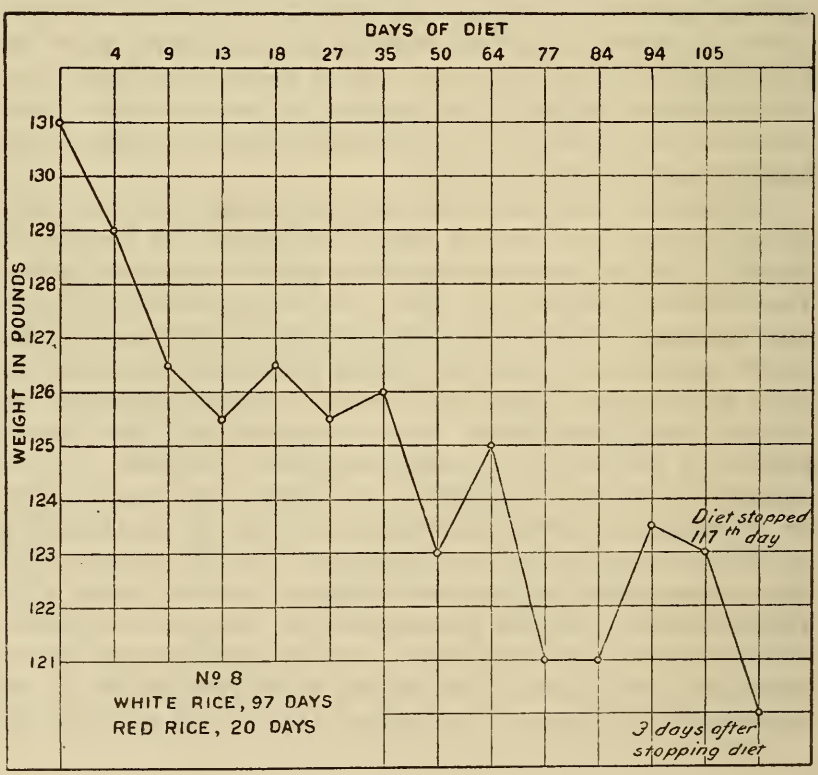
CASE NO. 8 (GROUP II).

Diet: White rice 97 days followed by red rice 20 days, together with the special diet common to all the groups. } Total period of experiment, 117 days.
Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Percussion of lungs shows no dulness; on auscultation, respiratory sounds slightly roughened at apices and somewhat enfeebled; no tubular modification of the sounds and no râles are present; posteriorly the respiratory sounds are normal; examination of the heart shows no increase in the area of dulness beyond the normal; the point of maximum impulse is invisible; it is palpable 7.5 centimeters to the left of the median line and 2 centimeters below the nipple line; the heart sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 88, and the systolic blood pressure 110 millimeters Hg; the spleen and liver are not enlarged; the knee jerks are active.

The notes of this case up to the sixty-fourth day are unimportant except that he had lost 2.7 kilograms (6 pounds) in weight. On this day there was slight bilateral prætibial pitting. There was no complaint of pain. On the seventy-first day the note was made: Point of maximum impulse invisible and not distinctly palpable; no heaving of chest wall; pulse slow and regular; heart sounds normal and normally spaced; œdema of legs distinct; knee jerks active. On the seventy-fourth day he complained of weakness and pains throughout the body. He remained in bed and ate no dinner or supper. The pulse was 88. On the seventy-seventh day the pulse was 80. He had been feeling better since the last note was made. On the seventy-eighth day he complained of pain and tenderness over the region of the right shoulder. On the eighty-first day the pain was better. The knee jerks were still active. On the eighty-fourth day the knee jerks were active. The œdema of the legs continued, and the calves were tender on pressure. On the following day the

systolic blood pressure was 85 millimeters Hg. On the ninetieth day the note was made as follows: He has constantly complained of pain all over the body and is perceptibly weaker; the legs are markedly œdematous; the knee jerks are present but weak; there is slight pulsation visible over the cardiac area; no murmurs are present; the second sounds are not accentuated; there is no distinct change in the cardiac dulness. On the ninety-fifth day the knee jerks could not be elicited; the pulse was 104; otherwise his condition had changed little since the last note. Red, unpolished rice was substituted on the ninety-seventh day for the white polished rice, and dried codfish and potatoes were added to the diet. It was necessary to make these changes, on account of the complaints of the prisoner. On the ninety-ninth day the pulse was 100. There was pulsation over the cardiac area. The first sound was prolonged at the apex, but there was no distinct murmur. The point of maximum impulse was 9 centimeters to the left of the median line, but there was no distinct increase in the area of cardiac dulness beyond the normal limits. There was marked œdema and tenderness of the calves



of the legs. The knee jerks were absent. On the following day the pulse was 92, and on the one hundred fourth day it was 76. The patient's condition did not change much during the next two weeks. During this time he had not gained in weight. On the one hundred seventeenth day the diet was discontinued, and he was placed upon the regular prison ration. Two days later the following note was made: Pulse 88; no epigastric pulsation; the point of maximum impulse is invisible; it is palpable 9.25 centimeters to the left of the median line; the first sound of the heart is prolonged at the apex; there is no distinct murmur; the cardiac dulness extends 2 centimeters to the left of the nipple line and to the right not beyond the edge of the sternum; the nutrition is fair; there is still marked pain and tenderness in the calves of the legs; the œdema of the legs has disappeared; the knee jerks are absent; the examination of the urine showed no albumin and no casts; he states that he feels somewhat stronger since the change in diet. Three days after his return to the regular prison ration he had lost 1.3 kilograms (3 pounds). He gradually recovered. This man evidently suffered from beriberi.

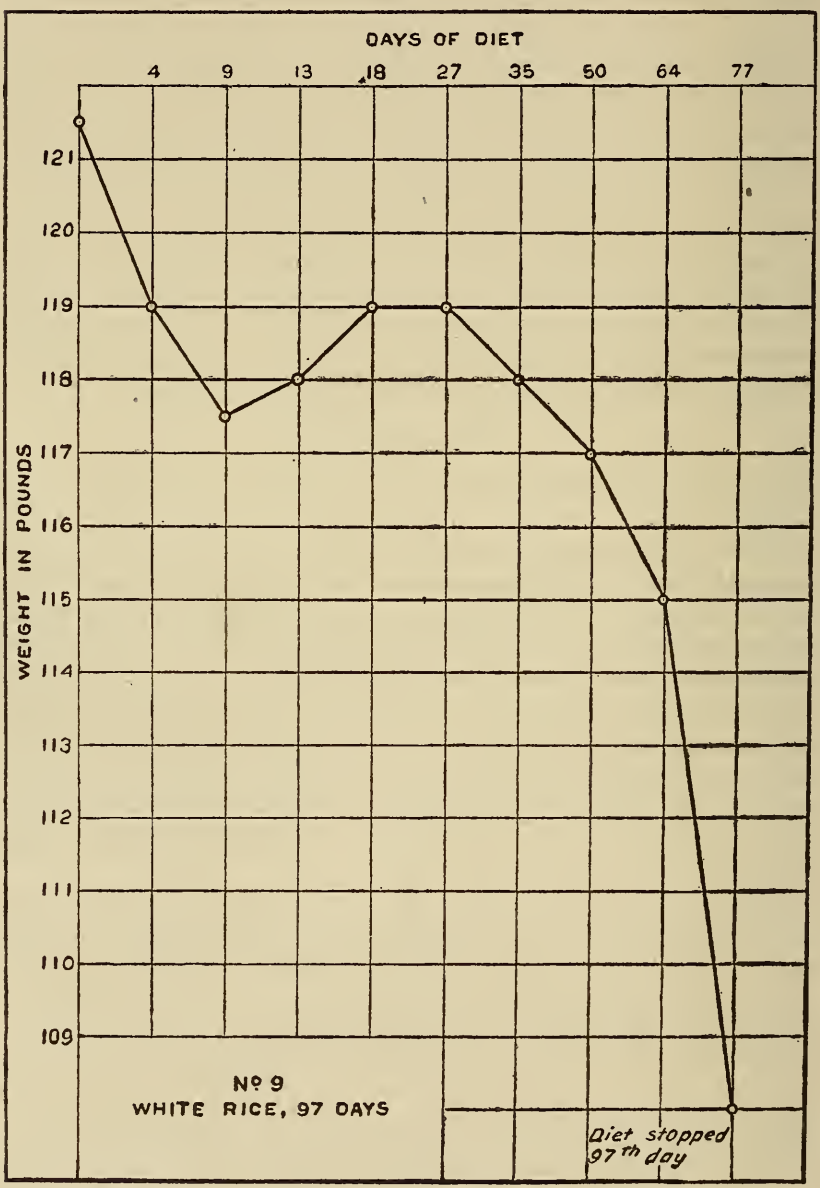
CASE NO. 9 (GROUP II).

Diet: White rice 97 days, together with the special diet common to all the groups.

Following is a summary of the notes of the case: Fairly well-nourished individual; percussion of the lungs shows no dulness; on auscultation the respiratory sounds are normal; examination of the heart shows no increase in the area of cardiac dulness beyond the normal; the point of maximum impulse is invisible; it is palpable 6.5 centimeters to the left of the median line and 3 centimeters below the nipple line; the heart sounds are clear at the apex and base; there is no visible epigastric pulsation; the pulse is 86, and the systolic blood pressure 100 millimeters Hg (Faught); the liver and spleen are not enlarged; the knee jerks are active.

The notes of this case are unimportant up to the thirty-fifth day, when erosions about the corners of the lips appeared. These were touched with a solution of silver nitrate. On the fifty-third day the note was made that for some days he has complained of soreness of the skin over the epigastrium, and has lost 2.2 kilograms (5 pounds) in weight since the beginning of the experiment. By the seventy-fourth day he had lost 9.5 kilograms (21 pounds). The note on this day reads: He has been complaining for some days of pain in the abdomen and chest and seems

much weaker; the pulse is normal; he remained in bed and ate no dinner nor supper. On the seventy-ninth day he was in bed, complaining of epigastric pain; pulse 80, rather weak. On the eightieth day the knee jerks were still present, but were weak; pulse 84 before and 96 after slight exertion; epigastric pulsation was visible; the respirations were 60 and very shallow; the first heart



sound was prolonged, but there was no distinct murmur; the second sounds were not accentuated nor reduplicated at the base. On the eighty-first day he was taken to the prison hospital on account of the persistent dyspnœa. Here he was given the same diet, and was isolated in a locked room. However, it is possible that he may have received some other food during the time he was in the hospital. On the eighty-fourth day the pulse was 100 and the respirations 40; the heart sounds were clear; the first sound was prolonged; there was no cardiac pulsation visible and no distinct increase in the area of dulness to the right or left; the knee jerks were doubtful; the legs were held rigidly. On the eighty-fifth day he stated his fingers felt as though they were made of rubber. There was slight anæsthesia over the finger tips. The systolic blood pressure was 85 millimeters Hg. On the eighty-eighth day the note states: Pulse 72; no epigastric nor cardiac throbbing; no marked tenderness of calves of the legs. On the eighty-ninth day, general condition very much the same; the knee jerks are absent. On the ninetieth day the pulse was 88; the patient complained of pain in the legs and chest; he was very weak, but could walk; his gait showed evidence of muscular weakness, but was not typically ataxic; there was hyperæsthesia of the muscles of the legs, and there was slight œdema over the tibiæ; there was no epigastric nor præcordial pulsation. The knee jerks were absent. On the ninety-first to the ninety-seventh days the jerks were always absent. The condition of the patient remained about the same, except that he grew weaker. On the ninety-seventh day there was slight œdema over the tibiæ. The diet was then discontinued. This man evidently suffered from beriberi. The urine was examined daily for the last three weeks of the experiment. It was always greatly decreased in amount but contained no albumin nor casts.

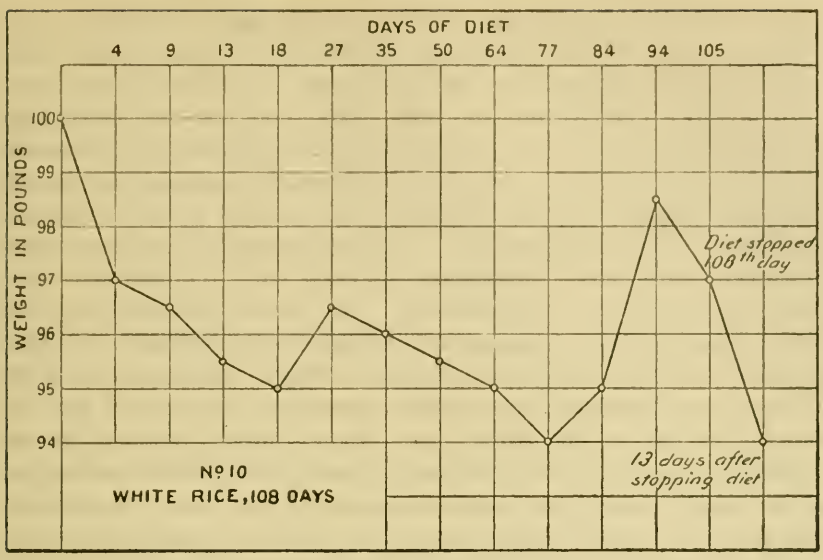
CASE NO. 10 (GROUP II).

Diet: White rice 108 days, together with the special diet common to all the groups.
Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Sparely nourished man of small stature; percussion and auscultation of the lungs normal; examination of the heart shows no increase of the area of dulness beyond the normal; the point of maximum impulse is invisible; it is palpable 6.25 centimeters to the left of the median line and 3 centimeters below the nipple line; the heart sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 84, and the systolic blood pressure 124 milli-

meters Hg (Faught); the liver and spleen are not enlarged; the knee jerks are active.

The patient at first lost 2.2 kilograms (5 pounds) in weight. The notes up to the seventy-fourth day of the diet are otherwise unimportant. On the seventy-fourth day he complained of headache and weakness. The pulse was 100. He ate no dinner nor supper. On the eighty-first day the knee jerks were still active. The patient seemed better and did not complain. On the eighty-fifth day the systolic blood pressure was 92 millimeters Hg. On the ninetieth day the knee jerks were weak; the patient stated that he felt well. On the ninety-fifth day the knee jerks were weak; there were no apparent changes in the condition of the heart. Owing to the complaints of this prisoner, on the ninety-seventh day dried codfish and potatoes were added to the diet. On the ninety-ninth day the following note was made: Point of maximum impulse 7.5 centimeters to the left of the median line and 3 centimeters below the nipple line; pulse 84; at the apex the first sound is accentuated; there is a tendency to pendulum spacing between the beats, while there is diffuse throbbing over the cardiac area, extending from the sternum to the nipple; there is slight visible epigastric pulsation and moderate œdema of the legs; there is pain and tenderness of the calves; no hyperæsthesia of the skin; the knee jerks are very weak. One hundred fifth day: Complains of pain in chest and legs; calves tender on pressure, and he walks with a slight limp; pulse 96; there is no œdema of the legs; the knee jerks are not elicited. On the one hundred sixth day the knee jerks could not be elicited. There was no œdema of the legs. The tenderness of the calves continued. On the one hundred eighth day it became necessary to discontinue the diet. The following note was then made: Sparely nourished individual; pulse 88; pulsation over cardiac area seems a little less marked than at the time of the last note, but is easily palpable over the whole cardiac area; slight epigastric pulsation; first sound at beginning much roughened and prolonged; pendulum spacing between the heart sounds has disappeared; the sounds are clear at the base; the point of maximum impulse is 9 centimeters to the left of the median line; the dulness extends to the left 2 centimeters outside the nipple line and to the right just beyond the edge of the sternum; there is slight œdema of the legs and hyperæsthesia of the calf muscles; the knee jerks are absent. Thirteen days after his return to the regular prison ration he had lost 4 pounds more. This man evidently suffered from beriberi.



CASE NO. 11 (GROUP II).

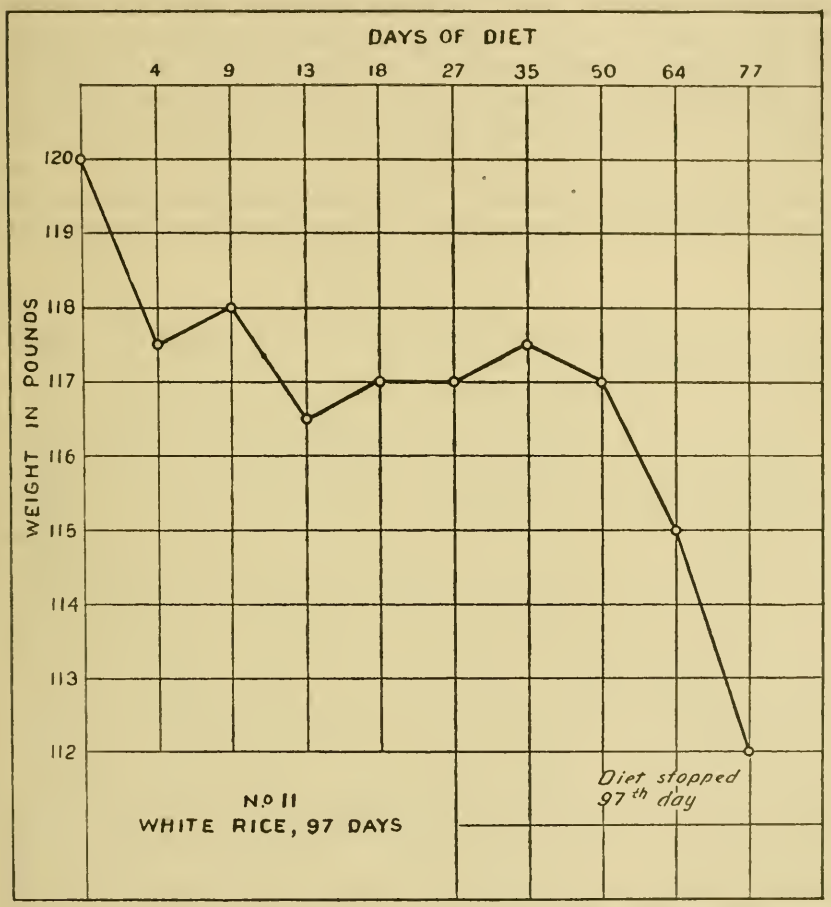
Diet: White rice 97 days, together with the special diet common to all the groups.

Following is a summary of the notes of the case: Fairly well-nourished man; auscultation and percussion of the lungs shows nothing abnormal; examination of the heart shows no increase in the area of cardiac dulness beyond the normal; the point of maximum impulse is not visible; it is palpable 8 centimeters to the left of the median line and 2 centimeters below the nipple line; there is no epigastric pulsation; the heart sounds are clear; the pulse is 80, and the systolic blood pressure 110 millimeters Hg (Faught); the liver dulness extends from the lower border of the fourth rib to the costal margin; the spleen is not palpable; the knee jerks are very active.

The patient lost but 1.3 kilograms (3 pounds) in weight up to the fiftieth day of the diet. On the thirty-fifth day erosions appeared on the corners of the lips. These were touched with a solution of silver nitrate. The notes are otherwise unimportant up to the forty-ninth day, when œdema of the right leg above the ankle was noted. The knee jerks were normal or increased. By the fiftieth day the œdema of the ankle had subsided. On the fifty-third day he complained of soreness of the left eye and of headache. On the sixty-fourth day at noon he vomited. He complained of no pain, and there was no fever. His food was left with him. On the sixty-fifth day he felt better and was eating

again. On the sixty-sixth day he complained of feeling cold; pulse 84; no fever and no pain. There was a slight cough, but apparently no disturbance of the lungs; the right knee jerk seemed more active than the left. His food was left with him as he did not care to eat. On the sixty-seventh day he ate bread and bacon, but no rice for dinner; however, he ate rice for supper. On the seventieth day he complained of general pain throughout the body. His pulse was 84. The first sound of the heart was distinctly prolonged, suggesting a very soft systolic murmur. The knee jerks were not obtained. On the seventy-first day the note states: Point of maximum impulse not distinctly visible; impulse of heart near apex visible between respirations; point of maximum impulse on palpation somewhat diffuse and may be felt as far out as the nipple line; slight visible pulsation in the vessels of the neck; the first heart sound is somewhat prolonged at the apex; there is no distinct murmur; the second sounds are not markedly accentuated; there is no abnormal spacing between the heart sounds. The cardiac dulness extends to the left, 3 centimeters outside of the nipple line; it is not increased to the right of the sternum; the pulse is 88 before and 94 after slight exertion; he complains of soreness over the chest and abdomen, and says that at night the skin feels as though being stretched. He also complains of soreness in the calves of the legs and pain on pressure over the calves of the legs. He winces slightly on pressure in this region. He says he has a sensation as if winds were blowing over the pores of the skin, especially over those of the chest and abdomen. There is apparently no marked loss of tactile or pain sense. The right knee jerk can not be elicited; the left jerk is very weak. On the seventy-fourth day the note reads: The patient has lost 3.6 kilograms (8 pounds) since the beginning of the experiment. He is in bed, and complains of pain over the abdomen, chest, and legs. The calves are tender on pressure. He states that he feels feverish. The pulse is 100. There is no rise in temperature. He ate no dinner nor supper. On the seventy-fifth day the note reads: Pulse 100; point of maximum impulse easily visible, rather diffuse; can be seen and felt as far out as the nipple line; no change in the heart sounds since the seventy-first day; heaving over heart more marked; knee jerks can not be elicited. On the seventy-seventh day the note states that he vomited his dinner. He is very weak; there is marked lameness and dyspnœa; the respirations are 40, and pulse 88. On the seventy-eighth day the note reads: Up at breakfast, in bed at dinner time; he complains chiefly of pain in the legs; there is

marked hyperæsthesia of the calf muscles; the pulse is 80 when lying down and 88 on sitting up; the respirations are 24. On the seventy-fourth day he was found to be suffering from severe suprapubic pain and could not void urine. He was taken to the prison hospital where he was catheterized. It was not necessary to use the catheter after the second day in the hospital. From the eightieth day on the patient was bedridden. On the eighty-



fourth day the following note was made: Pulse 80; marked epigastric pulsation; slight pulsation over the cardiac area; he complains of pain in the calves of the legs which are very tender on pressure; his gait is quite ataxic, the heart sounds are clear; the first sound is somewhat prolonged, but there is no distinct murmur; there is no foot nor wrist drop; the knee jerks are absent. On the eighty-fifth day the note reads: Patient says he feels no particular discomfort when lying down, but suffers from

discomfort in the chest and pains in the legs on getting up. Systolic blood pressure 95 millimeters Hg. Eighty-seventh day, pulse 72; still marked tenderness of calves and general weakness. No præcordial but slight epigastric pulsation. On the ninetieth day, pulse 84, respirations 24. Complains of much pain in the legs. He suffers from weakness and can no longer walk by himself. The knee jerks are absent. For the next few days the patient remained in about the same condition, but grew slightly weaker. On the ninety-seventh day the diet was discontinued. At this time he could just stand and was very weak. Pulse 80. Slight foot drop was present. This man evidently suffered from beriberi. During the last three weeks of the experiment the urine was examined each day and was always found to be greatly decreased in amount. Frequently the daily output was less than 500 cubic centimeters. It never contained albumin nor casts.

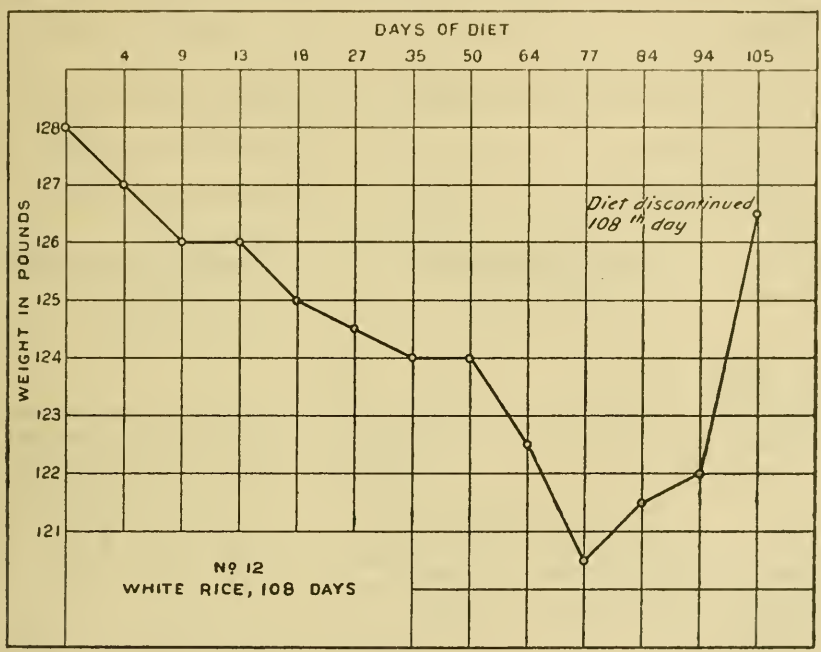
CASE NO. 12 (GROUP II).

Diet: White polished rice 108 days, together with the special diet common to all the groups.
Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Fairly well-nourished man; percussion and auscultation of the lungs show nothing abnormal; examination of the heart shows no increase in the area of cardiac dulness; the point of maximum impulse is invisible; it is palpable 8 centimeters to the left of the median line and 2.5 centimeters below the nipple line; the heart sounds are clear at the apex and base; the pulse is 88, and the systolic blood pressure 118 millimeters Hg (Faught); there is no epigastric pulsation; the liver and spleen are not palpable, and the liver dulness is not increased upward; the knee jerks are active.

The patient lost weight steadily up to the seventy-seventh day of the experiment. The knee jerks were active during this time. The earlier notes are otherwise unimportant, except that on the seventy-fourth day he complained of headache, dizziness, and marked weakness. The pulse was 110, and both knee jerks were found to be very weak. The apex beat of the heart was now palpable in the nipple line. The heart sounds were normally spaced, and there were no murmurs. The cardiac dulness was not distinctly changed. The patient remained in bed and ate no dinner nor supper. The following three days he stayed for the most of the time in bed, eating but little, but on the seventy-seventh day he was up and began to eat better. The knee jerks were active. On the eighty-fifth day the systolic blood pressure was

90 millimeters Hg. On the ninetieth day the note was made that he states that he feels well. The knee jerks are active. By the ninety-fifth day he had gained 0.6 kilogram (1.5 pounds) in weight. On the ninety-seventh day, as already mentioned, it became necessary to add codfish and potatoes to the diet. On the ninety-eighth day at noon he complained of pain and tenderness in the calves of the legs and of disturbance of vision. The pulse was 92. On the ninety-ninth day the note was made: Point of maximum impulse invisible; palpable in the same position as on the thirtieth day. No pulsation over cardiac area. Slight visible epigastric pulsation. There is a very faint systolic murmur at



the apex, which is not transmitted to the base. The second pulmonic sound is slightly accentuated. He states that his feet feel heavy, as though he could not lift them easily, and complains of pain in the calves of the legs and in his eyes. The calves are tender on pressure. There is very slight prætibial pitting. The knee jerks are present. On the one hundredth day the pulse was rather weak. The calves remained tender. On the one hundred first day the pulse was 100; the patient complained of headache, and marked œdema of the lower legs had developed. The knee jerks were active. The patient remained in about the same condition during the next few days. On the one hundred sixth day it was noted that the knee jerks were active and there

was still marked œdema of the legs but the calves seemed no longer tender. On the one hundred eighth day it was necessary to discontinue the diet, owing to the reasons already stated under the other cases. The following note was made on this day: Pulse 80, a little feeble; no throbbing over the cardiac area: point of maximum impulse not distinctly visible nor palpable; the first sound is considerably prolonged at the apex; he complains of pains in the legs and eyes; there is marked œdema of the legs and tenderness on pressure; the knee jerks are active.

TABLE IV.—*Record of rations consumed by prisoners of Group II.*

Prisoner number.	Kind of rice.	Duration of experiment.
7, 8	White rice, 97 days; red rice, 20 days	117 days, January 17 to May 12.
11, 9	White rice	97 days, January 17 to April 22.
10, 12	White rice	108 days, January 17 to May 3.

Diet.	Amount, in grams, consumed by prisoner number—						Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8		7	11	10	12	9	8
Day 1.							*Day 5.*						
Rice	300	300	300	300	300	300	Rice	200	200	200	200	200	200
Bacon	50	50	50	50	50	50	Bread	150	150	150	150	150	150
Day 2.							Bacon	30	30	30	30	30	30
Rice	300	300	300	300	300	300	Bread	200	200	200	200	200	200
Onions	100	100	100	100	100	100	Rice	100	100	100	100	100	100
Lard	15	15	15	15	15	15	Starch	50	0	50	50	50	0
Rice	300	300	300	300	300	300	Sugar	25	0	25	25	25	0
Bananas	150	150	150	150	150	150	Lard	20	0	20	20	20	0
Sugar	75	75	75	75	75	75	*Day 6.*						
Day 3.							Rice	300	300	300	300	300	300
Bread	150	100	100	150	100	100	Onions	100	100	100	100	100	100
Rice	100	100	100	100	100	100	Lard	15	15	15	15	15	15
Starch	50	50	50	25	25	50	Rice	300	300	300	300	300	300
Sugar	25	25	25	15	15	25	Bacon	50	50	50	50	50	50
Lard	20	20	20	10	10	20	*Day 7.*						
Rice	300	300	300	300	150	300	Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50	Bananas	100	100	100	100	100	100
Day 4.							Sugar	25	25	25	25	25	25
Rice	250	300	300	300	300	300	Bread	200	200	200	200	200	0
Onions	100	100	100	100	100	100	Rice	100	100	100	100	100	0
Lard	15	15	15	15	15	15	Starch	0	50	50	0	50	0
Rice	300	300	300	300	300	300	Sugar	0	25	25	0	25	0
Bananas	150	150	150	150	150	150	Lard	0	20	20	0	20	0
Sugar	75	75	75	75	75	75							

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 8.						
Rice	300	300	300	300	300	150
Bacon	50	50	50	50	50	50
Rice	0	175	175	175	175	0
Onions	0	0	150	0	75	75
Lard	0	0	20	0	10	10
Day 9.						
Bread	150	150	150	150	150	150
Rice	200	0	200	200	200	200
Bacon	30	30	30	30	30	30
Rice	0	0	300	0	300	0
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 10.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Bread	200	200	200	200	200	200
Rice	100	100	50	100	100	100
Starch	50	50	50	50	50	50
Sugar	25	25	25	25	25	25
Lard	20	20	20	20	20	20
Day 11.						
Rice	300	300	300	300	300	300
Onions	0	0	100	100	100	100
Lard	0	0	15	15	15	15
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 12.						
Bread	150	150	150	150	150	150
Rice	200	200	200	200	200	200
Bacon	30	30	30	30	30	30
Rice	300	300	350	350	300	350
Onions	25	25	125	150	25	150
Lard	0	0	15	20	0	20
Day 13.						
Bread	150	25	150	150	80	50
Rice	0	175	25	125	35	25
Starch	0	0	0	0	0	0
Sugar	0	0	0	0	0	0
Lard	0	0	0	0	0	0
Rice	300	300	300	300	300	300
Sugar	75	75	75	75	75	75
Bananas	150	150	150	150	150	150
Day 14.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 14—Ctd.						
Rice	350	350	350	350	350	350
Onions	25	100	50	25	25	125
Lard	0	10	10	0	0	15
Day 15.						
Rice	0	50	100	75	100	50
Starch	0	25	50	40	50	25
Sugar	0	125	25	15	25	125
Lard	0	10	20	15	20	10
Bread	150	150	150	(a)	150	150
Rice	200	200	200	(a)	200	200
Bacon	50	50	50	(a)	50	50
Day 16.						
Rice	300	300	300	300	300	300
Sugar	25	25	25	25	25	25
Bananas	100	100	100	100	100	100
Rice	300	350	350	350	350	350
Onions	130	150	150	150	150	150
Lard	15	20	20	20	20	20
Day 17.						
Bread	150	150	150	150	100	75
Rice	100	100	130	100	200	200
Bacon	30	30	30	30	30	30
Rice	225	225	300	275	200	100
Bananas	150	150	150	150	150	150
Sugar	75	38	75	75	75	75
Day 18.						
Rice	300	300	300	300	260	260
Onions	70	100	100	85	100	100
Lard	10	15	15	10	15	15
Bread	200	200	200	200	200	200
Rice	35	0	75	75	100	100
Starch	50	50	25	25	50	50
Sugar	25	25	13	13	25	25
Lard	20	20	10	10	20	20
Day 19.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	300	300	300	300	300
Sugar	75	75	75	75	75	75
Bananas	150	150	150	150	150	150
Day 20.						
Rice	75	300	300	300	300	300
Onions	100	100	100	30	100	100
Lard	15	15	15	5	15	15
Bread	200	200	200	200	200	150

[a] Prison rations.

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, cousumed by prisoner number—						Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8		7	11	10	12	9	8
Day 20—Ctd.							*Day 27.*						
Rice	30	75	65	65	75	85	Rice	100	260	300	200	300	150
Starch	20	40	35	35	40	45	Onions	0	100	100	50	100	50
Sugar	10	20	20	20	20	20	Lard	0	15	15	8	15	8
Lard	5	15	15	15	15	15	Bread	100	65	200	175	150	100
Day 21.							Rice	65	50	65	17	75	33
							Starch	33	25	33	10	37	17
Rice	300	300	300	300	300	300	Sugar	17	13	17	4	20	8
Bananas	100	100	100	100	100	100	Lard	7	10	7	4	15	7
Sugar	0	0	0	0	0	0	*Day 28.*						
Rice	300	300	300	300	300	300							
Bacon	50	50	50	50	50	50	Rice	150	300	300	300	300	275
Day 22.							Bacon	50	25	50	50	50	50
							Rice	200	150	300	40	200	40
Rice	200	200	200	200	200	200	Bananas	150	150	150	150	150	150
Bacon	30	30	30	30	30	30	Sugar	0	0	0	0	0	0
Bread	150	75	150	150	150	20	*Day 29.*						
Rice	350	350	350	350	350	350							
Onions	150	150	150	150	150	150	Bread	0	0	0	0	0	0
Lard	20	20	20	20	20	20	Rice	0	0	0	0	0	0
Day 23.							Starch	0	0	0	0	0	0
							Sugar	0	0	0	0	0	0
Rice	300	300	300	300	300	300	Lard	0	0	0	0	0	0
Bacon	50	50	50	50	50	50	Rice	175	175	350	250	250	310
Rice	300	300	300	300	300	300	Onions	150	0	150	150	75	0
Sugar	0	0	0	0	0	0	Lard	20	0	20	20	10	0
Bananas	150	150	150	150	150	150	*Day 30.*						
Day 24.													
							Rice	200	200	200	200	200	200
Bread	150	135	150	115	135	150	Bread	75	150	150	50	150	75
Rice	20	20	35	20	85	0	Bacon	30	30	30	30	30	30
Starch	10	10	15	10	40	0	Rice	150	200	200	300	150	200
Sugar	5	5	10	5	20	0	Bread	150	150	150	0	100	0
Lard	5	5	10	5	15	0	Bacon	50	50	50	50	50	50
Rice	300	300	300	300	300	300	*Day 31.*						
Bacon	50	50	50	50	50	50							
Day 25.							Rice	225	200	250	200	100	150
							Bananas	150	150	150	150	150	150
Rice	0	200	165	175	200	200	Sugar	0	0	0	0	0	0
Bread	150	0	150	150	150	0	Rice	0	150	225	300	150	150
Bacon	30	30	30	30	30	30	Onions	0	50	100	100	50	50
Dinner	No record.						Lard	0	7	15	15	7	7
Day 26.							*Day 32.*						
Rice	200	300	300	150	250	200	Rice	180	200	200	200	200	200
Bananas	100	100	100	100	100	100	Bread	135	35	135	150	135	0
Sugar	0	0	0	0	0	0	Bacon	30	15	30	30	30	30
Rice	300	300	300	300	300	300	Rice	260	300	300	260	225	260
Bacon	50	50	50	50	50	50	Bacon	50	50	50	50	50	50

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 33.						
Rice	260	260	300	260	300	260
Bacon	50	45	50	50	45	50
Rice	No record kept.					
Onions						
Lard						
Day 34.						
Bread	150	75	150	150	130	0
Rice	100	175	200	200	200	200
Bacon	30	30	30	30	30	30
Rice	225	150	200	300	260	100
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 35.						
Rice	100	260	275	200	200	200
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	235	260	350	350	235	350
Onions	50	75	150	150	150	150
Lard	7	10	20	20	20	20
Day 36.						
Rice	225	150	300	300	260	225
Bacon	50	50	50	50	50	50
Rice	No record kept.					
Bananas						
Sugar						
Day 37.						
Rice	150	150	200	200	200	175
Bacon	30	25	25	30	30	25
Bread	150	50	135	0	135	20
Rice	0	125	275	275	300	175
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 38.						
Rice	150	75	150	50	0	35
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	200	200	300	100	260	200
Bacon	50	50	50	50	50	50
Day 39.						
Rice	200	200	300	260	300	150
Bacon	50	50	50	50	50	50
Rice	45	235	175	310	235	45
Onions	0	150	75	150	150	0
Lard	0	20	10	20	20	0

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 40.						
Rice	200	135	200	180	200	200
Bread	150	150	150	0	150	150
Bacon	0	30	30	30	30	0
Rice	100	300	75	0	0	0
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 41.						
Rice	270	240	240	100	100	300
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	115	0	0	0	0	175
Onions	0	0	0	0	0	0
Lard	0	0	0	0	0	0
Day 42.						
Rice	40	40	240	150	275	30
Bacon	0	0	0	0	0	0
Rice	800	200	300	150	110	150
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 43.						
Rice	200	175	175	200	165	200
Bread	110	150	140	0	150	0
Bacon	0	0	30	30	30	30
Rice	300	300	300	300	300	300
Onions	150	75	150	150	75	150
Day 44.						
Rice	100	300	300	300	300	150
Onions	0	0	0	0	0	0
Rice	300	300	300	240	300	225
Bananas	150	150	150	150	150	150
Sugar	0	0	25	0	25	25
Day 45.						
Rice	270	225	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	350	225	350	300	350	350
Onions	150	0	150	150	150	0
Day 46.						
Rice	20	65	170	100	200	180
Bread	50	50	25	50	50	10
Bacon	0	15	15	0	30	0
Rice	300	260	260	200	200	300
Bananas	150	150	150	150	150	150
Sugar	0	0	25	0	10	0

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—						Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8		7	11	10	12	9	8
Day 47.							*Day 54.*						
Rice	225	240	300	100	260	200	Rice		100	200	300	300	100
Bananas	100	100	100	100	100	100	Bananas		100	100	100	100	100
Sugar	0	0	0	0	0	0	Sugar		0	0	0	0	0
Rice	0	125	0	125	35	125	Rice		300	350	315	350	310
Onions	0	0	0	0	0	0	Onions		0	0	0	0	0
Day 48.							*Day 55.*						
Rice	0	0	300	150	300	225	Rice		100	225	175	175	175
Bacon	50	25	50	50	50	50	Bacon		0	50	50	50	50
Rice	300	260	300	270	270	300	Rice		250	300	300	300	300
Bananas	150	150	150	150	150	150	Bananas		150	150	150	150	150
Sugar	0	0	0	0	0	0	Sugar		0	0	0	0	0
Day 49.							*Day 56.*						
Rice	175	200	175	175	200	200	Rice		200	200	160	0	200
Bread	150	135	110	50	75	0	Bread		0	120	135	110	135
Bacon	0	30	30	25	30	30	Bacon		0	30	30	30	15
Rice	350	235	315	300	350	300	Rice		350	350	300	260	350
Onions	0	150	150	0	75	75	Onions		50	50	150	0	0
Day 50.							*Day 57.*						
Rice	300	300	300	300	300	300	Rice		240	300	270	225	300
Onions	50	150	75	150	75	100	Onions		100	0	0	0	100
Rice	300	300	300	250	200	200	Rice	0	190	260	260	260	300
Bananas	150	150	150	150	150	150	Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0	Sugar	0	0	0	0	0	0
Day 51.							*Day 58.*						
Rice	300	250	150	300	270	360	Rice	0	0	0	225	35	150
Bananas	100	100	100	100	100	100	Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0	Sugar	0	0	0	0	0	0
Rice	300	300	300	300	300	300	Rice	300	300	225	300	240	240
Bacon	50	50	50	50	50	50	Bacon	50	50	50	50	50	25
Day 52.							*Day 59.*						
Rice	300	300	300	300	250	300	Rice	300	150	150	300	240	300
Bacon	50	35	0	0	50	50	Bacon	50	25	50	50	50	50
Rice	280	350	125	350	315	350	Rice	265	175	175	350	0	310
Onions	0	0	0	0	0	0	Onions	150	0	150	150	0	75
Day 53.							*Day 60.*						
Rice	160	150	70	200	200	200	Rice	150	100	200	200	200	70
Bread	75	75	75	150	75	150	Bread	110	65	110	0	150	150
Bacon	30	30	0	30	30	30	Bacon	0	30	30	30	30	30
Rice	300	300	300	300	300	300	Rice	300	250	300	260	250	260
Bananas	150	150	150	150	150	150	Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0	Sugar	0	0	0	0	0	0

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 61.						
Rice	300	150	225	300	150	150
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	175	175	85	35	45	125
Onions	0	0	0	0	0	0
Day 62.						
Rice	200	250	100	150	200	225
Bacon	0	50	25	50	50	25
Rice	270	250	250	100	100	100
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 63.						
Rice	200	175	50	200	160	25
Bread	150	150	150	135	150	150
Bacon	0	30	15	30	30	30
Rice	350	260	350	350	310	350
Onions	0	75	0	150	0	75
Day 64.						
Rice	300	300	300	300	300	300
Onions	0	75	0	0	0	0
Rice	300	(a)	225	300	300	260
Bananas	150	(a)	150	150	150	150
Sugar	0	(a)	25	25	25	0
Day 65.						
Rice	300	225	150	225	260	225
Bananas	100	100	100	100	100	100
Sugar	0	25	0	25	0	25
Rice	200	270	225	300	300	260
Bacon	50	50	25	50	50	50
Day 66.						
Rice	300	(b)	300	300	300	260
Onions	100	(b)	100	100	100	100
Lard	15	(b)	15	15	15	15
Rice	300	(b)	255	225	300	225
Bananas	150	(b)	150	150	150	0
Sugar	0	(b)	0	25	25	0
Day 67.						
Rice	0	0	170	170	200	100
Bread	150	75	150	150	150	100
Bacon	0	30	30	30	30	30
Rice	225	350	350	225	225	290
Onions	0	0	0	0	0	0

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 68.						
Rice	300	250	240	300	100	30
Bananas	150	150	150	150	150	150
Sugar	0	0	0	25	0	0
Rice	260	175	0	225	175	0
Onions	0	0	0	0	0	0
Day 69.						
Rice	150	200	0	300	50	40
Bacon	50	50	50	50	50	25
Rice	250	100	150	150	75	50
Bananas	150	150	150	150	150	150
Sugar	0	0	0	25	0	0
Day 70.						
Rice	0	0	35	250	0	250
Onions	0	0	0	0	0	0
Rice	0	(b)	150	260	300	30
Bacon	0	(b)	50	50	50	50
Day 71.						
Rice	200	25	200	175	200	50
Bread	150	150	150	100	150	0
Bacon	30	30	30	30	30	30
Rice	300	0	35	150	150	300
Bananas	150	150	150	150	150	150
Sugar	25	0	0	0	0	25
Day 72.						
Rice	240	0	150	260	30	0
Bacon	50	50	50	50	50	50
Rice	175	125	310	225	45	225
Onions	150	0	0	150	0	150
Lard	20	0	0	20	0	20
Day 73.						
Rice, Bananas, Sugar, Rice, Onions, Lard	No record kept.					
Day 74.						
Rice	0	0	0	0	0	0
Bread	0	0	0	0	0	0
Bacon	0	0	0	0	0	0
Rice	0	0	0	0	0	0
Bananas	0	0	0	0	0	0
Sugar	0	0	0	0	0	0

[a] Vomiting.

[b] Left with prisoner.

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 75.						
Rice	0	0	0	0	0	0
Bananas	0	0	0	0	0	0
Sugar	0	0	0	0	0	0
Rice	Food left with them and no record kept.					
Bacon						
Day 76.						
Rice	0	0	0	0	100	0
Onions	0	0	0	0	0	0
Rice	260	240	200	300	200	30
Bacon	50	50	50	50	50	0
Day 77.						
Rice	150	30	50	240	0	30
Bananas	100	100	100	100	100	100
Sugar	0	25	0	25	25	10
Rice	240	0	150	200	50	35
Bacon	0	0	0	50	50	50
Day 78.						
Rice	200	200	200	200	170	20
Bread	150	150	150	150	150	75
Bacon	30	30	30	30	30	0
Rice	260	(a)	225	290	70	175
Onions	150	(a)	50	150	150	150
Lard	20	(a)	10	20	20	20
Day 79.						
Rice	300	(a)	225	0	300	30
Bacon	0	(a)	0	50	50	0
Rice	300	(b)	100	150	150	200
Bananas	150	-----	150	150	150	150
Sugar	0	-----	0	0	0	0
Day 80.						
Rice	300	-----	250	260	0	100
Onions	0	-----	0	0	0	0
Rice	300	-----	150	200	150	50
Bacon	50	-----	50	50	50	50
Day 81.						
Rice	300	-----	250	150	150	25
Bananas	100	-----	100	100	100	100
Sugar	0	-----	0	0	0	10
Rice	260	-----	85	45	0	85
Onions	0	-----	40	0	0	0
Lard	0	-----	10	0	0	0
Day 82.						
Rice	200	-----	200	200	(b)	150
Bread	150	-----	150	150	-----	110
Bacon	30	-----	30	30	-----	30
Rice	35	-----	35	70	-----	35
Bacon	50	-----	50	50	-----	50

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 83.						
Rice	300	-----	225	300	-----	35
Onions	0	-----	0	0	-----	0
Rice	100	-----	150	75	-----	150
Bananas	150	-----	150	150	-----	150
Sugar	0	-----	0	0	-----	0
Day 84.						
Rice	300	-----	300	300	-----	300
Bacon	50	-----	50	50	-----	0
Rice	0	-----	125	0	-----	35
Onions	0	-----	0	0	-----	0
Day 85.						
Rice	300	-----	200	225	-----	260
Bananas	100	-----	100	100	-----	100
Sugar	0	-----	0	0	-----	0
Rice	300	-----	240	300	-----	150
Bacon	0	-----	0	0	-----	0
Day 86.						
Rice	200	-----	150	175	-----	50
Bread	150	-----	150	150	-----	150
Bacon	0	-----	0	30	-----	0
Rice	350	-----	35	125	-----	0
Onions	0	-----	0	0	-----	0
Day 87.						
Rice	225	-----	225	260	-----	225
Bacon	0	-----	50	50	-----	0
Rice	150	-----	35	75	-----	35
Bananas	150	-----	150	150	-----	150
Sugar	0	-----	0	0	-----	0
Day 88.						
Rice	0	-----	300	300	-----	150
Onions	0	-----	0	0	-----	0
Rice	150	-----	200	300	-----	75
Bacon	25	-----	50	50	-----	50
Day 89.						
Rice	0	-----	225	300	-----	100
Bananas	100	-----	100	100	-----	0
Sugar	25	-----	25	25	-----	25
Rice	60	-----	120	350	-----	35
Onions	0	-----	0	0	-----	0
Day 90.						
Rice	0	-----	150	200	-----	100
Bread	150	-----	0	150	-----	0
Bacon	30	-----	30	30	-----	15
Rice	0	-----	35	300	-----	25
Bacon	15	-----	25	50	-----	15

[a] Left with prisoner.

[b] In hospital, diet furnished; amount eaten not recorded from this date.

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 91.						
Rice	300		300	300		240
Onions	100		100	100		0
Lard	15		15	15		0
Rice	0		0	0		75
Bananas	0		150	150		150
Sugar	0		0	0		0
Day 92.						
Rice	300		300	300		185
Bacon	50		50	50		50
Rice	350		85	85		25
Onions	150		150	150		0
Lard	20		20	20		0
Day 93.						
Rice	185		35	185		200
Bananas	100		100	100		100
Sugar	5		25	5		0
Rice	300		300	300		240
Bacon	50		50	50		50
Day 94.						
Rice	175		100	200		0
Bread	150		120	150		35
Bacon	30		30	30		30
Rice	350		300	300		100
Onions	150		125	150		150
Day 95.						
Rice	300		300	300		75
Bacon	50		50	50		25
Rice	200		150	100		0
Bananas	150		150	150		150
Sugar	0		0	0		0
Day 96.						
Rice	300		150	240		0
Onions	0		0	0		0
Rice	150		200	250		75
Bacon	50		50	50		50
Day 97.						
Rice	150	[a]	250	200	[a]	0
Bananas	100		100	100		100
Sugar	0		0	0		0
Rice	300		150	225		25
Fish	30		30	30		30
Day 98.						
Rice	200		300	300		200
Fish	0		30	30		30
Rice	300		100	225		75

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 98—Ctd.						
Potatoes	150		150	150		150
Bacon	0		25	50		0
Day 99.						
Rice	0		[b]	[b]		150
Potatoes	150		[b]	[b]		75
Bacon	30		[b]	[b]		15
Rice	300		100	300		225
Fish	30		15	30		30
Day 100.						
Rice	300		260	300		0
Bananas	100		100	100		0
Sugar	0		0	0		0
Rice	200		175	165		200
Bread	150		135	135		150
Bacon	30		0	30		30
Day 101.						
Rice	300		300	300		300
Fish	25		25	25		25
Potatoes	100		100	100		100
Rice	350		175	350		85
Onions	0		0	0		0
Day 102.						
Rice	300		300	300		300
Fish	40		40	40		40
Rice	300		50	300		260
Potatoes	100		100	100		100
Bacon	30		30	30		30
Day 103.						
Rice	300		225	150		300
Potatoes	100		100	100		100
Fish	30		30	30		30
Starch	10		10	10		10
Lard	15		15	15		15
Rice	300		35	75		300
Bacon	0		0	0		50
Day 104.						
Rice	300		0	0		300
Potatoes	100		100	100		100
Bacon	30		30	30		30
Rice	300		75	150		260
Bananas	150		150	150		150
Sugar	5		0	0		0
Day 105.						
Rice	300		200	250		300
Fish	30		30	30		30

[a] Diet discontinued.

[b] Not recorded.

TABLE IV.—*Record of rations consumed by prisoners of Group II*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 105—Ctd.						
Rice	300		75	260		300
Potatoes	100		100	100		100
Bacon	30		30	30		30
Day 106.						
Rice	300		150	300		300
Potatoes	100		100	100		100
Fish	30		30	30		30
Rice	300		75	100		260
Bananas	150		150	150		150
Sugar	0		0	10		20
Day 107.						
Rice	300		150	300		300
Bacon	50		50	50		50
Rice, Potatoes, Fish	No record kept.					
Day 108.						
Rice	300		0	300		300
Bananas	100		0	100		100
Sugar	25		0	25		25
Rice	300		(a)	(a)		300
Potatoes	100					100
Bacon	30					30
Day 109.						
Rice	240					300
Fish	0					0
Starch	0					0
Lard	0					0
Dinner	No record kept.					
Day 110.						
Rice	300					300
Potatoes	100					100
Bacon	30					30
Rice	300					300
Potatoes	100					100
Day 111.						
Rice	300					300
Bananas	150					150
Sugar	25					25
Rice	190					300
Potatoes	100					100
Bacon	30					30

Diet.	Amount, in grams, consumed by prisoner number—					
	7	11	10	12	9	8
Day 112.						
Rice	300					300
Fish	30					30
Rice	300					300
Bananas	150					150
Sugar	25					0
Day 113.						
Rice	300					300
Potatoes	100					100
Fish	30					30
Rice	300					300
Bacon	50					50
Day 114.						
Rice	300					300
Potatoes	100					100
Fish	30					30
Rice	300					300
Bananas	150					150
Sugar	25					25
Day 115.						
Rice	300					300
Bacon	50					50
Rice	300					300
Fish	30					30
Day 116.						
Rice	300					300
Potatoes	100					100
Bacon	30					30
Rice	300					300
Sugar	25					25
Bananas	150					150
Day 117.						
Rice	300					300
Potatoes	100					100
Fish	30					30
Rice	300					300
Bacon	50					50
End of experiment.						

[a] Diet discontinued.

GROUP III.

CASE NO. 13 (GROUP III).

Diet: White rice + rice polishings for 17 days followed by red rice for 100 days, together with the special diet common to all the groups. } Total period of experiment, 117 days.

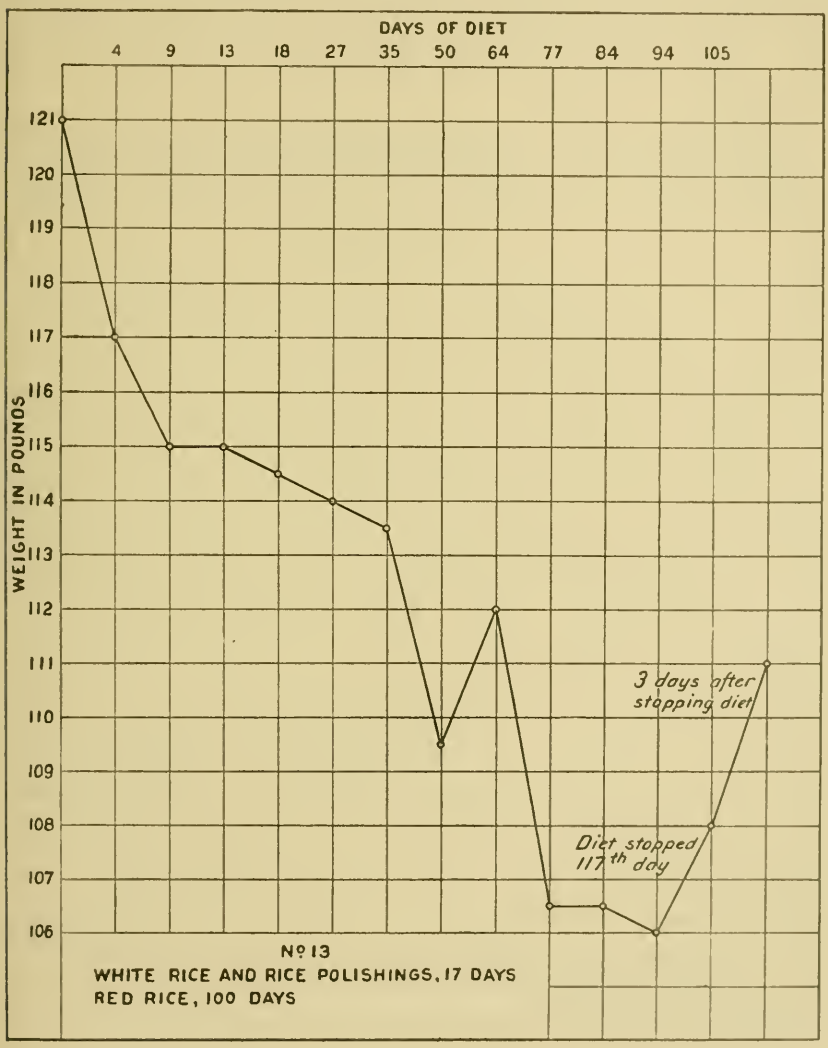
Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Well-nourished man; percussion and auscultation of the lungs reveal nothing abnormal; examination of the heart shows no increase in the area of cardiac dulness; the point of maximum impulse is visible and palpable 6.25 centimeters to the left of the median line and 3 centimeters below the nipple line; the heart sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 80, and the systolic blood pressure is 118 millimeters Hg (Faught); the spleen and liver are not enlarged; the knee jerks are active.

The notes during the earlier days of the experiment are unimportant, except that the patient lost steadily in weight. On the seventy-fourth day he complained of weakness and pain in the epigastrium, and the note states that he had been eating little for the past five days. On the seventy-fourth day the note made was as follows: Pulse 110; heart sounds clear; point of maximum impulse distinctly visible and palpable as far out as the nipple line; no distinct change in the area of cardiac dulness; no tenderness of the calves of the legs; the right knee jerk is present but is a little weak, the left is slightly stronger. He was eating his rice well until the sixty-ninth day of the experiment; since that day he has eaten but little. On the seventy-seventh day the pulse was 104, and he complained of pain in the epigastrium and back and of having sensations of cold below his elbows and below his knees; he states that his hands feel colder than his face or neck; there is marked throbbing over the cardiac area; the impulse is palpable over an area of 4 to 5 centimeters in diameter; the respirations are 40; the heart sounds at the apex are normal, while near the base the spacing of the beats is more nearly equal; there is still no distinct increase in the area of dulness; the knee jerks can not be elicited after repeated trials. At 4 p. m. the pulse was 110; there was marked dyspnœa. On the seventy-eighth day at noon the note reads: Still marked pulsation over cardia and well-marked dyspnœa; right knee jerk not elicited, left questionable; pulse 104 before and 112 after slight exertion; the first sound at the apex

seems a little less prolonged than yesterday; he complains of pain in the region of the heart; at 4 p. m. the pulse was 102; respirations 40. On the eighty-first day the note states: Complains of pain in chest and abdomen; both knee jerks are elicited to-day but are very weak; pulse 120; respirations 40; there is visible pulsation of the præcordial area, from about 2 centimeters to the left of the sternum extending transversely and obliquely downward to just below the nipple; the deep cardiac dulness begins at the lower border of the third rib; it extends to the left 2 centimeters outside of the nipple line and is not increased to the right of the sternum. On the eighty-third day the note reads: He says that he has felt better for the last two days, except at night, and that he sometimes feels hot and has pain in the abdomen and gastric distress; the pulse is not so rapid. On the eighty-fourth day the pulse was 90 and the respirations 44; the knee jerks were both elicited though weak. On the eighty-fifth day the systolic blood pressure was 100 millimeters Hg. From the ninetieth to the ninety-fifth day the knee jerks were present. He has lost 6.8 kilograms (15 pounds) since the beginning of the experiment, though he has been eating his rice fairly well since the eighty-fourth day. On the ninety-seventh day dried codfish and potatoes were added to the diet. On the ninety-eighth day he complained of some weakness; the pulse was 92. On the ninety-ninth day the note reads as follows: Complains of a sense of oppression in the epigastrium and over the chest and of headache; there is marked epigastric pulsation and marked visible throbbing over the cardiac area, extending outside of the nipple; the heart sounds are forcible, the second pulmonic is slightly accentuated; the knee jerks are very weak; the respirations are 48; pulse 104 and weak; the pains in the legs have disappeared but he complains of slight tenderness above the knees on pressure; there are no areas of distinct anæsthesia of the skin. On the one hundredth day the pulse had dropped to 88. On the one hundred second day there were some erosions on the corners of the lips which were touched with a solution of silver nitrate. On the one hundred seventeenth day it was necessary to discontinue the diet. He gradually improved from the ninety-seventh day. On the one hundred nineteenth day the following note was made: Nutrition fair; no epigastric pulsation; pulse 90, of fair volume; visible pulsation over the heart in the 4th and 5th interspaces within the nipple line; on palpation the impulse is felt even outside the

nipple line; the apex beat is rather diffuse; the point of maximum impulse is 7 centimeters to the left of the median line; the first sound at the apex is prolonged but there is no distinct murmur; the sounds at the base are clear; the deep area of dulness does not extend to the left outside of the nipple line, nor to the right of the right edge of the sternum; there is no tenderness of the calves of the legs, and no œdema of the legs; the knee jerks are present but are still weak. The examination of the urine shows no albumin and no casts.

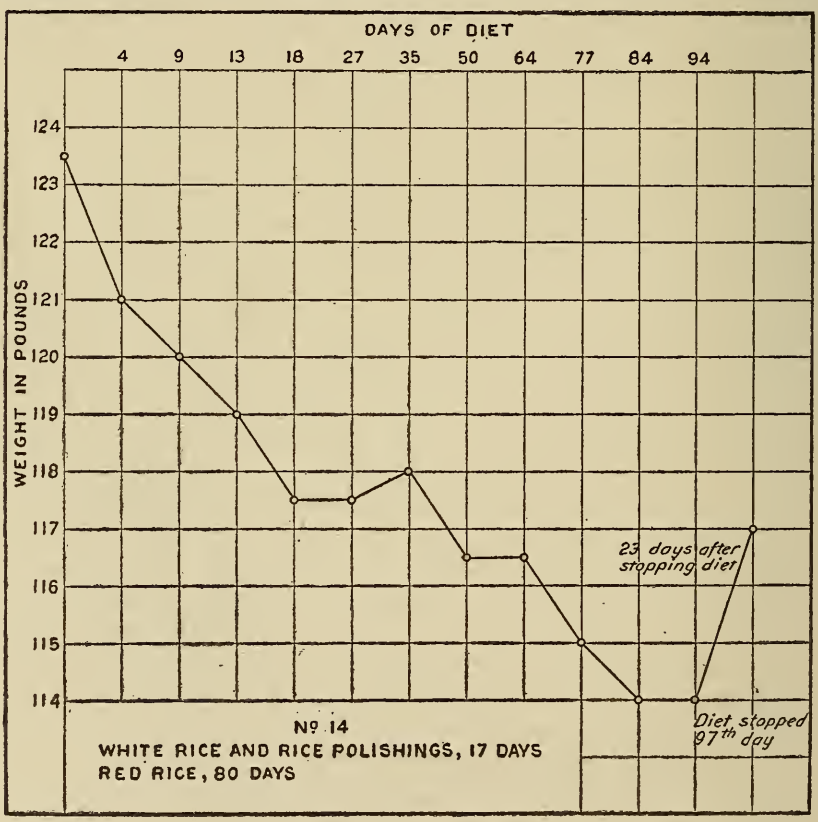


CASE NO. 14 (GROUP III).

Diet: White rice + rice polishings for 17 days followed by red rice for 80 days, together with the special diet common to all the groups. } Total period of experiment, 97 days.

Following is a brief summary of the notes of the case: Fairly well-nourished individual; percussion of lungs normal; respiratory sounds normal; area of cardiac dulness not increased beyond normal; point of maximum impulse visible 5.5 centimeters to the left of the median line and 2 centimeters below the nipple line; heart sounds clear at apex and base; no epigastric pulsation; spleen and liver not palpable below the costal margin; the knee jerks are active.

The notes of this case are unimportant except that the individual lost steadily in weight, and weighed 4.5 kilograms (10 pounds) less by the eightieth day of the experiment. On the



eighty-first day the note was made that the right knee jerk was very active but that the left seemed a little weak. On the eighty-fifth day the systolic blood pressure was 100 millimeters Hg. On the ninety-fifth day the knee jerks were both active. On the ninety-seventh day it became necessary to discontinue the diet as he refused to continue the experiment longer. At this time his condition was good, although he had lost 4.5 kilograms (10 pounds) in weight. The condition of the heart remained unchanged. The knee jerks were active and there was no œdema of the legs, tenderness of the calves of the legs, nor areas of anæsthesia of the skin. The urine was normal.

CASE NO. 15 (GROUP III).

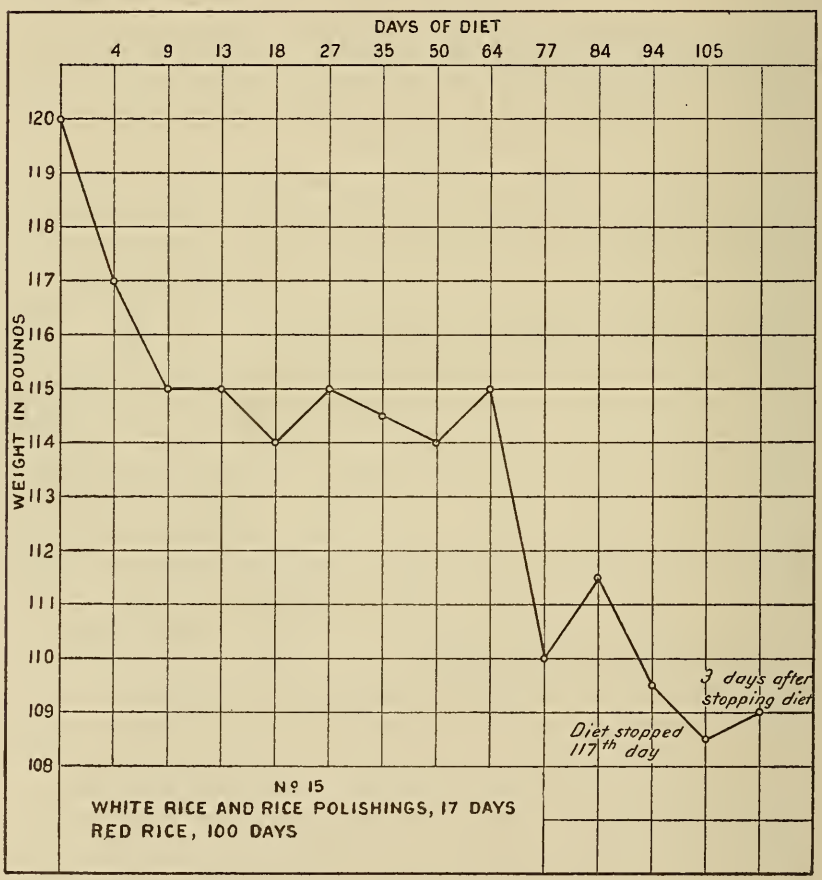
Diet: White rice + rice polishings for 17 days followed by red rice for 100 days, together with the special diet common to all the groups. } Total period of experiment, 117 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Percussion and auscultation of the lungs reveal nothing abnormal; the examination of the heart shows no increase in the area of cardiac dulness beyond the normal; the point of maximum impulse is palpable 7 centimeters to the left of the median line and 1 centimeter below the nipple line; the heart sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 72 and the systolic blood pressure 130 millimeters Hg (Faught); the spleen and liver are not enlarged; the knee jerks are active.

The earlier notes of this case show no important changes in the condition of the individual except that he lost weight gradually up to the seventy-seventh day of the experiment when he weighed 4.5 kilograms (10 pounds) less than when the experiment was begun. On the eighty-first day the systolic blood pressure was 100 millimeters Hg. On the ninetieth day the note states: He has eaten little for two days and complains of headache; there are no cardiac symptoms; his headache and loss of appetite were relieved by purgation; the knee jerks have been active throughout. On the ninety-seventh day dried codfish and potatoes were added to the diet. On the ninety-ninth day the following note was made: No throbbing over cardiac area; pulse 80; point of maximum impulse invisible; palpable within the nipple line; heart sounds clear and slightly accentuated at the base; the knee jerks are active; no increase in the cardiac

dulness; no œdema of the legs. On the one hundred fifth day his condition remained good. On the one hundred seventeenth day the diet was discontinued. On the one hundred nineteenth day the following note was made: Nutrition fair; pulse 80; no epigastric nor præcordial pulsation visible; point of maximum impulse not distinctly palpable; area of cardiac dulness not increased; heart sounds normal; knee jerks active; no œdema; no pain nor tenderness in the legs. He has had severe conjunctivitis and some erosions at the edges of the lips at times during the experiment, and has lost steadily in weight; in all 5.6 kilograms (11.5 pounds). The urine contains no albumin and no casts.

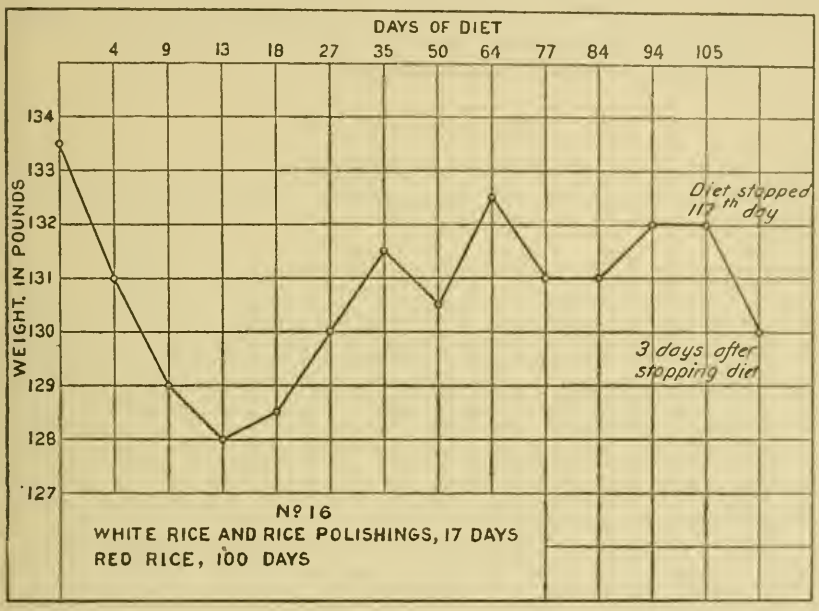


CASE NO. 16 (GROUP III).

Diet: White rice + rice polishings for 17 days followed by red rice for 100 days, together with the special diet common to all the groups. } Total period of experiment, 117 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Examination of the lungs shows nothing abnormal; examination of the heart shows the area of dulness is not increased beyond the normal limits; the point of maximum impulse is invisible; it is palpable 6 centimeters to the left of the median line and 4 centimeters



below the nipple line; the heart sounds are clear at the apex, and are faintly heard at the base; there is no epigastric pulsation; the pulse is 88, and the systolic blood pressure 120 millimeters Hg (Faught); the spleen and liver are not enlarged; the knee jerks are active.

The patient lost 2.2 kilograms (5 pounds) in weight before red rice was substituted for the white rice mixed with the rice polishings; then he began to gain in weight. On the fiftieth day of the diet the note reads: No hypertrophy nor dilatation of the heart; the sounds are clear; the knee jerks are active. The other notes are unimportant regarding the case. On the eighty-

fifth day the systolic blood pressure was 105 millimeters Hg. On the ninety-seventh day dried codfish and potatoes were added to the diet. On the ninety-ninth day the note reads as follows: Patient has had no physical complaint; there are no apparent changes in the condition of the heart; the pulse is 84; the knee jerks are very active; there is no œdema nor tenderness of the calves of the legs. On the one hundred seventeenth day it became necessary to discontinue the diet. On the one hundred nineteenth day the following note was made: Well nourished; pulse slow and regular; point of maximum impulse not visible; heart sounds unchanged; there is no pain in the calves of the legs and no œdema of the legs; the knee jerks are active; he says he feels as well as before he began the experiment. The urine contains no albumin and no casts.

CASE NO. 17 (GROUP III).

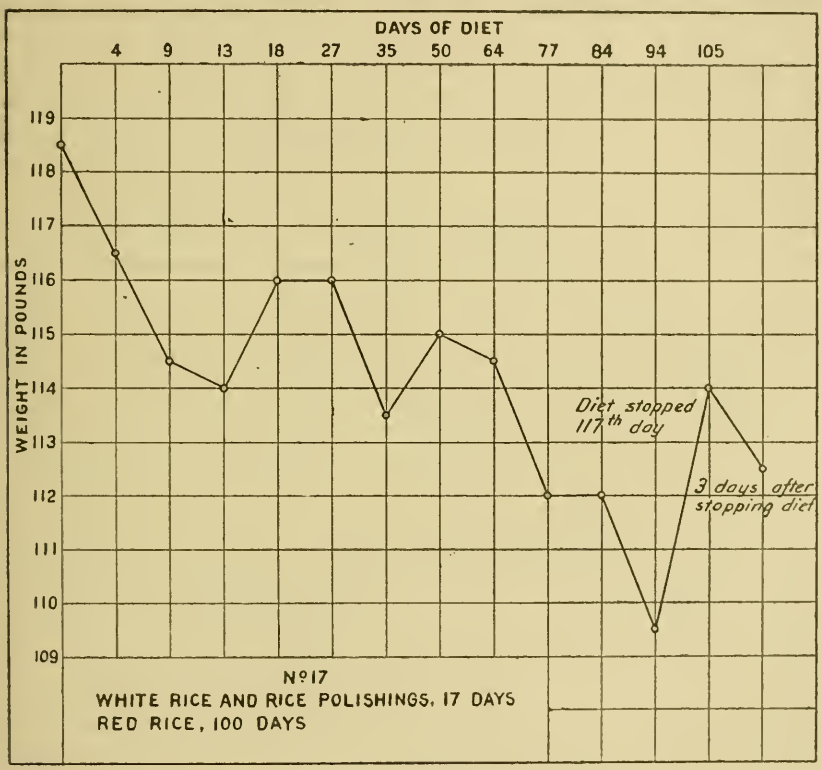
Diet: White rice + rice polishings for 17 days followed by red rice for 100 days, together with the special diet common to all the groups. } Total period of experiment, 117 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Percussion and auscultation of the lungs reveal nothing abnormal; examination of the heart shows no increase in the area of dulness beyond the normal; the point of maximum impulse is visible and palpable 7.5 centimeters to the left of the median line and 3.5 centimeters below the nipple line; the second sound at the apex is accentuated; at the base the sounds are not accentuated nor reduplicated; there are no murmurs, and no epigastric pulsation is visible; the pulse is 88, and the systolic blood pressure is 108 millimeters Hg (Faught); the liver and spleen are not palpable below the costal margin.

The notes of the case are unimportant except that the patient had lost 9 pounds (4 kilograms) in weight by the ninety-fourth day of the experiment. On the eighty-fifth day the systolic blood pressure was 95 millimeters Hg; the knee jerks remained active, and there was no complaint of pain. On the ninety-seventh day the following note was made: Point of maximum impulse not distinctly visible; palpable well within the nipple line; no pulsation over the cardiac area; the heart sounds have not changed since the previous note; the pulse is slow and regular; there is no œdema of the legs; the knee jerks are very active. On the one hundred fifth day the note states that his condition is good. During the experiment he has had at times catarrhal conjunctivitis but this has now disappeared. On the one hundred

seventeenth day the diet was discontinued and the prisoner returned to the regular prison ration. The next day the following note was made: Well-nourished individual; pulse 80; no epigastric nor præcordial pulsation; point of maximum impulse is not visible nor palpable; the heart sounds appear to be as at the beginning of the experiment; the area of cardiac dulness is not increased beyond the normal limits; there is no complaint of pain in the legs, and there is no œdema and no tenderness; the knee jerks are active; he says he feels well. From the ninety-seventh to the one hundred fifth day he gained 2.04 kilograms (4.5 pounds). The urine contained no albumin and no casts.



CASE NO. 18 (GROUP III).

Diet: White rice + rice polishings for 17 days followed by red rice for 100 days, together with the special diet common to all the groups. } Total period of experiment, 117 days.

Dried codfish and potatoes were added to the diet on the 97th day.

Following is a summary of the notes of the case: Percussion and auscultation of the lungs reveal nothing abnormal; the area

of cardiac dulness is not increased beyond the normal; the point of maximum impulse is not visible, and is but faintly palpable 7 centimeters to the left of the median line and 3 centimeters below the nipple line; the heart sounds are rapid but clear at the apex and base; there is no epigastric pulsation; the pulse is 100; the systolic blood pressure is 100 millimeters Hg (Faught); the spleen and liver are not palpable below the costal margin; the knee jerks are very active.

The earlier notes of the case are unimportant. On the forty-fourth day a vesiculo-pustular eruption appeared over the back and shoulders; this disappeared in a few days under local treatment. The patient lost 5 pounds in weight at the beginning of the experiment but later there was no further loss. The knee jerks remained active and the patient remained in good health. On the eighty-fifth day the systolic blood pressure was 105 millimeters Hg. On the ninety-seventh day of the experiment dried codfish and potatoes were added to the diet. On the ninety-ninth day the following note was made: Complains of headache; pulse 120, it misses a beat about every 10th pulsation; epigastric pulsation is visible; there is slight throbbing over the cardiac area; the impulse is palpable as far out as the nipple; the heart sounds are evenly spaced; they are forcible at the apex and much weaker at the base; there is no œdema of the legs, and the knee jerks are active. On the one hundred seventeenth day it became necessary to discontinue the diet. On the one hundred nineteenth day the following note was made: Fairly well nourished; no epigastric pulsation; pulse 100, occasionally intermitting a beat; the point of maximum impulse is not visible; it is palpable 7.5 centimeters to the left of the median line; just below the apex, the first and second heart sounds are of equal length; just above the apex, the first sound is a little more prolonged than the second sound; the sounds at the base are clear but weak; the area of cardiac dulness is not increased beyond normal; there is no œdema nor tenderness of the legs; he says he felt stronger before beginning the experiment. The urine showed no albumin and no casts.

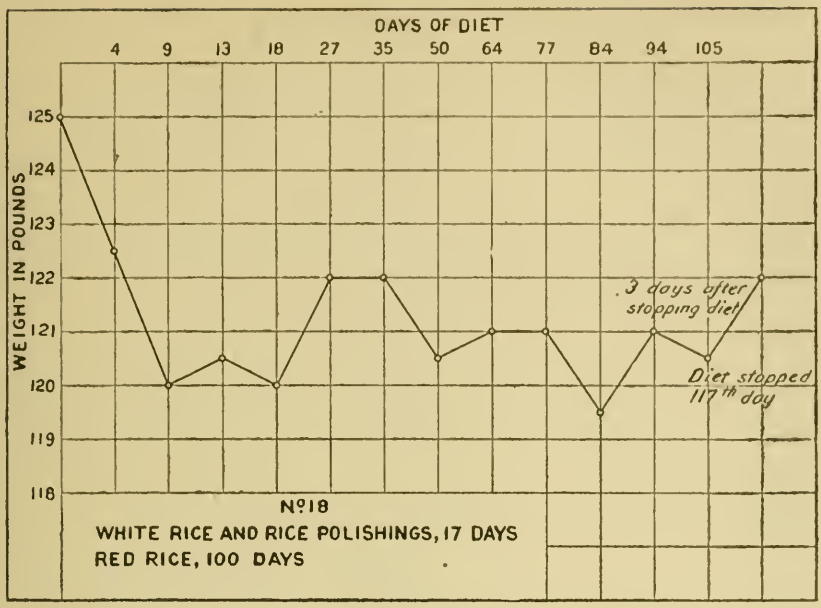


TABLE V.—*Record of rations consumed by prisoners of Group III.*

Prisoner number.	Kind of rice.	Duration of experiment.
14	White rice + rice polishings, 17 days; and red rice 80 days.	97 days, January 17 to April 22.
16, 18, 13, 15, 17	White rice + rice polishings, 17 days; and red rice 100 days.	117 days, January 17 to May 12.

Diet.	Amount, in grams, consumed by prisoner number—						Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15		14	16	18	13	17	15
Day 1.							*Day 3.*						
Rice	150	150	150	150	150	150	Bread	150	150	150	150	150	150
Bacon	50	50	50	50	50	50	Rice	100	100	100	100	100	100
Day 2.							Starch	0	0	0	0	25	0
							Sugar	0	0	0	0	15	0
Rice	0	0	0	0	0	0	Lard	0	0	0	0	10	0
Onions	50	50	50	50	50	50	Rice	150	150	150	150	150	150
Lard	8	8	8	8	8	8	Bacon	0	0	0	0	0	0
Rice	300	300	300	300	300	300	*Day 4.*						
Bananas	150	150	150	150	150	150	Rice	50	50	50	50	50	50
Sugar	25	25	75	75	75	75	Onions	100	100	100	100	100	100

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 4—Ctd.						
Lard	15	15	15	15	15	15
Rice	50	50	50	50	50	50
Sugar	75	75	75	75	75	75
Bananas	150	150	150	150	150	150
Day 5.						
Rice	50	50	50	50	50	50
Bread	150	150	150	150	150	150
Bacon	30	30	30	30	30	30
Bread	200	200	200	200	200	200
Rice	50	50	50	50	50	50
Starch	50	50	50	50	50	50
Sugar	25	25	25	25	25	25
Lard	20	20	20	20	20	20
Day 6.						
Rice	0	0	0	0	0	0
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	0	0	0	0	0	0
Bacon	50	50	50	50	50	50
Day 7.						
Rice	0	0	0	0	0	0
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Bread	200	200	200	200	200	200
Rice	0	0	0	0	0	0
Starch	10	10	10	10	10	10
Sugar	5	5	5	5	5	5
Lard	5	5	5	5	5	5
Day 8.						
Rice	0	0	0	0	0	0
Bacon	50	0	50	50	50	0
Rice	0	0	0	0	0	0
Onions	150	150	0	150	150	0
Lard	20	20	0	20	20	20
Day 9.						
Bread	150	150	150	150	150	150
Rice	0	0	0	0	0	0
Bacon	30	30	30	30	30	30
Rice	0	0	0	0	0	0
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 10.						
Rice	0	0	0	0	0	0
Bacon	50	50	50	50	50	50
Bread	200	200	200	200	200	200

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 10—Ctd.						
Rice	0	0	0	0	0	0
Starch	0	0	0	0	0	0
Sugar	0	0	0	0	0	0
Lard	0	0	0	0	0	0
Day 11.						
Rice	0	0	0	0	0	0
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	0	0	0	0	0	0
Bacon	50	50	50	50	50	50
Day 12.						
Rice	0	0	0	0	0	0
Bread	150	150	150	150	150	150
Bacon	30	30	30	30	30	30
Rice	0	0	0	0	0	0
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 13.						
Bread	150	150	150	150	150	150
Rice	0	0	0	0	0	0
Starch	0	0	0	0	0	0
Sugar	0	0	0	0	0	0
Lard	0	0	0	0	0	0
Rice	240	240	225	240	250	250
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 14.						
Rice	300	300	250	300	225	300
Bacon	50	50	50	50	50	50
Rice	275	350	300	275	300	250
Onions	100	150	150	100	150	150
Lard	15	20	20	15	20	20
Day 15.						
Rice	0	0	50	0	0	0
Starch	0	0	0	0	0	0
Sugar	0	0	0	0	0	0
Lard	0	0	0	0	0	0
Rice	75	75	75	75	75	75
Bread	150	150	150	150	150	150
Bacon	50	50	50	50	50	50
Day 16.						
Rice	260	260	300	225	75	40
Sugar	25	25	25	25	25	25
Bananas	100	100	100	100	100	100
Rice	310	260	350	350	175	235

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 16—Ctd.						
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 17.						
Bread	130	150	150	150	0	150
Rice	75	0	20	100	200	0
Bacon	0	0	0	0	30	0
Rice	0	40	0	0	40	150
Bananas	150	150	150	150	150	0
Sugar	25	25	25	25	25	0
Day 18.						
Rice	0	0	0	0	0	0
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Bread	200	200	100	200	200	200
Rice	100	100	100	100	100	100
Starch	20	50	50	50	50	50
Sugar	8	25	25	25	25	25
Lard	6	20	20	20	20	20
Day 19.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	260	300	300	300	300
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 20.						
Rice	300	300	300	300	300	300
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Bread	140	175	150	175	200	150
Rice	100	85	100	100	100	100
Starch	50	40	50	50	50	50
Sugar	25	20	25	25	25	25
Lard	20	15	20	20	20	20
Day 21.						
Rice	260	260	300	300	300	300
Bananas	100	100	50	50	100	100
Sugar	10	25	25	25	10	25
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 22.						
Rice	200	200	200	200	200	200
Bacon	30	30	30	30	30	30
Bread	135	135	150	150	135	135
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 23.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	300	300	300	300	300
Sugar	0	0	0	0	0	0
Bananas	150	150	150	150	150	150
Day 24.						
Bread	150	150	150	150	150	150
Rice	15	85	75	50	15	15
Starch	10	45	40	25	10	10
Sugar	5	20	20	15	5	5
Lard	5	15	15	10	5	5
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 25.						
Rice	200	200	200	200	200	200
Bread	150	150	150	150	150	150
Bacon	30	30	30	30	30	30
Dinner	No record.					
Day 26.						
Rice	300	300	300	300	300	300
Bananas	100	100	100	100	100	100
Sugar	25	25	25	10	25	10
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 27.						
Rice	300	300	300	270	0	300
Onions	100	100	100	100	0	100
Lard	15	15	15	15	0	15
Bread	150	200	200	200	200	200
Rice	0	35	15	25	0	0
Starch	0	15	10	15	0	0
Sugar	0	10	5	10	0	0
Lard	0	5	2	5	0	0
Day 28.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	225	300	300	260	150	300
Bananas	150	150	150	150	150	150
Sugar	0	0	0	25	0	0
Day 29.						
Bread	150	150	150	150	150	150
Rice	75	15	0	0	0	0
Starch	40	10	0	0	0	0
Lard	15	5	0	0	0	0
Sugar	25	25	25	25	25	25

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 29—Ctd.						
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 30.						
Rice	200	200	200	200	200	200
Bacon	15	30	30	30	30	30
Bread	150	150	150	150	150	150
Rice	200	200	150	150	150	150
Bacon	30	30	30	30	0	30
Bread	0	100	150	75	0	150
Day 31.						
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Rice	300	300	300	300	300	300
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Day 32.						
Rice	200	200	200	200	200	200
Bread	150	150	150	150	150	150
Bacon	30	30	30	30	30	30
Rice	300	300	300	300	150	270
Bacon	50	50	50	50	50	50
Day 33.						
Rice	300	300	300	300	300	260
Bacon	25	20	0	25	25	25
Rice, Onions, Lard	No record.					
Day 34.						
Rice	200	200	200	200	200	175
Bread	75	150	150	150	150	150
Bacon	30	0	30	30	30	30
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 35.						
Rice	300	300	200	270	150	260
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 36.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice, Bananas, Sugar	No record.					
Day 37.						
Rice	200	200	200	200	175	200
Bacon	30	30	30	30	30	30
Bread	75	150	135	150	135	150
Rice	350	350	310	350	350	350
Onions	150	150	150	150	150	75
Lard	20	20	20	20	20	10
Day 38.						
Rice	200	300	200	270	270	300
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 39.						
Rice	300	300	300	300	270	300
Bacon	50	50	50	50	50	50
Rice	275	350	350	275	350	350
Bread	0	0	0	0	0	0
Onions	150	0	150	0	0	150
Lard	20	0	20	0	0	20
Day 40.						
Rice	200	200	200	200	0	200
Bread	50	150	135	150	150	150
Bacon	30	30	30	30	30	30
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Sugar	75	75	75	75	75	75
Day 41.						
Rice	150	300	225	0	250	240
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	350	315	350	0	310	350
Onions	150	75	150	0	150	0
Lard	20	10	20	0	20	0
Day 42.						
Rice	300	300	260	300	250	300
Bacon	50	50	50	50	50	50

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 42—Ctd.						
Rice	260	300	150	300	260	300
Bananas	150	150	150	150	150	150
Sugar	25	10	10	25	10	25
Day 43.						
Rice	200	200	200	160	200	200
Bread	0	110	150	150	150	150
Bacon	30	30	30	30	30	30
Rice	350	350	225	225	350	350
Onions	75	150	0	75	110	110
Day 44.						
Rice	300	300	40	270	250	300
Onions	100	100	30	30	75	100
Lard	15	15	5	5	10	15
Rice	300	300	0	300	240	300
Bananas	150	150	0	150	150	150
Sugar	0	0	0	0	0	0
Day 45.						
Rice	300	300	200	300	300	300
Bacon	50	50	0	50	50	50
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 46.						
Rice	300	300	300	300	300	300
Bread	35	50	50	50	50	50
Bacon	30	30	0	30	30	30
Rice	75	260	200	260	260	300
Bananas	100	150	0	150	150	100
Sugar	5	0	5	0	0	5
Day 47.						
Rice	150	300	300	150	250	200
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 48.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	300	300	0	240	300
Bananas	150	150	150	0	150	150
Sugar	0	0	0	0	0	0

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 49.						
Rice	200	200	200	200	200	200
Bread	150	150	150	150	150	150
Bacon	30	30	30	30	30	30
Rice	290	350	175	350	315	350
Onions	0	150	0	0	75	50
Lard	0	20	0	0	10	5
Day 50.						
Rice	300	300	300	300	300	300
Onions	50	100	0	50	0	100
Lard	10	15	0	10	0	15
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Sugar	25	25	25	25	25	25
Day 51.						
Rice	300	300	300	300	300	300
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	10
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 52.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	350	350	350	350	350	350
Onions	50	150	150	150	150	150
Lard	5	20	20	20	20	20
Day 53.						
Rice	300	300	300	300	300	300
Bread	75	75	75	75	150	75
Bacon	30	30	30	30	30	30
Rice	300	300	300	150	300	300
Bananas	150	150	150	150	150	150
Day 54.						
Rice	300	300	300	300	300	300
Bananas	100	100	100	100	100	100
Sugar	25	25	0	0	0	25
Rice	350	350	350	350	350	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 55.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	300	300	200	300	300
Bananas	150	150	150	150	150	150

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 56.						
Rice	200	200	200	200	200	200
Bread	50	135	150	0	150	50
Bacon	30	30	30	30	30	30
Rice	175	350	350	310	350	350
Onions	75	0	0	20	0	30
Lard	10	0	0	5	0	5
Day 57.						
Rice	260	300	300	300	300	300
Onions	50	100	50	100	50	100
Lard	10	15	10	15	10	15
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Day 58.						
Rice	300	300	300	300	300	300
Bananas	100	100	100	100	100	100
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 59.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	0	350	260	175	350	350
Onions	0	100	0	150	75	0
Lard	0	10	0	20	10	0
Day 60.						
Rice	200	200	200	200	200	200
Bread	0	110	150	150	150	100
Bacon	30	30	30	30	30	30
Rice	250	300	300	300	300	300
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0
Day 61.						
Rice	300	300	300	300	300	240
Bananas	100	100	100	100	100	100
Sugar	0	0	25	0	25	25
Rice	260	310	175	350	290	350
Onions	150	150	150	0	150	150
Lard	20	20	20	0	20	20
Day 62.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	270	300	300	300	300	300
Bananas	150	150	150	150	150	150

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 63.						
Rice	200	200	200	200	200	150
Bread	0	120	150	150	125	150
Bacon	30	30	30	30	30	30
Rice	125	310	310	225	350	310
Onions	75	150	0	150	0	0
Lard	10	20	0	20	0	0
Day 64.						
Rice	300	250	260	300	300	300
Onions	50	25	0	15	0	50
Lard	10	5	0	5	0	10
Rice	300	300	300	300	300	300
Bananas	50	150	150	150	150	150
Sugar	25	0	0	0	0	0
Day 65.						
Rice	300	300	300	300	300	300
Bananas	100	100	100	100	100	100
Sugar	0	0	5	0	25	0
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 66.						
Rice	300	300	300	300	300	300
Onions	50	100	100	0	100	0
Lard	10	20	20	0	20	0
Rice	150	270	250	225	300	270
Bananas	150	150	150	150	150	150
Sugar	0	0	25	0	0	25
Day 67.						
Rice	200	200	200	200	200	200
Bread	0	150	150	150	150	150
Bacon	30	30	30	30	30	30
Rice	350	350	310	350	350	350
Onions	75	0	0	0	0	150
Lard	10	0	0	0	0	20
Day 68.						
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Sugar	0	25	0	25	0	25
Rice	350	315	350	85	350	260
Onions	150	0	75	150	75	75
Lard	20	0	10	20	10	10
Day 69.						
Rice	300	250	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	40	300	100	0	300	300

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 69—Ctd.						
Bananas	150	150	150	0	150	150
Sugar	25	25	25	0	25	25
Day 70.						
Rice	300	300	300	0	300	270
Onions	100	100	100	0	100	70
Lard	15	15	15	0	15	10
Rice	300	300	270	300	300	300
Bacon	50	50	50	50	50	50
Day 71.						
Rice	200	200	200	70	175	100
Bread	0	50	150	0	150	100
Bacon	30	30	30	30	30	30
Rice	260	300	300	40	300	300
Bananas	150	150	150	150	150	150
Sugar	25	25	25	25	25	25
Day 72.						
Rice	260	300	300	0	300	300
Bacon	50	50	50	50	50	50
Rice	310	260	225	175	350	310
Onions	50	50	20	150	20	50
Lard	5	5	5	20	5	5
Day 73.						
Rice Bananas Sugar Rice Onions Lard	No record kept.					
Day 74.						
Rice	175	150	70	0	150	175
Bread	0	100	150	0	150	100
Bacon	30	30	30	0	30	30
Rice	100	300	300	0	300	75
Bananas	150	150	150	100	150	150
Sugar	25	25	25	25	25	25
Day 75.						
Rice	0	0	100	0	0	0
Bananas	100	0	0	100	0	0
Sugar	0	0	0	25	0	0
Rice	300	300	300	(a)	300	300
Bacon	50	50	50	(a)	50	50
Day 76.						
Rice	300	150	300	0	100	75
Onions	100	100	100	0	40	0

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 76—Ctd.						
Lard	15	15	15	0	10	5
Rice	300	300	300	30	300	300
Bacon	50	50	50	50	50	50
Day 77.						
Rice	100	150	260	30	150	75
Bananas	100	100	100	50	100	100
Sugar	25	25	0	0	25	25
Rice	150	225	260	0	50	100
Bacon	50	50	50	0	50	50
Day 78.						
Rice	200	200	200	200	260	260
Bread	0	75	150	0	150	150
Bacon	30	30	30	30	30	30
Rice	175	225	350	25	265	265
Onions	150	150	25	150	25	25
Lard	20	20	5	20	5	5
Day 79.						
Rice	300	250	260	25	300	250
Bacon	50	50	50	50	50	50
Rice	150	150	150	0	0	0
Bananas	150	150	150	150	150	150
Day 80.						
Rice	150	25	150	0	0	25
Onions	0	0	0	0	0	0
Rice	300	250	270	40	260	260
Bacon	50	50	50	50	50	50
Day 81.						
Rice	240	200	300	0	300	150
Bananas	100	100	100	50	100	100
Rice	260	175	45	45	45	0
Onions	20	75	0	0	0	0
Lard	5	10	0	0	0	0
Day 82.						
Rice	200	200	200	200	200	0
Bread	150	150	150	150	150	150
Bacon	30	30	30	30	30	30
Rice	225	225	35	75	260	75
Bacon	50	50	50	50	50	30
Day 83.						
Rice	150	200	200	25	200	150
Onions	0	0	0	0	0	0
Rice	75	50	30	30	75	50
Bananas	150	150	150	150	150	150
Sugar	0	0	0	0	0	0

[a] Left with prisoner.

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 84.						
Rice	300	300	300	300	250	300
Bacon	50	50	50	50	50	50
Rice	85	0	85	25	45	0
Onions	0	0	0	0	0	0
Day 85.						
Rice	300	300	300	300	300	300
Bananas	100	100	100	100	100	100
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Day 86.						
Rice	200	150	150	200	175	25
Bread	110	150	150	150	150	150
Bacon	30	30	30	30	30	30
Rice	0	0	125	0	290	125
Onions	0	0	0	0	0	0
Day 87.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	200	185	225	225	260	0
Bananas	150	150	150	150	150	150
Sugar	25	25	0	0	25	0
Day 88.						
Rice	300	300	260	260	270	0
Onions	100	100	100	100	100	0
Lard	15	15	15	15	15	0
Rice	300	300	300	300	300	260
Bacon	50	50	50	50	50	50
Day 89.						
Rice	150	75	150	150	50	0
Bananas	100	100	100	100	100	100
Rice	175	60	0	60	60	0
Onions	0	0	0	0	0	0
Day 90.						
Rice	200	200	200	200	200	200
Bread	75	150	150	150	75	150
Bacon	30	30	30	30	30	30
Rice	225	200	225	300	185	260
Bacon	50	50	50	50	50	50
Day 91.						
Rice	300	300	240	260	300	300
Onions	100	100	100	100	100	100
Lard	15	15	15	15	15	15
Rice	200	200	150	150	0	100
Bananas	150	150	150	150	150	150

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 92.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	85	220	85	85	25	85
Onions	0	20	150	150	0	20
Day 93.						
Rice	75	75	150	225	200	225
Bananas	100	100	100	100	100	100
Sugar	0	0	0	0	0	0
Rice	300	300	240	300	300	300
Bacon	50	50	50	50	50	50
Day 94.						
Rice	200	200	200	200	200	200
Bread	0	50	135	150	150	135
Bacon	30	30	30	30	30	30
Rice	260	260	225	280	175	350
Onions	150	150	150	150	150	150
Lard	20	20	20	20	20	20
Day 95.						
Rice	300	300	300	300	300	300
Bacon	50	50	50	50	50	50
Rice	300	300	300	300	300	300
Bananas	150	150	150	150	150	150
Day 96.						
Rice	200	150	300	150	200	150
Onions	0	0	0	0	0	0
Rice	0	150	0	0	150	0
Bacon	50	50	50	50	50	50
Day 97.						
Rice	0	0	0	0	0	0
Bananas	0	0	0	0	0	0
Rice	225	150	300	75	225	75
Fish	30	30	30	30	30	30
Day 98.						
Rice	(a)	300	240	300	300	250
Fish		30	30	30	30	30
Rice		260	300	150	225	200
Potatoes		75	150	150	150	150
Bacon		50	50	50	50	50
Day 99.						
Rice		75	225	0	200	0
Potatoes		20	20	0	150	0
Bacon		5	5	0	50	0
Rice		0	260	0	0	0
Fish		0	30	0	0	0

[a] Diet discontinued.

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 100.						
Rice		100	300	40	300	150
Bananas		100	100	0	100	100
Sugar		0	0	0	0	0
Rice		200	200	135	150	175
Bread		150	150	150	150	150
Bacon		30	30	0	30	30
Day 101.						
Rice		240	300	300	300	260
Fish		25	25	25	25	25
Potatoes		100	100	100	100	100
Rice		0	0	0	0	0
Onions		0	0	0	0	0
Day 102.						
Rice		300	300	300	300	300
Fish		40	40	40	40	40
Rice		300	300	300	300	300
Potatoes		100	100	100	100	100
Bacon		30	30	30	30	30
Day 103.						
Rice		300	300	300	240	150
Potatoes		100	100	50	100	100
Fish		30	30	30	30	30
Starch		10	10	10	10	10
Lard		15	15	15	15	15
Rice		225	260	300	260	300
Bacon		50	50	50	50	50
Day 104.						
Rice		300	300	300	300	300
Potatoes		100	100	100	100	100
Bacon		30	30	30	30	30
Rice		225	260	150	225	225
Bananas		150	150	150	150	150
Day 105.						
Rice		260	300	240	225	300
Fish		30	30	30	30	30
Rice		225	300	300	260	225
Potatoes		100	100	100	100	100
Bacon		30	30	30	30	30
Day 106.						
Rice		300	300	300	300	300
Potatoes		100	100	100	100	100
Fish		30	30	30	30	30
Rice		225	40	100	260	225
Bananas		150	150	150	150	150
Sugar		0	25	25	25	0

Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15
Day 107.						
Rice		225	300	200	250	300
Bacon		50	50	50	50	50
Rice, Potatoes, Fish	No record kept.					
Day 108.						
Rice		300	300	300	300	200
Bananas		100	100	100	100	100
Sugar		25	25	25	25	25
Rice		300	260	300	300	270
Potatoes		100	100	100	100	100
Bacon		30	30	30	30	30
Day 109.						
Rice		225	225	200	300	150
Fish		30	30	30	30	30
Starch		15	15	15	15	15
Lard		10	10	10	10	10
Dinner	No record kept.					
Day 110.						
Rice		200	300	300	300	225
Potatoes		100	100	100	100	100
Bacon		30	30	30	30	30
Rice		300	200	100	200	100
Potatoes		100	100	100	100	100
Day 111.						
Rice		200	200	240	225	225
Bananas		150	150	150	150	150
Sugar		25	0	25	25	25
Rice		225	150	150	225	150
Potatoes		100	100	100	100	100
Bacon		30	30	30	30	30
Day 112.						
Rice		300	300	300	300	300
Fish		30	30	30	30	30
Rice		225	300	150	200	225
Bananas		150	150	150	150	150
Day 113.						
Rice		300	300	300	300	225
Potatoes		100	100	100	100	100
Fish		30	30	30	30	30
Rice		200	300	185	200	200
Bacon		50	50	50	50	50

TABLE V.—*Record of rations consumed by prisoners of Group III*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—						Diet.	Amount, in grams, consumed by prisoner number—					
	14	16	18	13	17	15		14	16	18	13	17	15
Day 114.							*Day 116*—Ctd.						
Rice		150	300	300	225	225	Bacon		30	30	30	30	30
Potatoes		100	100	100	100	100	Rice		240	300	240	240	240
Fish		30	30	30	30	30	Bananas		150	150	150	150	150
Rice		40	150	75	75	75	Sugar		25	25	25	25	25
Bananas		150	150	150	150	150	*Day 117.*						
Day 115.													
Rice		200	300	150	225	225	Rice		240	300	300	200	300
Bacon		50	50	50	50	50	Potatoes		100	100	100	100	100
Rice		185	75	150	150	150	Fish		30	30	30	30	30
Fish		30	30	30	30	30	Rice		300	300	300	300	300
Day 116.							Bacon		50	50	50	50	50
Rice		300	300	300	240	300			End of experiment.				
Potatoes		100	100	100	100	100							

GROUP IV.

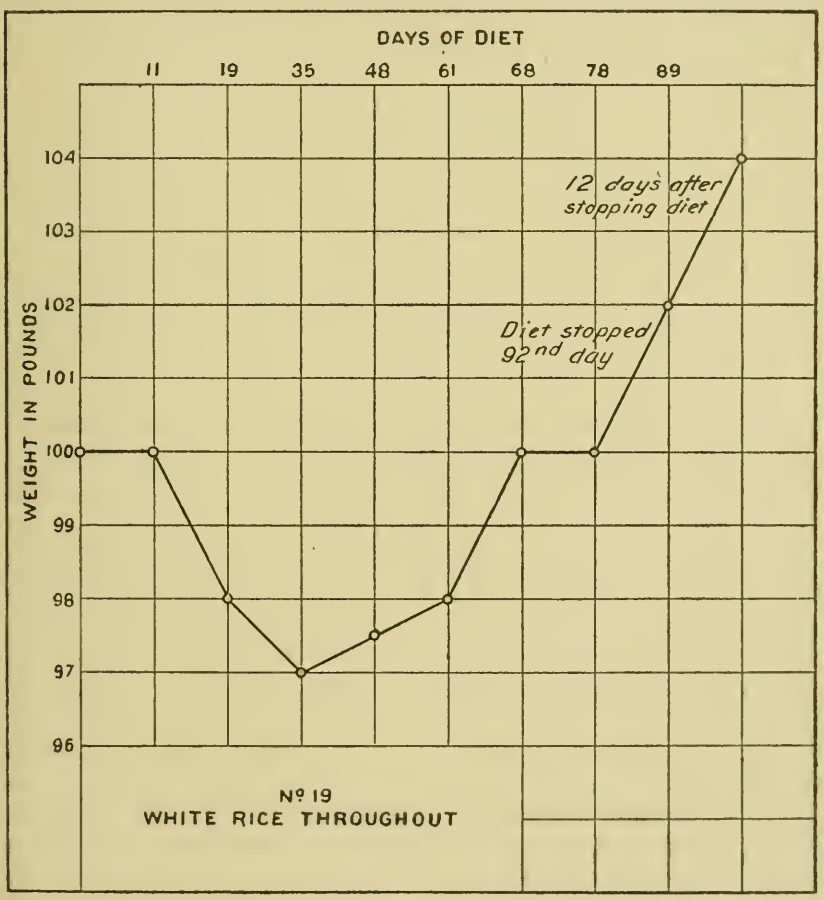
CASE NO. 19 (GROUP IV).

Diet: White rice for 92 days, together with the special diet common to all the groups. } Total period of experiment, 92 days.
Dried codfish and potatoes were added to the diet on the 81st day.

Following is a summary of the notes on the case: Sparely nourished man of small stature; examination of lungs reveals no abnormality. The area of cardiac dulness is not increased beyond the normal limits; the point of maximum impulse is palpable 7 centimeters to the left of the median line and 2 centimeters below the nipple line; the heart sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 80, and systolic blood pressure 115 millimeters Hg (Faught); the liver and spleen are not enlarged; the knee jerks are active.

The earlier notes of the case are unimportant. The patient lost 1.3 kilograms (3 pounds) in the first thirty-five days of the experiment. Then he began to gain and by the sixty-eighth day he had regained his original weight. The knee jerks remained active and he complained of no distress. On the sixty-ninth day the systolic blood pressure was 100 millimeters Hg. On the eighty-first day dried codfish and potatoes were added to the diet. On the eighty-third day the following note was made: Cardiac

pulsation visible in the second left interspace; the apex beat is diffuse but not visible outside the nipple; the area of dulness is not distinctly increased; both heart sounds are forcible and clear; the second pulmonic sound is accentuated; the pulse is 100; he complains of pain in the legs and in the arms; slight œdema of the legs has developed; the knee jerks are very weak. On the eighty-ninth day the following note was made: Slight œdema of the legs continues; there is no complaint of pain; the pulse is slow. On the ninetieth day the note reads: Knee jerks very weak; slight œdema of the legs and no tenderness. On the ninety-second day it became necessary to discontinue the diet. The note made on this date reads as follows: Fairly well nourished; pulse 88 before and 104 after slight exercise, of good volume, tension somewhat increased; epigastric pulsation visible; the point of maximum impulse is visible and palpable 7.5 centi-



meters to the left of the median line; slight cardiac impulse visible and palpable in the third and fourth interspaces; throbbing more marked near the apex; the heart sounds are very forcible after slight exertion; there are no distinct murmurs; he complains of pain in the legs and arms; the grip of the hands is feeble; there is slight tenderness of the calves and there is slight œdema over the tibiæ; the knee jerks are still present but very weak; the patient complains of tingling and numbness over the feet and legs; there is no distinct loss of sensation; the urine shows no albumin and no casts; he weighed 2 pounds (0.9 kilogram) more at the close of the experiment than at the beginning of it. He was placed on the regular prison diet, and in twelve days had gained 2 more pounds.

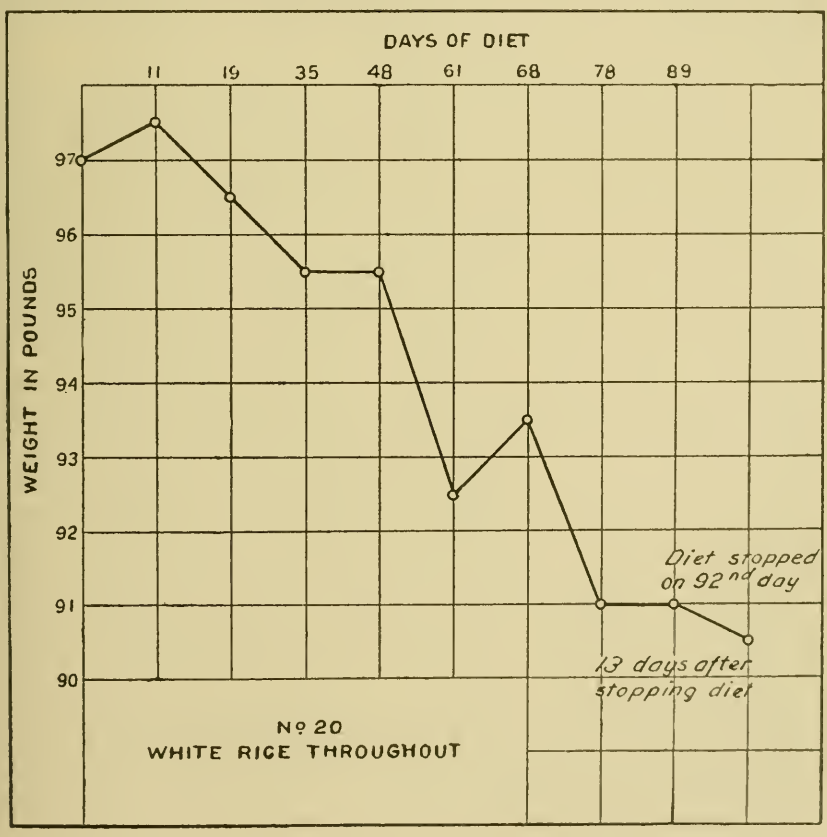
CASE NO. 20 (GROUP IV).

Diet: White rice for 92 days, together with the special diet common to all the groups. } Total period of experiment, 92 days.
Dried codfish and potatoes were added to the diet on the 81st day.

Following is a summary of the notes of the case: Sparely nourished man of small stature; examination of the lungs reveals no abnormality; the area of cardiac dulness is not increased beyond the normal limits; the point of maximum impulse is visible and palpable 6 centimeters to the left of the median line and 0.5 centimeter below the nipple line; there is no epigastric pulsation; the pulse is 88; the systolic blood pressure is 100 millimeters Hg (Faught); the liver and spleen are not enlarged; the knee jerks are active.

The early notes of the case are unimportant except that he lost 2.2 kilograms (5 pounds) in weight during the first sixty-one days. The knee jerks remained active throughout this time. On the sixty-ninth day the systolic blood pressure was 90 millimeters Hg. On the eighty-first day dried codfish and potatoes were added to the diet. On the eighty-third day the following note was made: Epigastric pulsation marked; visible throbbing over the cardiac area; point of maximum impulse palpable 8 centimeters to the left of the median line; the cardiac dulness extends to the left 3 centimeters outside of the nipple, but is not increased to the right of the sternum; the second pulmonic sound is markedly accentuated at the base; there is a slight systolic murmur at the apex transmitted about halfway to the base; the pulse is 88; the heart sounds are occasionally irregular; he complains of pains and tenderness of the calves of the legs; there is no œdema of the legs and no areas of anæsthesia of the

skin; the knee jerks are active; he says he can not see well at night. On the eighty-ninth day the knee jerks were doubtful. There was no œdema of the legs, but the calves were tender on pressure; the pulse was 108. On the ninetieth day the knee jerks were absent; there was still no œdema, but there was marked tenderness of the calves of the legs. On the ninety-second day it became necessary to discontinue the diet and to return him to the regular prison ration. On this date the following note was made: Fairly well nourished; pulse 108, of good volume; the point of maximum impulse is visible and palpable 8 centimeters to the left of the median line; the first sound is still considerably prolonged at the apex; the second pulmonic and second aortic sounds are accentuated; there is moderate epigastric and cardiac pulsation; he complains of pain in the chest and in the stomach; the pain and tenderness in the legs still persist; there is no œdema of the legs; the knee jerks are still absent; the urine contains no albumin nor casts; the patient



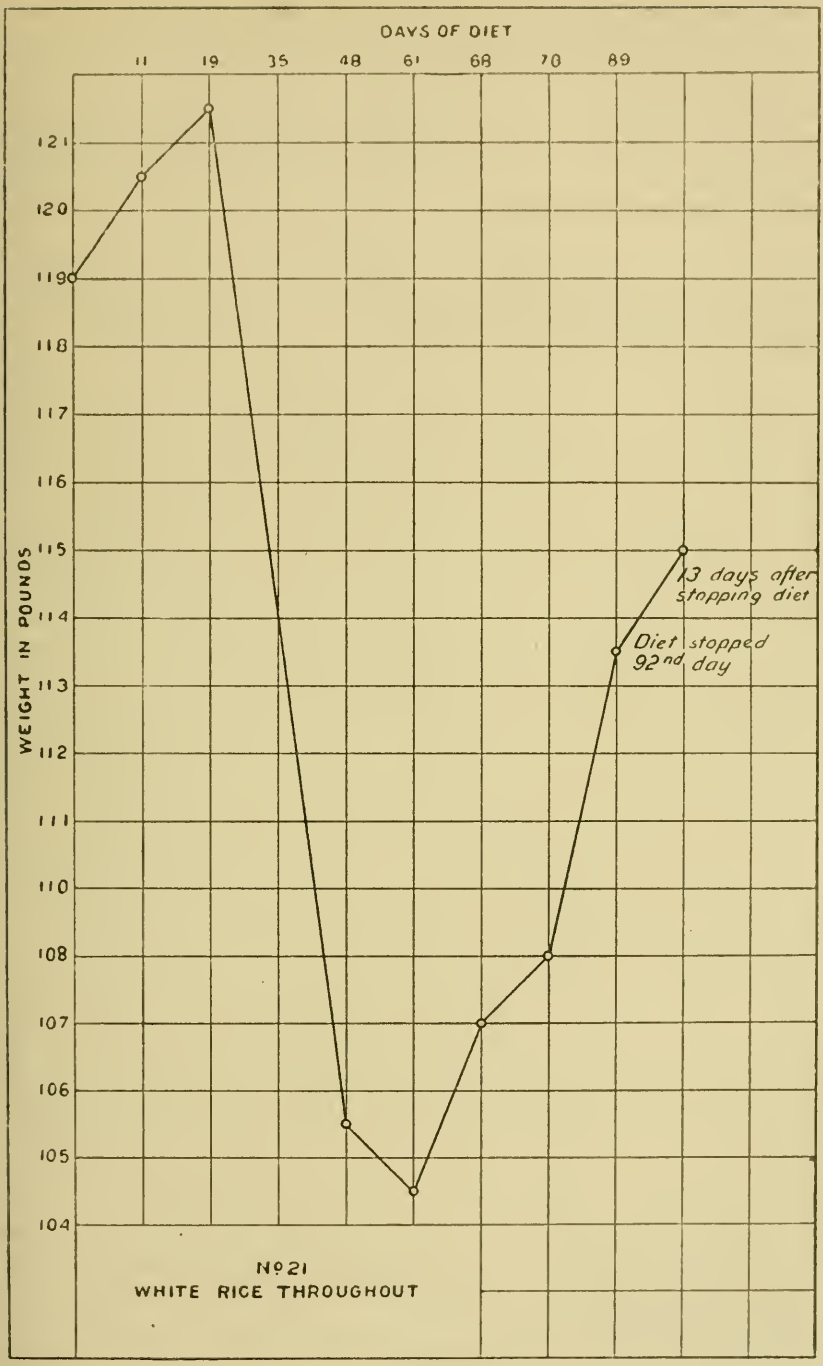
lost 2.7 kilograms (6 pounds) during the experiment; he had not gained any in weight during the first thirteen days after he received the regular prison ration.

CASE NO. 21 (GROUP IV).

Diet: White rice for 92 days, in addition to the special diet common to all the groups. } Total period of experiment, 92 days.
Dried codfish and potatoes were added to the diet on the 81st day.

Following is a summary of the notes of the case: Fairly well-nourished man; percussion and auscultation of the lungs reveal no abnormality; examination of the heart shows no increase in the area of cardiac dulness beyond the normal limits; the point of maximum impulse is invisible; it is palpable 8 centimeters to the left of the median line and 1 centimeter below the nipple line; the first sound is slightly prolonged at the apex; both sounds are clear at the base; no epigastric pulsation is visible; the pulse is 76, and the systolic blood pressure 160 millimeters Hg (Faught); the liver is not palpable below the costal margin, and the dulness is not increased; the edge of the spleen is just palpable; the knee jerks are active.

The earlier notes of the case are otherwise unimportant. The patient gained 1.1 kilograms (2.5 pounds) during the first 19 days of the experiment. He then gradually lost in weight and by the forty-eighth day had lost 7.2 kilograms (16 pounds). On the sixty-ninth day the systolic blood pressure was 110 millimeters Hg. On the eighty-first day dried codfish and potatoes were added to the diet. On the eighty-third day the note shows that there was marked epigastric pulsation but no throbbing over the cardiac area; the point of maximum impulse was palpable 8.5 centimeters to the left of the median line; there was a soft systolic murmur at the apex not transmitted to the base; the second pulmonic sound was distinctly accentuated; the pulse was 80 before and 88 after slight exercise; there was slight œdema of the legs; some pain in the calves was complained of; the knee jerks were very active; the patient gained in weight since the sixty-first day, in all 3.6 kilograms (8 pounds). On the eighty-ninth day the note reads: Pulse slow; no complaint of pain; the knee jerks are very active; there is marked œdema of the legs; the urine contains no albumin nor casts. On the ninety-first day the knee jerks were very active; the legs were œdematous; there was no tenderness of the calves and no areas of anæsthesia of the skin of the feet and hands; he was still fairly well nourished; the pulse was 84; there was slight


DAYS OF DIET
11
19
35
48
61
68
70
89
WEIGHT IN POUNDS
121
120
119
118
117
116
115
114
113
112
111
110
108
107
106
105
104
13 days after stopping diet
Diet stopped 92nd day
No 21
WHITE RICE THROUGHOUT

epigastric pulsation but no cardiac throbbing; the point of maximum impulse was not distinctly visible nor palpable; there were no murmurs; he complained of pain from his waist down; the legs were distinctly œdematous; there was slight tenderness of the calves; the knee jerks were active; the urine contained no albumin nor casts. It became necessary to change to the regular prison diet two days later.

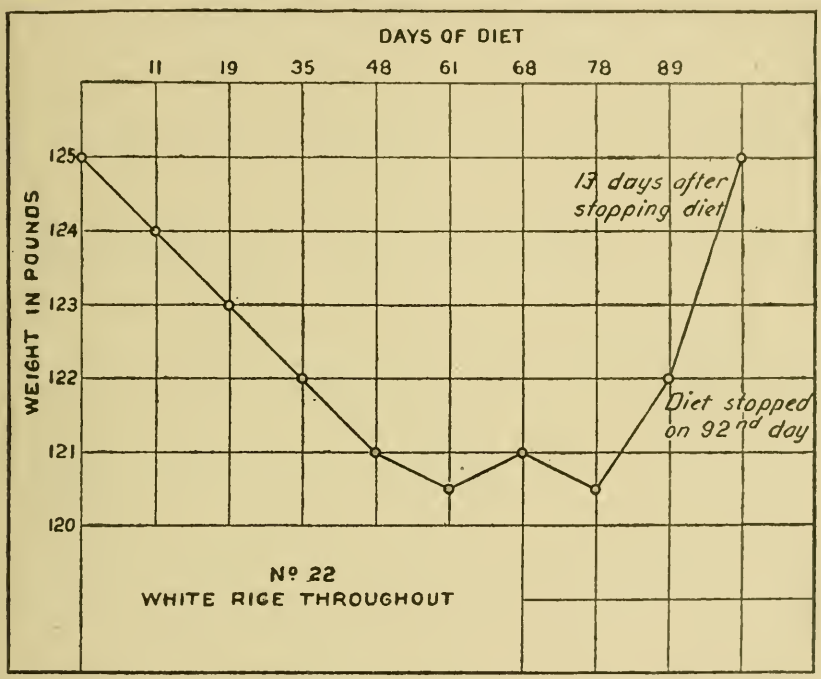
CASE NO. 22 (GROUP IV).

Diet: White rice 92 days, together with the special diet common to all the groups. } Total period of experiment, 92 days.
Dried codfish and potatoes were added to the diet on the 81st day.

Following is a summary of the notes of the case: Sparely nourished man; percussion of the lungs shows no distinct area of dulness; the respiratory sounds are somewhat enfeebled at the apices; there is no tubular modification and no râles are present; the area of cardiac dulness is not increased beyond the normal limits; the point of maximum impulse is not visible nor palpable; the sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 72, and the systolic blood pressure 120 millimeters Hg (Faught); the abdomen is prominent. The liver and spleen are not enlarged; the knee jerks are active.

The earlier notes of the case are otherwise not important. The patient lost but 1.8 kilograms (4 pounds) in weight during the first sixty-one days of the experiment. The knee jerks remained active. On the sixty-eighth day the systolic blood pressure was 110 millimeters Hg. On the seventy-second day he complained of soreness of the throat. There was nothing apparent to account for the complaint, though he continued to complain of this symptom during the following days. On the eighty-first day dried codfish and potatoes were added to the diet. On the eighty-third day he complained of no pain except in the throat after eating. The heart sounds were clear; the cardiac dulness was apparently not changed; there was no throbbing over the cardiac area, and but slight epigastric pulsation; the pulse was 70; there was marked œdema of the legs, but no tenderness; the knee jerks were very active. On the eighty-eighth day the pulse was 72. There was no complaint of pain, but the throat was still sore; there was marked œdema of the legs, but the knee jerks were active. On the ninetieth day the knee jerks were still active. The marked œdema of the legs continued; there was no tenderness of the calves. On the ninety-second day it became necessary to discontinue the diet. The

following note was made on this date: Fairly well nourished; the conjunctivæ are of very good color; the abdomen is prominent; the pulse is slow and full; he complains of pain over the abdomen; there is a little tenderness on pressure over the abdominal wall; there is very slight epigastric pulsation; the point of maximum impulse is not visible nor palpable; the heart sounds are clear; the area of dulness is not increased; the knee jerks are very active; there is very marked œdema of the legs and some tenderness of the calves; the respirations are 20; he complains of pain from the waist down to the feet, and says he feels very ill; there is apparently no fluid in the abdominal



cavity; the urine contains no albumin nor casts. The patient had lost but 1.3 kilograms (3 pounds) in weight during the course of the experiment.

CASE NO. 23 (GROUP IV).

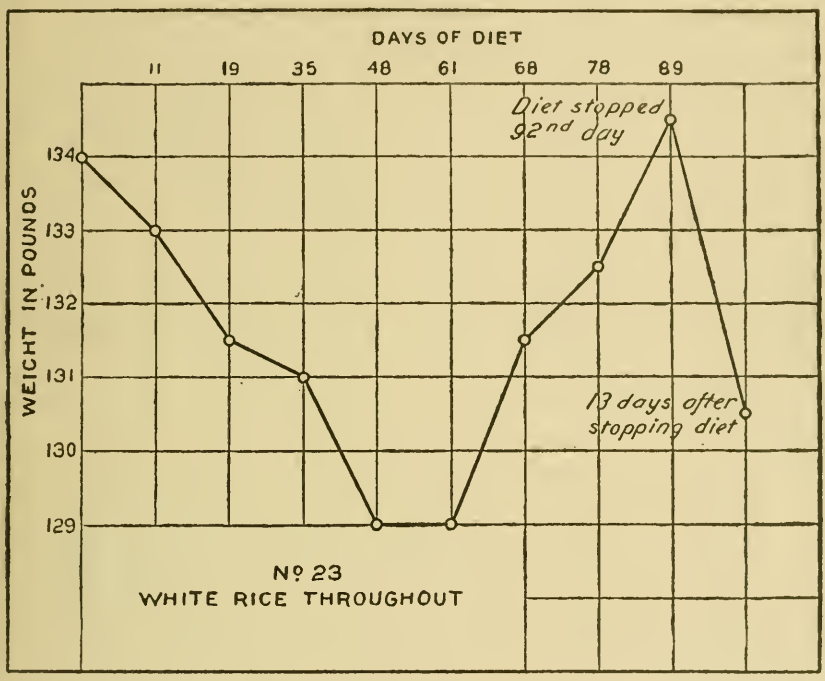
Diet: White rice 92 days, together with the special diet common to all the groups. } Total period of experiment, 92 days.
Dried codfish and potatoes were added to the diet on the 81st day.

Following is a summary of the notes of the case: Well-nourished man; examination of the lungs reveals nothing abnormal;

examination of the heart shows the area of dulness not increased beyond the normal limits; the point of maximum impulse is invisible; it is palpable 7 centimeters to the left of the median line and 1.5 centimeters below the nipple line; the mamma moves very slightly with the systole of the heart; the heart sounds are somewhat rapid but clear; the pulse is 98; the systolic blood pressure is 120 millimeters Hg. The liver and spleen are not palpable below the costal margin. The knee jerks are active.

The earlier notes of this case are otherwise not important; the patient had lost 5 pounds by the forty-eighth day of the experiment; the knee jerks remained active. On the sixty-ninth day the systolic blood pressure was 120 millimeters Hg. On the eighty-first day dried codfish and potatoes were added to the diet. On the eighty-third day the note reads: Visible throbbing over the cardiac area from the third interspace and sternum downward to below the nipple and outward 1 centimeter beyond the nipple; the point of maximum impulse is 9 centimeters to the left of the median line; the area of dulness extends 2.5 centimeters to the left of the nipple line, a slight distinct increase; there is slight epigastric pulsation; a soft systolic murmur is heard at the apex, but is not transmitted to the base; the second pulmonic sound is moderately accentuated; there is visible pulsation of the vessels of the neck; the respirations are 24, the pulse 104 before and 124 after slight exertion; he complains of pain in the calves of the legs, and there is marked œdema of the legs; the knee jerks are active. On the eighty-fourth day the pulse was 110 and of full volume. On the eighty-fifth day the note reads: Pulse 96; complains still of pains in the legs; there is marked œdema; the knee jerks are active; the urine contains no albumin nor casts. On the eighty-eighth day the pulse was 92. There were no pains in the legs this date, but some œdema was present. The knee jerks were active. On the ninetieth day the knee jerks were very active. The œdema of the legs continued. There was no hyperæsthesia of the calves of the legs. On the ninety-second day it became necessary to discontinue the diet. The following note was made on that date: Pulse 92 and of good volume. Well-nourished individual. Cardiac pulsation visible; extends to the left as far as the nipple line, and distinctly 1.5 centimeters outside the nipple line. Point of maximum impulse 9.75 centimeters to the left of the median line. Dulness extends to the left 3.5 centimeters outside the nipple. The first sound is roughened and prolonged at the

apex. There is no complaint of pain in the legs, and the calves are not tender on being pressed. No areas of anæsthesia of the skin can be discovered. There is some œdema of the legs. The knee jerks are exaggerated. The urine contains no albumin nor casts. The patient gained 2.2 kilograms (5 pounds) in weight from the sixty-first to the eighty-ninth days of the experiment, when he had reached his original weight. Thirteen days after resuming the ordinary prison ration he had again lost 5.5 pounds.



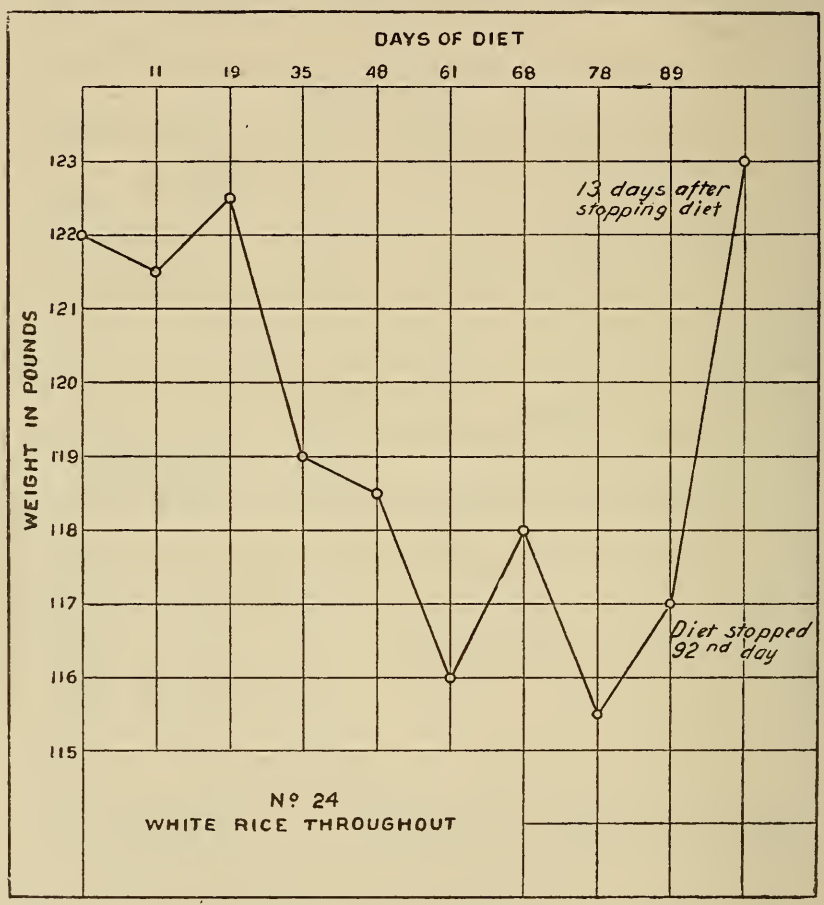
CASE NO. 24 (GROUP IV).

Diet: White rice 92 days, together with the special diet common to all the groups. } Total period of experiment, 92 days.
Dried codfish and potatoes were added to the diet on the 81st day.

The following is a summary of the notes of the case: Fairly well-nourished man; percussion of the lungs shows no abnormal dulness; the respiratory sounds are normal; examination of the heart shows no increase in the area of dulness beyond the normal; the point of maximum impulse is visible and palpable 8 centimeters to the left of the median and 3 centimeters below the nipple line; the heart occasionally intermits a beat; the first sound at the apex is roughened; the second aortic sound is

slightly accentuated; there is no visible pulsation over the epigastrium; the pulse is 76, and the systolic blood pressure 128 millimeters Hg (Faught); the liver and spleen are not enlarged; the knee jerks are active.

The earlier notes of the case show otherwise nothing of importance except that the patient lost 2.7 kilograms (6 pounds) in weight by the sixty-first day. On the sixty-ninth day the



systolic blood pressure was 105 millimeters Hg. On the eighty-first day dried codfish and potatoes were added to the diet. On the eighty-third day the note reads: Complains of no pain, but of general weakness; has lost 2.7 kilograms (6 pounds) in weight; there is epigastric pulsation, but no visible throbbing over the cardiac area; the point of maximum impulse is 8.5

centimeters to the left of the median line; the area of dulness is not distinctly increased either to the right or to the left; the first sound at the apex is prolonged, the second aortic markedly accentuated; there is no reduplication of the sounds; the pulse is 90; there is no œdema of the legs and no pain in the calves; the knee jerks are active. On the eighty-ninth day the note shows that there was no apparent change in his condition. The knee jerks were active. There was no œdema and no pain in the legs. The pulse was slow. He had gained 0.68 kilogram (1.5 pounds) in weight. His condition remained about the same until it became necessary to discontinue the diet on the ninety-second day of the experiment. On this day the following note was made: Nutrition good; abdomen prominent; pulse 80; very slight epigastric pulsation; no visible pulsation over the cardiac area; point of maximum impulse not visible; palpable 7.5 centimeters to the left of the median line; there is no tenderness of the calves and no œdema of the legs; the knee jerks are active; he states that he feels a little weaker than when he began the diet; the urine was normal. Thirteen days after resuming the regular prison ration he had gained 2.7 kilograms (6 pounds) and stood at the same weight as at the time the experiment was commenced.

CASE NO. 25 (GROUP IV).

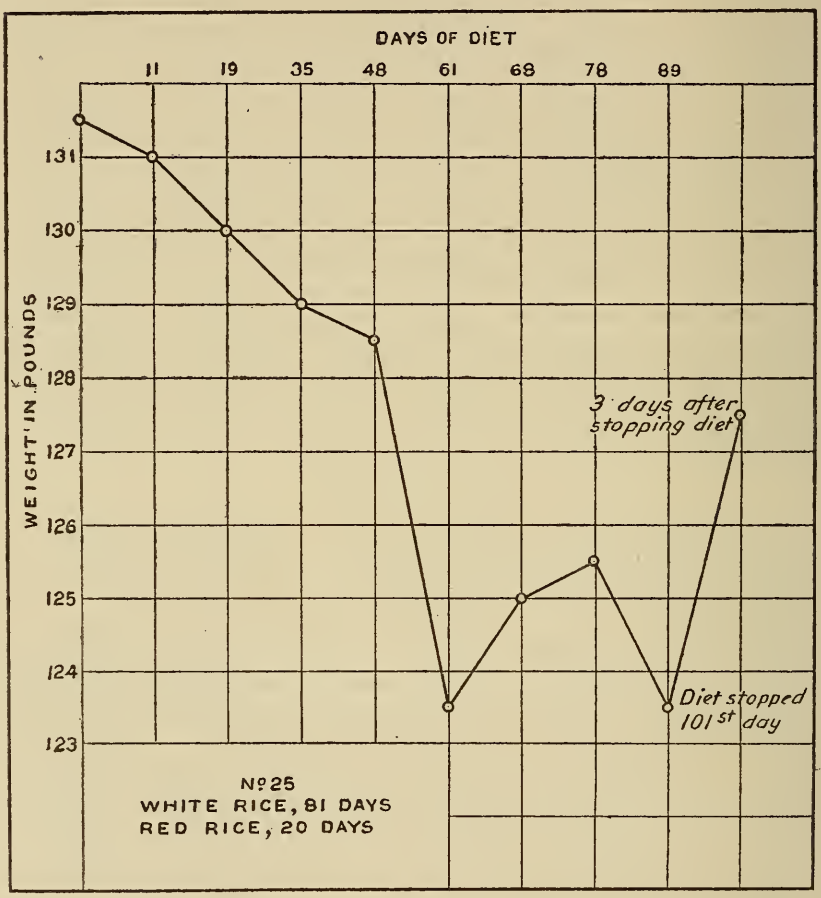
Diet: White rice for 81 days followed by red rice for 20 days, in addition to the special diet common to all the groups. } Total period of experiment, 101 days.

Dried codfish and potatoes were added to the diet on the 81st day.

Following is a summary of the notes of the case: Well-nourished man; examination of the lungs reveals nothing abnormal; the examination of the heart shows no increase in the area of cardiac dulness beyond the normal; the point of maximum impulse is invisible; it is palpable 7.5 centimeters to the left of the median line and 1.5 centimeters below the nipple line; the heart sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 76, and the systolic blood pressure 100 millimeters Hg (Faught); the spleen is not palpable; the liver flatness extends from the lower border of the fourth rib; the liver is not palpable below the costal margin; the knee jerks are active.

The earlier notes concerning the case contained nothing of importance, except that the patient lost in weight and by the sixty-first day weighed 3.6 kilograms (8 pounds) less than when

he began the experiment. On the sixty-third day the knee jerks could no longer be obtained. There was no œdema of the legs. The cardiac impulse could be seen after slight exertion. The heart sounds remained clear; there was no murmur. The subsequent notes show that the knee jerks remained absent. On the sixty-ninth day the systolic blood pressure was 80 millimeters Hg. On the seventy-fifth day the following note was made:



Pulse 96; complains of pain in the calves of the legs; no œdema of legs; knee jerks not elicited. No change in the condition of the heart. On the seventy-eighth day, marked weakness of the legs and difficulty in walking; knee jerks not elicited; no œdema of legs; pulse 100. On the seventy-ninth day the note reads: Pulse 84; knee jerks absent; complains of pain and weakness in

the calves of the legs. On the eighty-first day, the knee jerks were still absent. Slight œdema of the legs had appeared. There was marked hyperæsthesia of the muscles of the calves of the legs. The patient said he felt weak in his legs. The gait was not ataxic. The condition of the heart was not distinctly changed. Red rice was substituted for white rice in the diet on this date, and dried codfish and potatoes were also added. On the eighty-second day the pulse was 120. The pains in the calves of the legs and tenderness on pressure continued. There were no distinct areas of anæsthesia of the skin. There was slight prætibial pitting on pressure over the ankles. On the eighty-third day the note reads: Visible throbbing over the cardiac area; no distinct increase in the area of dulness; the heart sounds are clear; the first sound is short; the œdema of the legs has almost disappeared; the pulse is 100. On the eighty-ninth day it was noted that the strength of the legs was gradually returning. On the one hundred first day the diet was discontinued. The note at the end of the experiment reads: Pulse 88, regular; fairly well nourished; no epigastric nor præcordial pulsation; the point of maximum impulse is not visible nor distinctly palpable; the heart sounds are clear; the area of dulness extends to about 1.5 to 2 centimeters to the left of the nipple line and just to the right edge of the sternum; there is no definite increase since the beginning of the experiment; the pain, tenderness, and weakness in the legs are still present; there is no œdema of the legs; the knee jerks are still absent; the urine contains no albumin nor casts. Three days after resuming the regular prison ration he had gained 1.8 kilograms (4 pounds).

CASE NO. 26 (GROUP IV).

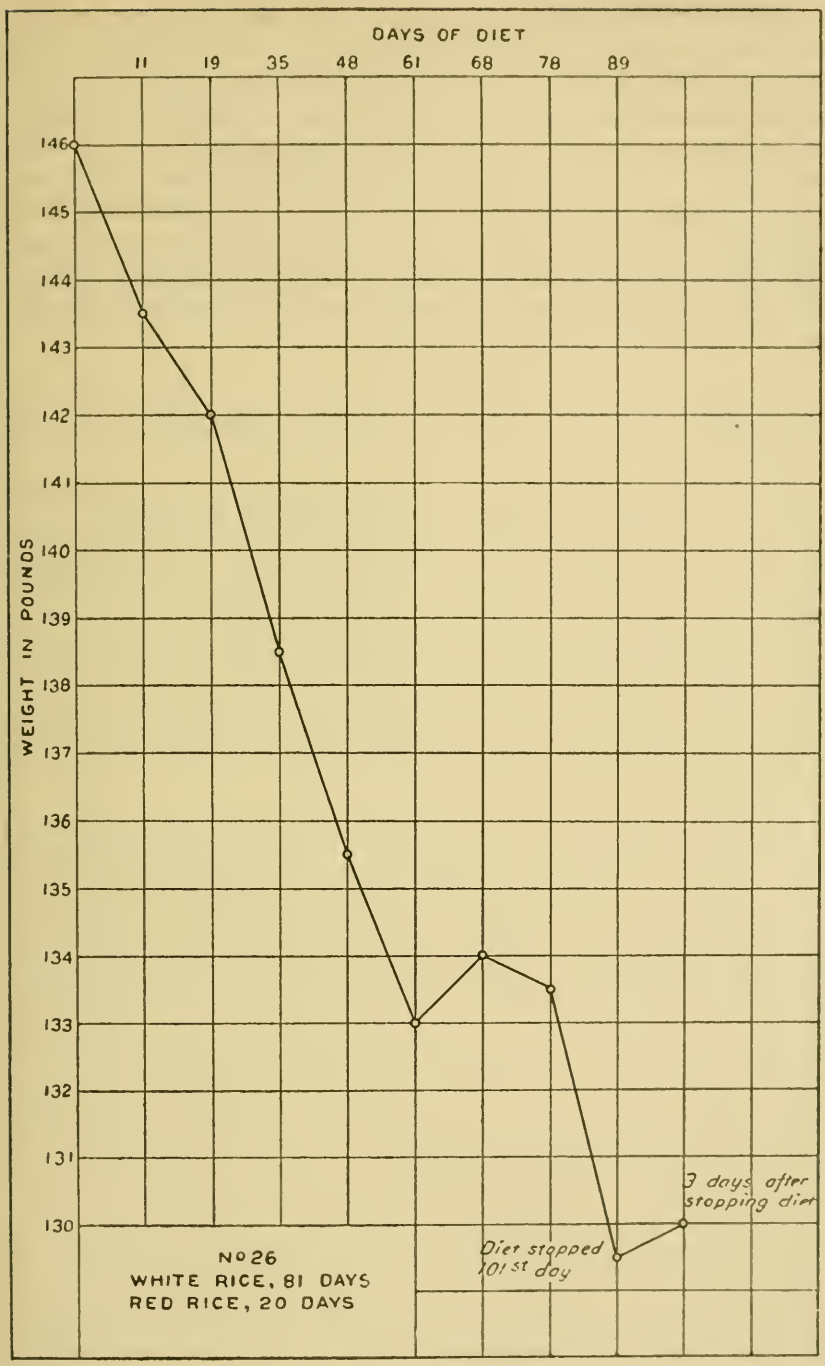
Diet: White rice for 81 days followed by red rice for 20 days, together with the special diet common to all the groups. } Total period of experiment, 101 days.

Dried codfish and potatoes were added to the diet on the 81st day.

Following is a summary of the notes of the case: Well-nourished man; auscultation and percussion of the lungs reveal nothing abnormal; the examination of the heart shows that the area of cardiac dulness is not increased beyond the normal limits; the point of maximum impulse is visible and not distinctly palpable; both sounds are clear at the apex; the second aortic sound is a little muffled, but there is no murmur; there is no epigastric pulsation; the pulse is 88 and the systolic blood pres-

sure is 108 millimeters Hg (Faught); the spleen is not palpable; the liver dulness begins at the lower border of the fifth rib; the edge is palpable just below the costal margin; the knee jerks are active.

The earlier notes of this case are not important except that the patient steadily lost in weight and by the sixty-third day of the experiment he weighed 5.8 kilograms (13 pounds) less than when he began the diet. The note made on this date reads as follows: Apex beat not visible nor distinctly palpable; pulse 86; no change in the condition of the heart apparent; the knee jerks are present but are weak. There was no change in his condition for the next few days. On the sixty-ninth day the systolic blood pressure was 90 millimeters Hg; he complained on this date of sharp pains in his fingers: From the sixty-ninth to the seventy-fifth day he continued to complain of pain in the ends of his fingers. On the latter day the pulse was 84 and he also complained of tenderness in his toes. On the seventy-sixth day the following note was made: There is marked weakness of the hands which are held semiflexed, and the grip of the hands is weak; the pulse is 100; the knee jerks are not elicited; there is no change in the heart sounds; there is slight epigastric but no præcordial pulsation and no œdema of the legs; there is hyperæsthesia of the skin of the fingers and toes and ankles; the patient winces when pressure is made over the calves of the legs. On the seventy-eighth day the note reads as follows: Pulse 78; patient in bed and not eating—complains of pains in the legs and arms; knee jerks not elicited; there is no œdema of the legs; the power in the hands is very weak. On the seventy-ninth day he was up and walking about; the pulse was 76; the gait was a little unsteady but not ataxic, though his body swayed when he stood with his eyes closed; the heart sounds were clear; there was no visible pulsation over the cardiac area; the hands were held semiflexed but could be extended; there was no wrist drop. On the eighty-first day it became necessary to substitute red rice for white rice, and on the following day dried codfish and potatoes were added to the diet. On the eighty-second day the note reads: The grip of the hands seems stronger but he still complains of pains in the fingers, legs, and toes. On the eighty-third the point of maximum impulse is not visible; the heart sounds are rapid and clear at the apex and feeble at the base; there is marked visible pulsation over the cardiac area; the pulse is 100; there is no distinct increase in the area of cardiac dulness. On the eighty-ninth day the strength of the hands seemed to continue to


DAYS OF DIET
11
19
35
48
61
68
78
89
WEIGHT IN POUNDS
146
145
144
143
142
141
140
139
138
137
136
135
134
133
132
131
130
No 26
WHITE RICE, 81 DAYS
RED RICE, 20 DAYS
Diet stopped
101st day
3 days after
stopping diet

increase. On the one hundred first day the diet was discontinued and the patient returned to the regular prison ration. On the following day the note reads: Nutrition fair; slight epigastric but no præcordial pulsation visible; point of maximum impulse not visible nor palpable; pulse 100; heart sounds clear at apex and feeble at base; there is no increase in the cardiac dulness; some tenderness in the calves of the legs is still present; the knee jerks are still present; there is no œdema of the legs; the fingers and toes are still weak. The urine showed no albumin and no casts. The patient gradually recovered. He had lost 7.7 kilograms (17 pounds) during the experiment.

CASE NO. 27 (GROUP IV).

Diet: White rice 82 days, together with the special diet common to all the groups.

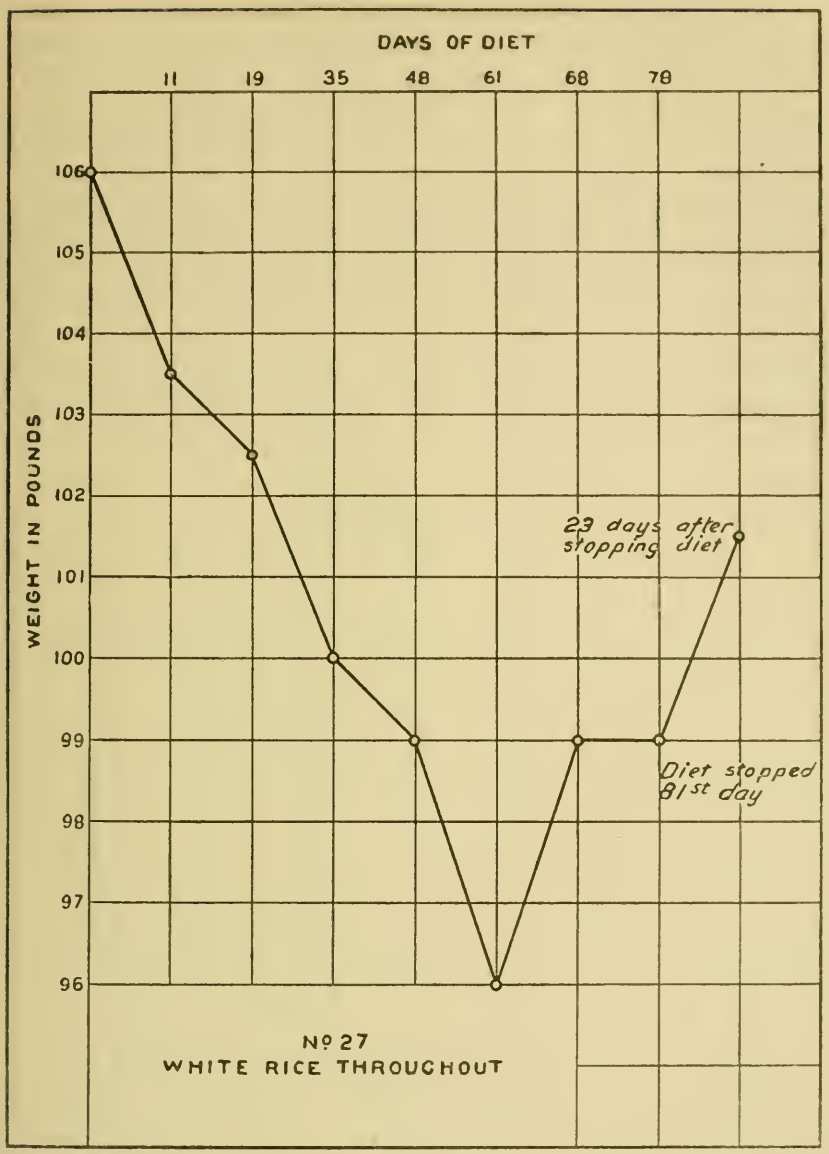
Following is a summary of the notes of the case: Well-nourished man of small stature; examination of the lungs shows nothing abnormal; the area of cardiac dulness is not increased beyond the normal limits; the point of maximum impulse is visible and palpable 6.5 centimeters to the left of the median line and 2.5 centimeters below the nipple line; the heart sounds are clear at the apex and base; there is no epigastric pulsation; the pulse is 96, and the systolic blood pressure 120 millimeters Hg (Faught); the spleen and liver are not enlarged; the knee jerks are active.

The earlier notes of this case are also not important. The patient lost steadily in weight until he weighed 10 pounds less than when he began the experiment. The knee jerks were always present. On the sixty-ninth day the systolic blood pressure was 120 millimeters Hg. No change had been noted in the condition of the heart. On the eighty-second day it became necessary to discontinue the diet. At this time he was in good condition. No change had occurred in the condition of the heart, and no symptoms of beriberi had developed during the course of the experiment. The urine showed no albumin nor casts. Twenty-three days after his return to prison ration he had gained 1.1 kilograms (2.5 pounds).

CASE NO. 28 (GROUP IV).

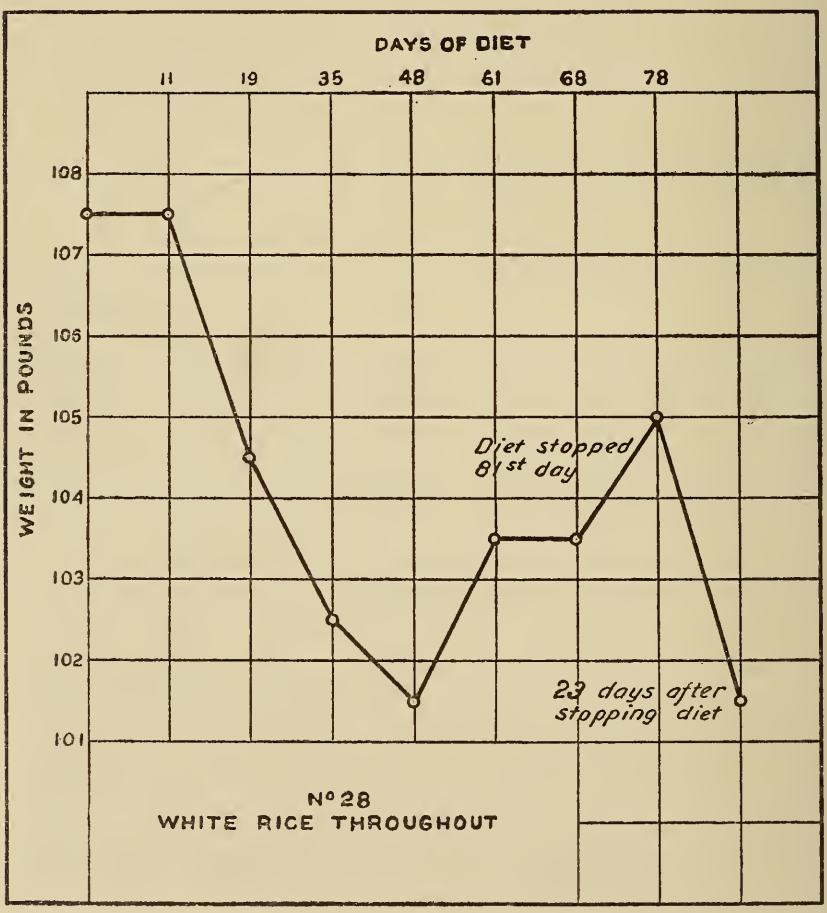
Diet: White rice for 82 days, together with the special diet common to all the groups.

Following is a summary of the notes of the case: Sparely nourished man; examination of the lungs reveals no abnormality; examination of the heart shows no increase of cardiac dulness



beyond the normal limits; the point of maximum impulse is just visible and palpable 7 centimeters to the left of the median line and 2 centimeters below the nipple; the heart sounds are clear at the apex and base; there is no epigastric pulsation visible; the pulse is 72, and the systolic blood pressure 100 millimeters Hg; the liver and spleen are not palpable below the costal margin; the knee jerks are active.

The other notes regarding this case are not important, except that the patient lost gradually in weight until the forty-eighth day of the experiment, 2.7 kilograms (6 pounds) in all. He then began to gain, and on the seventy-eighth day had regained 1.5 kilograms (3.5 pounds). The notes from the sixty-third to the sixty-eighth day show the knee jerks to have been very active. They were not lost throughout the time of the experiment. On the sixty-ninth day the systolic blood pressure was 98 millimeters Hg. There was no important change in his condition from now on. On the eighty-second day it became necessary to discontinue the diet, and he was returned to the regular prison ration. At this time he was in good condition. No changes had occurred in the condition of the heart, and no symptoms of beriberi had developed. The urine showed no albumin nor casts. Twenty-

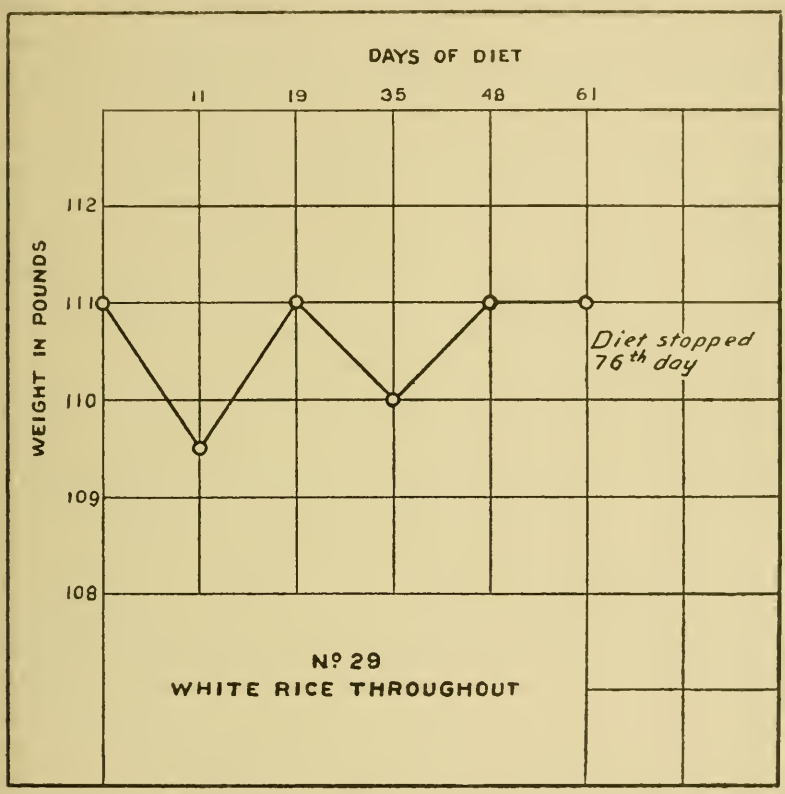


three days after resuming the regular prison ration he had lost again 1.5 kilograms (3.5 pounds).

CASE NO. 29 (GROUP IV).

Diet: White rice for 75 days, together with the special diet common to all the groups.

Following is a summary of the notes of the case: Sparely nourished man, moderately small in stature; percussion of the lungs reveals no area of dulness; on auscultation there is slight



roughening of the breath sounds over the right lung posteriorly near the base, but no tubular modification of the breath sounds and no râles; the area of cardiac dulness is not increased; the point of maximum impulse is neither visible nor palpable; there is no visible epigastric pulsation; the pulse is 104, and the systolic blood pressure 118 millimeters Hg (Faught); the liver and spleen are not enlarged; the knee jerks are active.

The earlier notes of the case are not important. The patient did not lose in weight. On the fifty-sixth day he complained of

swelling and pain in both legs. There was no particular pain on pressure over the calves. The right knee jerk was exaggerated, but the left seemed slightly diminished. The pulse was 104. On the sixty-first day the note reads as follows: Point of maximum impulse of the heart distinctly visible 10 centimeters to the left of the median line; no visible pulsation of the vessels of the neck; the heart sounds are clear at the apex and base. There is no tenderness of the calf muscles; the œdema of the legs has disappeared. The knee jerks are active. On the sixty-second day it was noted that the impulse over the cardiac area was not so marked. On the sixty-third day the note reads: Impulse just visible 10 centimeters from the middle line 5 centimeters below the nipple. Pulse 110 after exercise. Knee jerks active. On the sixty-fourth day œdema of the legs again appeared. On the sixty-fifth day the note made was as follows: Complains of pain in the chest, abdomen, and neck; pulse 120; epigastric and præcordial pulsation visible; there is marked œdema of both legs; the knee jerks are active. On the sixty-seventh day at noon the note was as follows: Not eating; pulse 96; respirations increased; marked præcordial and epigastric pulsation. He complains of weakness and epigastric pain. At 4 p. m. the pulse was 100; the respirations 40; and the epigastric pulsation marked. He ate but little. On the sixty-eighth day the knee jerks were still active, but he complained particularly of pain in the abdomen and legs. On the sixty-ninth day he complained of pain over the abdomen and in the thighs. There was marked epigastric pulsation, and the pulse was 106, full, and bounding. The knee jerks were active. There was still œdema of the legs. On the seventieth day the systolic blood pressure was 100 millimeters Hg. On account of the general condition of this patient, he was sent to the prison hospital. On the seventy-first day the pulse was 100, the knee jerks were active, the patient appeared drowsy. On the seventy-second day at noon the following note was made: Complains of feeling sore all over the body, and there is marked hyperæsthesia of the muscles of the calves; he is very drowsy; the face is puffy; there is marked œdema of the legs; the point of maximum impulse is not distinctly visible; it is palpable about 2 centimeters outside the nipple line and 4 centimeters below the nipple. On the seventy-third day the pulse was 104, and the knee jerks doubtful. He was still drowsy. On the seventy-fourth day the pulse was 120, respirations 24. He complained of pain in the chest and in the muscles of the legs and arms. There was slight epigastric

pulsation but no præcordial throbbing was visible. The knee jerks could not be elicited. On the seventy-fifth day the note made was as follows: Pulse 120; respirations 50; point of maximum impulse visible outside the nipple line; area of cardiac dulness increased transversely; there is slight præcordial pulsation; at the apex the first sound is short, and the spacing between the sounds equal; there are no definite murmurs, and no accentuation of the sounds at the base; there is marked dyspnœa, and the legs are œdematous; the knee jerks are absent. He complains of pain and tenderness over the chest and in the shoulders, neck, and calves of the legs. At 4 p. m. the pulse was 120, respirations 40, and the pulse very weak. The patient was placed on a general nourishing diet, and stimulation started. On the seventy-sixth day the pulse was very weak. The patient was very drowsy and responded slightly when spoken to. He was only semiconscious. The heart sounds were rapid and evenly spaced. On the seventy-seventh day the note was made as follows: Still weaker; there is marked general twitching of the muscles all over the body and some coarse tremors of the muscles of the shoulders; there is marked general œdema and general tenderness; no ascites; the pulse is very rapid and very weak; respirations 40; the temperature has been practically normal since he entered the hospital. The patient gradually sank and died at 2 p. m. on the following day. The urine in this case was greatly diminished in amount. On April 13, six days before his death, the amount for twenty-four hours was only 360 cubic centimeters, and the amount diminished each day until the day before his death, when only 60 cubic centimeters were passed. The specific gravity during this time varied between 1022 and increased gradually so that the day before death it was 1030. The urine contained no albumin at any time and no casts.

NECROPSY. ONE-HALF HOUR AFTER DEATH.

Anatomical diagnosis.—Acute beriberi; degeneration of heart muscle; epicardial, pleural, peritoneal, renal, hepatic, gastric, and duodenal ecchymoses; congestion and œdema of lungs; acute gastro-duodenitis; acute parenchymatous degeneration of kidney; acute congestion and degeneration of liver; pial œdema; hydrothorax; anasarca.

The cadaver is that of an adult male Filipino of about 40 years of age, measuring about 150 centimeters in length. The body is still warm. There is marked general subcutaneous œdema which is most marked over the legs, scrotum, and face. Hair of the head abundant, black, and straight. Beard moderate. Scant axillary and thoracic hair. Pubic hair of the male Caucasian type. No scars found on the body. Pupils are equal,

dilated, circular; corneæ and conjunctivæ clear. Ears, nose, and mouth normal. Superficial lymphatic glands not enlarged. Thorax broad and short; abdomen tense, but not distended. Rigor mortis not present. No post-mortem hypostases.

On section the rather abundant and yellow subcutaneous adipose is very moist, a clear fluid exuding from all cut surfaces. The skeletal muscles are pale, soft, friable, and moist. The abdominal cavity contains only a small amount of clear fluid in the fossæ, the peritoneum being everywhere smooth and glistening, without adhesions. The intestines are somewhat distended, their serosa pale. Liver reaches 2 centimeters below the right costal margin and 6 centimeters below the xyphoid. The dome of the diaphragm stands at the upper margin of the 5th rib on the right and the lower border of the 6th on the left.

Thorax.—On removal of the sternum the tissues of the anterior mediastinum are found to be somewhat œdematous. Both lungs are retracted beyond the cut costal margin, exposing a very large præcordial area. Each pleural sac contains about 200 cubic centimeters of clear yellowish fluid. The thymic pad is moist and fatty without recognizable glandular remnant.

Heart.—The præcordial area is large and the pericardium very tense. Before opening the pericardium, the apex is felt impinging upon the parietal pleura in the midaxillary line at the 6th rib, and the right border of the pericardium is 2.5 centimeters to the right of the sternal margin. On opening the pericardium, its inner wall is found smooth, and not more than about 30 cubic centimeters of clear fluid is found in its sac, the heart filling up and distending the sac. Both ventricles present anteriorly, the right a little more than the left, and the distension of the right heart (both auricle and ventricle) is the more marked. The right edge of the heart is very much rounded. In the right auriculo-ventricular groove anteriorly are a few small punctate epicardial ecchymoses. The apex is formed by both ventricles with a groove between them. Epicardial fat is not over abundant and the coronary vessels are not prominent. On section of the heart, abundant dark fluid blood escapes from both sides and the heart collapses, diminishing greatly in size. Both right auricle and ventricle are, however, evidently dilated after opening the heart in the usual way, and the calumnæ carneæ and papillary muscles are somewhat flattened. The tricuspid ring admits three and one-half fingers, the tricuspid leaflets being large, thin, and pliable with rather long and slender chordæ tendineæ. The entire endocardium of the right heart is smooth and pale except for the presence of small punctate hæmorrhages on the outer wall of the ventricle just beneath the mural flap of the tricuspid valve. The muscle of the right ventricle is thin, pale brown, and rather friable. The pulmonary orifice and valves are normal. The left side of the heart is less dilated, and its endocardium is intact, the mitral ring admitting 2 fingers with ease. The aortic ring and leaflets are normal. Muscle of the left ventricle measures about 12 millimeters at mitral insertion and is firmer than that of the right ventricle; its cut surface is smooth, rather more of a yellowish tinge than normal, although not flecked, and has a glassy appearance. No hæmorrhages are found in the left heart.

Lungs.—Both lungs are diminished in volume and are free from pleural adhesions. The pleura is smooth and moist, and the pigmented lines of the interlobular septa are readily visible. Elasticity of the lungs is diminished,

and the lungs are less crepitant than normal. A few ecchymoses are present on the pleura covering the outer margin of the right lower lobe. On section of the lungs the cut surfaces are smooth, dark red throughout, exuding abundant blood and a moderate amount of frothy fluid. No consolidated areas are found, but the general consistence is increased by the diminished air content, this being especially true of the left lower lobe. The mucosa of the larger bronchi is reddened, its longitudinal striations prominent, and there is present considerable frothy pale fluid.

Organs of neck.—Tongue broad and flat, the papillæ at its base being not prominent. Faucial tonsils not enlarged. Walls of the pharynx are congested. Mucosa of œsophagus is smooth and pale. Mucosa of larynx and trachea is somewhat reddened and a small amount of frothy fluid is found in the trachea. Thyroid gland is not enlarged, and is dark and moist showing the presence of moderate colloid. Cervical lymphatic glands not enlarged.

Spleen lies well posteriorly and is nonadherent. It is somewhat increased in size, and its capsule tense and steel-blue in color. On section, the consistence is somewhat increased, the pulp prominent but firm, being of a dark red color. Lymphoid tissue is scarcely visible, and there is no apparent interstitial increase. No hæmorrhages are seen in the capsule or substance of the gland.

Adrenals are of normal size, the cortex being yellowish with a rather broad pigmented zone. The medulla is relatively prominent.

Kidneys are embedded in a moderate amount of perinephric fat, there being a small hæmorrhage into the peritoneum at the lower pole of the right kidney. The kidneys are of about normal size, and the capsules strip readily from the surfaces, which are smooth and of a dark red color with a few punctate hæmorrhages. On section the cortex is a little broadened and bulges considerably. The cut surface of the cortex is pale reddish brown with a moist glassy appearance. The vascular striæ are not prominent, and the glomeruli are easily visible, enlarged, and for the most part of a red color. The pyramids are very pale and firm. The mucosa of the calyces, pelves, and ureters is pale with the exception of a few small ecchymoses in the pelvis of the left kidney. Renal vessels are in good condition. Urinary bladder, prostate gland, urethra, testes, and seminal vesicles are normal in appearance. A few ecchymoses are present over the dome of the bladder.

Intestines.—The mesentery is fatty and œdematous, its lymphatic glands being small and pink. The large intestine shows no appreciable lesions; it contains a small amount of formed dark fæces. There is possibly a slight excess of mucus in the small intestine. The lymphoid structures of the lower part of the ileum are not unduly prominent. The duodenum shows marked changes in its mucosa. The mucosa is thickened, œdematous, boggy, and as a whole is very red. In addition to its general red color, very numerous small hæmorrhages are readily visible after removing the excessive mucus. The papilla of Vater is unchanged and delivers a golden yellow bile on pressure on the gall bladder.

Stomach is somewhat dilated and contains a small amount of watery fluid. On its posterior surface in the region of the pylorus are very numerous ecchymoses scattered over a rather large area, and the mucosa as a whole is reddened and swollen.

Pancreas is of normal size, firm, pale with distinct lobular markings and patent duct.

Liver and gall bladder.—The gall bladder is small and contains a small amount of golden yellow bile which is readily expressed through the ducts. Common, cystic, and hepatic ducts normal. Liver is of about normal size, its capsule thin, smooth, and transparent. The edges are slightly rounded and the surface smooth and a deep red color with small areas of yellowish mottling. On section the organ is soft and the cut surface smooth. In color it is very deep red, the red masses and strands being rather prominent above the surface, surrounding and including small pin-head-sized areas of a much paler parenchyma. Some few small yellowish foci are seen in the parenchyma. The general architecture of the cut surface is destroyed by the prominence and distribution of the elevated red areas which obliterate the normal markings.

Lymphatic glands of mesentery, retroperitoneal space, and lesser sac are small and pink on section.

Brain.—Structures of scalp are œdematous. Calvarium normal. Dura mater is nonadherent. Longitudinal sinus free. Inner surface of dura mater smooth. There is a slight excess of clear fluid in the meshes of the pia arachnoid over the hemispheres. The meningeal vessels are prominent. Vessels at the base in good condition. Ventricles are not dilated and ependyma is smooth. Section of brain substances shows no gross lesions.

Sections of the viscera were preserved in Zenker's fluid and in 10-per-cent formalin. Sections of the two vagi, anterior tibial, and popliteal nerves were preserved in Müller's fluid.

HISTOLOGICAL EXAMINATION.

Heart.—There is considerable œdema and some increase of the adipose tissue beneath the epicardium and of that between the muscle bundles. The muscle fibers themselves are swollen and granular. When seen in longitudinal section the muscle fibrils are very distinct and in many the nuclei are poor in chromatin. Occasionally vacuoles are seen in the protoplasm of the fibers. Each of these features is much exaggerated when the bundles are seen in transverse section. The fibrils of the muscles are comparatively widely separated and much more readily visible than normal. Irregular vacuolated areas are very frequent, and the nuclei are frequently entirely gone, being replaced by a vacuole or a homogeneous mass which does not take the hæmotoxylin stain. Staining with Sudan III shows very little fat in the muscle fibers. No round-celled foci and no marked multiplication of the nuclei are seen.

Liver.—In the liver the cells in the immediate neighborhood of the central veins are much swollen and granular with indistinct outlines and the portal spaces have a more or less normal appearance. The architecture of the entire remaining portions of the liver is destroyed. In the mid-zone and periphery of the

lobules and sometimes in the central portions the capillaries are widely distended with blood and the arrangement of the cells is distorted. The individual cells show various grades of changes. In some the protoplasm is the seat of small vacuoles while in others the protoplasm has entirely disappeared, leaving a more or less intact nucleus enclosed by the cell membrane—all grades of this change from slight vacuolation up to complete disappearance of the protoplasm may be traced. The nucleus sometimes remains intact, while in others can be seen various stages of disappearance of the chromatin, until simply the shadows of some cells are left. In other areas another type of cell change takes place in which the cell outline is clear but distorted and the cell protoplasm is much more opaque, more homogeneous, and more highly acidophilic than normal. Some of this latter type of cell contain apparently intact nuclei and some even double nuclei, while in others various grades of disappearance of the chromatin are seen down to those in which the nucleus is no longer visible.

While the congestion in these areas is intense, in no place has actual hæmorrhage taken place. No marked bile stasis is recognizable; sections stained with Sudan III show only a very small amount of fatty degeneration.

A few leucocytes surround some of the central veins, and, if regeneration be present, it is certainly not a prominent feature.

Spleen.—The spleen shows some congestion and a rather loose arrangement of the reticulum of the pulp. The congestion is especially marked in the region of the lymphoid follicles. The follicles are relatively small. No other notable changes are seen.

Pancreas.—The pancreas is well formed and shows no changes outside of the islands of Langerhans. Here the cells are very pale and very poorly differentiated from one another, while the nuclei are relatively prominent. Occasionally double nuclei are seen. No changes are seen in the periacinar tissue. The average size of the islands is large, but not larger than within normal limits.

Kidneys.—These show a very severe acute parenchymatous degeneration and some congestion. Little, if any, exudation of cells has taken place. Dilated veins are seen on the surface and a few very small areas of superficial fibrosis.

The convoluted tubules show a marked degeneration of the epithelial cells, and practically all are filled up with a substance which is acidophilic and arranged in the form of a granular reticulum—this is evidently a coagulated, albuminous fluid. The

vessels of the glomeruli are much congested and the cytoplasm of the epithelial cells of the tufts is frequently granular and sometimes vacuolated. Some of the glomerular spaces contain a material similar to that described in the convoluted tubules, but no cellular exudate. The cells lining Bowman's capsule are sometimes high and swollen. In the pyramids the cells of the excretory tubules are intact and no casts are seen, but the tissue between the tubules is very œdematous. Sections stained with Sudan III show no fat.

Stomach and duodenum.—The sections show hæmorrhages in the mucosa without inflammatory condition other than slight catarrh. Marked prominence of acidophilic parietal cells is observed in the pyloric glands.

Nerves.—These were fixed in Müller's fluid and prepared by the Marchi method for the study of the degeneration of nerves. The hæmatoxylin and eosin stain was also employed.

All nerves examined (vagi, phrenics, anterior crural, popliteal, and sciatic) show equally marked changes. The degeneration of the myelin sheaths is very advanced and a large majority of the fibers are affected. In longitudinal sections this degeneration is shown after the Marchi treatment to consist of a marked swelling and fragmentation of the myelin sheath and its collection in masses and globules, giving a varicose or honeycombed appearance to the fibers. No leucocytic infiltration or proliferation of the nuclei of the neurilemma is seen in the sections. Cross sections show fibrils, some partly and some completely surrounded by the degenerated sheath. There is apparently some fragmentation of the nerve fibers themselves. (Plates IV, V, VI, and VII.)

TABLE VI.—*Record of rations consumed by prisoners of Group IV.*

Prisoner number.	Kind of rice.	Duration of experiment.
26 25	White rice 81 days; red rice 20 days	101 days, February 2 to May 12.
22 24 19 20 21 23	White rice	92 days, February 2 to May 3.
27 28	White rice	81 days, February 2 to April 23.
29	White rice	76 days, February 2 to April 17.

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 1.											
Rice	300	300	300	300	300	300	225	150	200	150	300
Bananas	150	150	150	150	150	150	150	50	150	150	0
Sugar	75	75	75	75	75	75	35	35	35	75	35
Day 2.											
Rice	300	300	300	300	300	300	300	300	300	300	300
Onions	100	100	100	100	100	100	100	100	100	100	100
Lard	15	15	15	15	15	15	15	15	15	15	15
Bread	200	0	200	175	65	200	150	100	200	200	200
Rice	70	100	100	100	100	100	70	85	70	100	50
Starch	35	50	50	50	50	50	35	45	35	50	25
Sugar	20	25	25	25	25	25	20	20	20	25	10
Lard	15	20	20	20	20	20	15	15	15	20	10
Day 3.											
Rice	300	300	300	300	300	300	300	300	300	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	300	300	300	300	300	300	265	265	300	265	300
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	65	75	65	75	65	75	55	65	65	75	65
Day 4.											
Rice	300	300	300	300	300	300	300	300	300	300	300
Onions	100	100	100	100	100	100	100	100	100	100	100
Lard	15	15	15	15	15	15	15	15	15	15	15
Bread	200	200	175	200	175	200	200	100	200	200	200
Rice	65	75	100	75	100	75	50	65	65	75	65
Starch	35	40	50	40	50	40	25	35	35	40	35
Sugar	15	20	25	20	25	20	15	15	15	20	15
Lard	10	15	20	15	20	15	10	10	10	15	10
Day 5.											
Rice	300	300	300	300	300	300	200	200	200	265	300
Bananas	100	100	100	100	100	100	100	100	100	100	100
Sugar	15	25	0	10	10	25	15	15	15	15	0
Rice	300	50	50	300	300	300	300	300	50	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 6.											
Rice	200	200	200	175	200	200	200	200	175	65	175
Bread	75	75	75	150	75	75	150	150	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	350	350	350	350	350	350	350	350	350	350	350
Onions	150	150	150	150	150	150	150	150	150	150	150
Lard	20	20	20	20	20	20	20	20	20	20	20
Day 7.											
Rice	300	300	300	300	300	300	300	300	300	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	300	300	300	300	300	300	300	300	300	300	300
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	75	75	75	75	75	75	75	75	75	75	75

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 8.											
Bread	150	150	150	150	100	150	150	150	150	150	150
Rice	10	50	50	65	35	65	50	50	90	50	50
Starch	5	25	25	35	15	35	25	25	45	25	25
Sugar	5	15	15	15	5	15	15	15	20	15	15
Lard	5	10	10	10	5	10	10	10	15	10	10
Rice	300	300	300	300	300	300	300	300	300	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 9.											
Bread	150	150	150	150	150	150	150	150	150	150	150
Rice	200	200	25	200	200	65	200	200	200	200	200
Bacon	30	30	0	30	30	30	30	30	30	30	30
Dinner	No record kept.										
Day 10.											
Rice	300	300	300	300	300	300	300	300	300	250	300
Bananas	100	100	100	100	100	100	100	100	100	100	100
Sugar	0	25	0	25	10	0	25	25	10	25	25
Rice	300	300	300	300	300	300	300	300	300	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 11.											
Rice	270	300	300	270	265	265	300	300	265	300	300
Onions	100	100	100	100	100	100	100	100	100	100	100
Lard	15	15	15	15	15	15	15	15	15	15	15
Bread	200	65	200	200	100	200	200	200	175	200	200
Rice	30	60	60	50	50	30	100	100	100	100	60
Starch	15	30	30	25	25	15	50	50	50	50	30
Sugar	10	20	20	10	10	10	25	25	25	25	20
Lard	5	10	10	10	10	5	20	20	20	20	10
Day 12.											
Rice	300	300	300	300	150	300	300	300	300	300	300
Bacon	50	50	0	50	0	50	50	50	50	50	50
Rice	300	150	100	300	150	200	300	150	200	150	300
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	75	75	75	75	35	75	75	75	75	75	75
Day 13.											
Bread	150	150	150	150	20	150	150	150	150	150	150
Rice	60	85	50	60	50	50	100	100	60	100	100
Starch	30	40	25	30	25	25	50	50	30	50	50
Sugar	20	20	10	20	10	10	25	25	20	25	25
Lard	10	15	10	10	10	10	20	20	10	20	20
Rice	350	230	350	350	230	230	350	305	230	305	350
Onions	150	150	150	150	150	150	150	150	150	150	150
Lard	20	20	20	20	20	20	20	20	20	20	20
Day 14.											
Rice	200	200	200	200	200	200	200	200	200	200	200
Bacon	30	30	30	0	30	30	30	30	30	30	30
Rice	300	225	300	300	265	200	300	300	200	300	265
Bacon	50	50	50	50	50	50	50	50	50	50	50
Bread	150	150	150	150	100	150	150	150	150	150	150

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 15.											
Rice	300	300	300	300	265	200	300	300	265	150	300
Bananas	150	150	100	150	150	150	150	150	150	150	150
Rice	305	350	350	350	350	350	305	305	230	230	305
Onions	150	150	150	150	150	150	150	150	150	150	150
Lard	20	20	20	20	20	20	20	20	20	20	20
Day 16.											
Rice	175	200	200	175	200	175	200	200	150	200	200
Bread	150	150	125	150	150	150	150	150	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	300	225	265	265	265	265	225	225	265	265	265
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 17.											
Rice	265	300	300	265	265	265	300	300	270	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	No record kept.										
Onions											
Lard											
Day 18.											
Rice	200	200	200	135	200	200	200	200	175	200	200
Bread	150	150	135	150	100	100	150	75	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	265	150	40	265	225	200	265	75	150	150	300
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	75	0	0	0	0	0	0	75	75	75	0
Day 19.											
Rice	300	300	300	265	300	270	300	225	265	300	265
Bananas	100	100	100	100	100	100	100	100	100	100	100
Sugar	0	0	10	0	10	25	0	0	0	0	0
Rice	350	350	350	350	350	350	350	350	350	350	350
Onions	150	150	150	150	150	150	150	150	150	150	150
Lard	20	20	20	20	20	20	20	20	20	20	20
Day 20.											
Rice	270	300	300	270	300	300	300	300	270	300	300
Bacon	0	50	50	50	50	50	50	50	50	50	50
Rice	No record kept.										
Bananas											
Sugar											
Day 21.											
Rice	175	175	200	150	180	175	180	200	180	200	175
Bacon	30	30	30	30	30	30	30	30	30	30	30
Bread	150	150	150	150	135	150	150	20	150	150	150
Rice	265	175	0	175	175	230	265	265	280	230	230
Onions	150	150	0	150	0	150	150	150	150	0	150
Lard	20	20	0	20	0	20	20	20	20	0	20
Day 22.											
Rice	300	150	0	300	150	200	300	270	150	300	300
Bananas	100	100	50	100	100	100	100	100	100	100	100
Sugar	0	0	0	0	0	0	0	0	0	0	0

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 22—Continued.											
Rice	265	265	300	265	150	265	100	300	270	150	225
Bacon	50	50	50	50	50	50	50	25	50	50	50
Day 23.											
Rice	225	225	300	300	275	300	225	300	270	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	150	150	200	40	100	100	200	100	0	300	300
Bread	150	150	150	150	100	150	150	150	150	150	150
Onions	0	75	50	75	50	150	150	150	150	150	150
Day 24.											
Rice	180	100	100	200	180	180	180	200	150	100	200
Bread	150	150	75	150	100	150	150	150	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	225	200	225	240	150	240	150	100	200	225	200
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	75	75	75	75	75	75	75	75	75	75	75
Day 25.											
Rice	0	150	75	300	0	225	150	150	225	0	150
Bananas	100	100	50	100	50	100	100	100	100	100	100
Sugar	25	25	25	25	10	25	25	0	25	0	0
Rice	150	240	225	40	100	265	100	240	200	100	300
Onions	0	150	75	0	0	150	75	0	150	150	0
Lard	0	20	10	0	0	20	10	0	20	20	0
Day 26.											
Rice	300	300	300	200	300	300	240	300	300	270	275
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	240	150	75	180	200	225	60	100	150	225	200
Bananas	150	150	100	150	150	150	150	150	150	150	150
Sugar	75	75	0	75	75	75	75	75	75	75	75
Day 27.											
Rice	200	200	200	200	200	200	130	180	180	180	200
Bread	150	150	75	150	150	150	150	150	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	310	230	265	350	45	280	350	45	280	45	350
Onions	0	75	75	150	0	150	150	50	150	50	150
Day 28.											
Rice	300	150	300	300	300	300	300	200	200	200	200
Onions	15	50	100	30	30	75	0	75	taste	50	0
Lard	5	10	15	5	5	10	0	10	taste	10	0
Rice	200	300	200	240	200	240	300	100	200	240	300
Bananas	150	150	100	150	150	150	150	150	150	150	150
Sugar	75	75	75	75	75	75	75	75	75	75	75
Day 29.											
Rice	0	200	300	300	300	300	300	300	250	300	300
Bacon	0	50	50	50	50	50	50	50	50	50	50
Rice	0	315	305	175	280	280	350	315	305	350	350
Onions	0	150	0	0	150	150	150	150	150	150	150
Lard	0	20	0	0	20	20	20	20	20	20	20

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 30.											
Rice	130	175	180	150	175	175	150	200	150	175	200
Bread	100	135	150	150	150	150	140	150	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	200	200	100	300	200	200	150	100	225	225	200
Bananas	100	150	100	100	100	100	100	100	100	100	100
Sugar	0	0	0	25	25	0	25	25	0	0	25
Day 31.											
Rice	100	100	200	300	250	200	150	300	225	250	300
Bananas	100	100	100	100	100	100	100	100	100	100	100
Sugar	0	0	0	0	0	0	0	0	0	0	0
Rice	115	230	175	350	230	230	115	305	115	265	175
Onions	0	50	50	150	50	100	50	150	75	0	150
Lard	0	5	5	20	5	10	10	20	10	0	20
Day 32.											
Rice	300	300	300	300	300	0	150	300	150	300	300
Bacon	50	50	50	50	50	0	50	50	50	50	50
Rice	200	100	100	200	135	(?)	135	180	160	160	150
Bananas	150	150	100	150	150	(?)	150	150	150	150	150
Sugar	75	75	0	35	25	(?)	75	75	75	0	0
Day 33.											
Rice	265	265	100	75	225	(?)	200	265	35	265	200
Bread	20	40	120	150	20	.....	20	0	150	25	75
Bacon	30	30	30	0	30	.....	30	30	30	30	30
Rice	0	115	0	115	0	(?)	175	230	115	230	175
Onions	75	75	0	75	0	(?)	100	100	0	0	150
Lard	10	10	0	10	0	(?)	15	15	0	0	20
Day 34.											
Rice	275	250	270	300	150	.....	300	300	300	240	300
Onions	50	50	0	50	0	.....	100	0	100	0	100
Lard	10	10	0	10	0	.....	15	0	15	0	15
Rice	270	240	240	300	240	.....	225	225	150	240	270
Bananas	150	150	150	150	150	.....	150	150	150	150	150
Sugar	75	25	75	75	75	.....	75	0	75	75	0
Day 35.											
Rice	270	270	240	300	270	.....	200	300	225	225	200
Bananas	100	100	100	100	100	.....	100	100	100	100	100
Sugar	10	25	25	25	25	.....	0	25	25	25	10
Rice	200	300	300	300	225	.....	270	300	240	200	300
Bacon	50	50	50	50	50	.....	50	50	50	50	50
Day 36.											
Rice	270	265	225	265	200	.....	200	270	270	265	300
Bacon	50	50	50	50	50	.....	50	50	50	50	50
Rice	265	265	280	350	115	.....	350	350	350	350	350
Onions	75	75	0	75	0	.....	150	150	150	150	150
Lard	10	10	0	10	0	.....	20	20	20	20	20

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 37.											
Rice	200	100	180	180	150	------	100	200	200	200	200
Bread	120	150	150	150	50	------	75	150	150	150	140
Bacon	30	30	30	30	30	------	30	30	30	30	30
Rice	265	200	150	300	275	------	225	250	200	250	300
Bananas	150	150	150	150	150	------	150	100	150	150	150
Sugar	0	0	0	40	0	------	75	75	75	75	0
Day 38.											
Rice	240	225	0	200	250	------	240	250	100	300	275
Bananas	100	100	100	100	100	------	100	100	100	100	100
Sugar	0	0	0	0	25	------	0	0	0	0	0
Rice	210	305	45	280	175	------	230	230	280	280	230
Onions	0	75	0	0	0	------	0	150	0	150	0
Lard	0	10	0	0	0	------	0	20	0	20	0
Day 39.											
Rice	270	300	275	300	200	------	240	300	225	300	300
Bacon	50	50	50	50	50	------	50	50	50	50	50
Rice	240	225	150	300	240	------	300	75	0	300	240
Bananas	150	150	150	150	150	------	150	150	150	150	150
Sugar	75	75	75	75	75	------	75	75	75	75	75
Day 40.											
Rice	175	175	130	175	200	------	130	165	180	170	150
Bread	150	150	75	75	75	------	75	75	150	75	75
Bacon	30	30	15	30	30	------	30	30	30	30	30
Rice	240	200	150	240	150	------	300	300	200	300	300
Onions	50	0	50	100	0	------	150	0	50	0	150
Lard	5	0	5	10	0	------	20	0	5	0	20
Day 41.											
Rice	250	225	150	300	240	------	265	300	300	300	300
Onions	100	100	0	100	0	------	100	100	50	35	100
Lard	15	15	0	15	0	------	15	15	10	5	15
Rice	225	265	150	265	200	------	200	250	200	275	300
Bananas	150	150	150	150	150	------	150	150	150	150	150
Sugar	0	0	0	75	50	------	0	75	0	75	0
Day 42.											
Rice	300	240	60	300	200	------	200	300	150	300	300
Bananas	100	100	100	100	100	------	100	50	100	100	100
Sugar	10	0	0	0	20	------	25	0	10	25	0
Rice	240	265	265	240	275	------	265	200	200	300	300
Bacon	50	50	50	50	50	------	50	50	50	50	50
Day 43.											
Rice	265	240	240	300	275	------	150	300	225	265	300
Bacon	50	50	35	50	50	------	0	25	50	50	50
Rice	175	0	85	280	280	------	230	350	310	350	350
Onions	75	0	0	0	0	------	75	150	150	150	150
Lard	10	0	0	0	0	------	10	20	20	20	20

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 44.											
Rice	100	100	150	.....	65	.....	200	135	200	200	135
Bread	150	150	150	.....	75	.....	0	150	150	150	75
Bacon	30	30	15	.....	15	.....	30	30	30	30	30
Rice	240	250	75	250	150	250	200	240	265	300	265
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	0	75	0	75	75	75	75	0	75	75	0
Day 45.											
Rice	200	150	0	200	150	100	200	265	225	300	265
Bananas	100	100	50	100	100	100	100	100	100	100	100
Sugar	0	25	0	25	25	0	25	0	0	0	0
Rice	115	265	175	115	60	230	175	175	0	175	230
Onions	75	150	0	100	0	0	150	150	0	75	75
Lard	10	20	0	15	0	0	20	20	0	10	10
Day 46.											
Rice	225	240	225	240	240	225	100	75	150	300	240
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	150	265	75	200	100	250	225	150	150	300	200
Bananas	150	150	50	150	150	150	150	150	150	150	150
Sugar	75	75	75	75	35	75	75	0	0	75	0
Day 47.											
Rice	100	135	135	100	80	135	100	200	160	160	100
Bread	150	100	75	150	150	100	50	150	120	75	75
Bacon	30	30	30	30	30	0	15	30	30	30	30
Rice	115	230	115	230	175	230	80	280	350	350	350
Onions	75	50	0	35	75	75	150	80	75	150	0
Lard	10	5	0	5	10	10	20	15	10	20	0
Day 48.											
Rice	75	60	60	150	75	200	240	300	225	300	300
Onions	25	100	20	100	25	35	100	100	100	0	0
Lard	5	15	3	15	5	5	15	15	15	0	0
Rice	250	265	40	300	265	265	300	0	300	300	300
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	75	75	75	35	0	75	75	0	35	75	35
Day 49.											
Rice	240	200	0	200	200	150	275	240	265	300	225
Bananas	100	100	100	100	100	100	100	100	100	100	100
Sugar	0	25	5	5	25	0	25	25	25	25	10
Rice	150	300	300	225	265	200	100	275	100	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 50.											
Rice	150	150	300	100	75	150	200	300	200	300	300
Onions	100	100	100	100	100	50	50	100	100	100	100
Lard	15	15	15	15	15	10	10	15	15	15	15
Rice	150	150	taste	225	150	225	275	100	240	300	275
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	35	35	35	75	20	0	0	75	75	35	35

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 51.											
Rice	135	170	165	200	175	165	175	200	170	200	150
Bread	100	150	150	150	150	150	150	150	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	0	230	85	265	175	175	230	350	175	350	350
Onions	150	75	0	75	0	75	150	150	150	150	150
Lard	20	10	0	10	0	10	20	20	20	20	20
Day 52.											
Rice	150	200	240	300	225	225	240	265	0	300	225
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	25	25	0	25	25	25	25	25	0	0	10
Rice	70	230	40	175	40	265	230	290	265	350	305
Onions	150	150	0	150	150	40	150	150	40	150	40
Lard	20	20	0	20	20	5	20	20	5	0	5
Day 53.											
Rice	35	225	300	300	75	300	300	300	300	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	150	225	30	300	35	250	150	225	0	300	225
Bananas	150	150	150	150	100	150	150	150	150	150	150
Sugar	40	75	0	75	40	75	75	40	0	40	40
Day 54.											
Rice	100	300	300	300	75	300	300	300	200	300	300
Onions	50	100	100	100	100	50	100	100	50	100	100
Lard	10	15	15	15	15	10	15	15	10	15	15
Rice	240	300	300	300	30	250	300	300	275	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 55.											
Rice	100	80	160	200	65	175	50	35	0	180	160
Bread	150	150	150	150	0	110	150	125	75	150	75
Bacon	30	30	30	30	15	30	30	30	30	30	30
Rice	275	180	50	265	100	200	265	280	35	275	200
Bananas	150	150	100	150	100	150	150	150	100	150	150
Sugar	15	75	20	0	0	0	0	0	0	75	0
Day 56.											
Rice	300	150	300	300	100	265	200	150	225	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Rice	230	265	230	230	90	265	280	280	175	305	280
Onions	0	0	150	150	0	150	150	150	75	75	150
Lard	0	0	20	20	0	20	20	20	10	10	20
Day 57.											
Rice	265	225	75	300	100	240	150	300	240	265	240
Bananas	100	100	100	100	100	100	100	0	100	100	100
Sugar	0	0	0	25	5	0	0	0	25	10	0
Rice	305	305	315	350	230	230	305	350	305	305	350
Onions	0	150	150	150	0	0	150	150	50	150	150
Lard	0	20	20	20	0	0	20	20	10	20	20
Day 58.											
Rice	150	160	150	175	135	150	175	200	175	175	175
Bread	50	150	50	150	50	150	150	150	150	50	110

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 58—Continued.											
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	100	265	150	150	150	240	300	225	100	300	300
Bananas	150	150	150	150	150	150	150	150	150	150	150
Sugar	0	0	5	10	0	25	0	0	0	25	10
Day 59.											
Rice	150	265	100	225	150	265	200	35	0	225	200
Bananas	100	100	100	100	50	100	100	0	0	100	100
Sugar	0	0	10	10	0	0	0	0	0	25	0
Rice	100	300	200	300	100	225	150	75	150	300	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 60.											
Rice	200	35	100	100	35	200	0	0	0	150	30
Onions	100	100	30	50	100	50	100	0	0	50	50
Lard	15	15	5	10	15	10	15	0	0	10	10
Rice	300	200	250	225	150	265	150	300	0	300	300
Bacon	50	50	50	50	50	50	50	50	0	50	50
Day 61.											
Rice	35	150	100	225	35	150	225	300	0	300	250
Bananas	100	0	100	100	0	100	100	100	100	100	100
Sugar	25	0	0	0	0	0	0	0	0	0	25
Rice	225	225	250	300	225	250	225	100	250	225	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 62.											
Rice	135	150	150	150	135	175	175	200	175	175	200
Bread	50	150	150	150	50	150	100	150	135	150	135
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	175	175	45	60	35	265	230	350	300	150	350
Onions	150	taste	0	taste	150	taste	150	150	75	100	150
Lard	20	taste	0	taste	20	taste	20	20	10	15	20
Day 63.											
Rice	(?)	75	250	150	30	200	150	275	150	300	250
Bacon	(?)	50	50	50	50	50	50	50	50	50	50
Rice	(?)	100	0	250	225	250	225	250	225	300	250
Bananas	(?)	50	100	150	100	150	150	150	150	150	150
Sugar	(?)	0	20	0	15	0	0	0	20	25	20
Day 64.											
Rice	150	taste	taste	300	150	200	240	300	40	275	200
Onions	0	0	0	0	0	0	0	0	0	0	0
Rice	150	150	150	300	150	200	300	300	265	265	240
Bacon	0	0	0	0	0	0	0	0	0	0	0
Day 65.											
Rice	265	200	40	225	265	265	200	200	225	40	225
Bananas	100	100	50	100	50	100	100	100	100	100	100
Sugar	0	25	5	25	0	25	25	25	25	0	0
Rice	175	265	265	265	265	265	175	265	115	175	175
Onions	0	110	75	110	0	110	150	0	75	110	75
Lard	0	15	10	15	0	15	20	0	10	15	10

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 66.											
Rice	175	165	150	200	160	200	200	200	0	65	200
Bread	150	150	150	150	75	150	150	150	150	150	150
Bacon	30	30	30	30	30	30	30	30	30	30	30
Rice	185	200	150	185	150	150	185	300	150	75	300
Bacon	50	50	50	50	50	50	50	50	50	50	50
Day 67.											
Rice	250	250	200	300	150	270	75	300	200	0	300
Onions	100	100	50	100	100	50	100	100	50	0	50
Lard	15	15	10	15	15	10	15	15	10	0	10
Rice	200	100	100	225	150	265	200	265	265	300	300
Bananas	150	150	100	150	150	150	150	150	150	0	150
Sugar	75	75	0	75	35	0	0	75	taste	0	taste
Day 68.											
Rice	300	300	300	300	300	300	300	300	300	(a)	300
Bacon	50	50	50	50	50	50	50	50	50	(a)	50
Rice	230	175	175	350	0	230	350	350	305	(a)	305
Onions	150	taste	0	taste	150	75	150	0	100	(a)	0
Lard	20	taste	0	taste	20	10	20	0	15	(a)	0
Day 69.											
Rice	265	225	225	265	265	225	275	300	300	(a)	300
Bananas	100	100	50	100	100	100	0	100	100	(a)	100
Sugar	25	25	10	25	10	10	taste	25	25	(a)	10
Rice	100	250	265	225	200	265	300	300	265	(a)	300
Bacon	50	50	50	50	50	50	50	50	50	(a)	50
Day 70.											
Rice	150	150	125	175	150	175	100	175	150	(a)	175
Bread	150	110	135	150	110	135	150	150	150	(a)	135
Bacon	30	30	30	30	30	30	30	30	30	(a)	30
Rice	40	115	175	60	115	230	175	175	45	(a)	175
Onions	150	75	0	150	150	150	150	150	150	(a)	50
Lard	20	10	0	20	20	20	20	20	20	(a)	5
Day 71.											
Rice	240	225	200	240	225	275	240	300	240	(a)	300
Bacon	50	50	50	50	50	50	50	50	50	(a)	50
Rice	75	0	60	0	100	100	200	150	150	(a)	270
Bananas	100	150	50	150	100	50	100	0	150	(a)	150
Sugar	0	75	taste	0	0	0	0	0	0	(a)	0
Day 72.											
Rice	225	300	300	240	200	275	300	300	300	(b)	300
Onions	0	100	30	50	30	50	100	0	65	------	100
Lard	0	15	5	10	5	10	15	0	10	------	15
Rice	240	300	300	300	265	300	250	300	265	------	265
Bacon	50	50	50	50	50	50	50	50	50	------	50
Day 73.											
Rice	150	240	150	225	150	200	0	150	0	------	300
Bananas	100	100	100	100	100	100	0	0	100	------	50
Sugar	10	10	10	0	10	0	0	0	taste	------	10

[a] Left with prisoner. [b] Diet discontinued.

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 73—Continued.											
Rice	230	230	175	175	45	230	175	175	350	.....	290
Onions	150	150	0	150	150	0	0	150	150	.....	75
Lard	20	20	0	20	20	0	0	20	20	.....	10
Day 74.											
Rice	135	150	135	200	135	175	150	200	160	.....	165
Bread	150	150	150	150	75	75	75	150	150	.....	120
Bacon	30	30	30	30	30	30	30	30	30	.....	30
Rice	200	150	150	200	150	265	200	75	300	.....	300
Bacon	50	50	50	50	50	50	50	50	50	.....	50
Day 75.											
Rice	100	150	225	225	225	240	225	200	300	.....	200
Onions	25	30	25	25	30	50	50	0	100	.....	0
Lard	5	5	5	5	5	10	10	0	15	.....	0
Rice	150	225	240	200	200	265	265	265	240	.....	300
Bananas	0	150	150	150	100	150	50	0	0	.....	150
Sugar	0	75	15	25	20	25	0	0	20	.....	0
Day 76.											
Rice	150	240	250	300	200	240	265	265	300	.....	300
Bacon	50	50	50	50	50	50	50	50	50	.....	50
Rice	75	200	100	175	115	175	230	230	230	.....	265
Onions	0	0	50	0	0	50	0	0	0	.....	0
Lard	0	0	10	0	0	10	0	0	0	.....	0
Day 77.											
Rice	200	200	150	200	100	150	300	240	265	.....	300
Bananas	100	100	100	100	100	100	100	100	100	.....	100
Sugar	0	0	10	5	0	10	0	0	0	.....	0
Rice	75	200	200	250	150	225	240	0	225	.....	275
Bacon	50	50	50	50	50	50	0	0	50	.....	50
Day 78.											
Rice	0	0	0	100	taste	100	0	0	0	.....	0
Bread	150	20	150	150	150	150	150	150	150	.....	150
Bacon	30	30	30	30	30	30	30	30	10	.....	30
Rice	0	175	85	175	115	280	85	35	175	.....	350
Onions	0	75	20	150	150	20	taste	0	0	.....	150
Lard	0	10	5	20	20	5	taste	0	0	.....	20
Day 79.											
Rice	0	100	150	150	150	200	240	300	150	.....	300
Bacon	50	50	50	50	50	50	50	0	0	.....	50
Rice	0	240	200	240	240	225	300	200	265	.....	265
Bananas	0	150	150	150	150	150	150	150	150	.....	150
Sugar	0	0	35	taste	taste	taste	0	0	0	.....	35
Day 80.											
Rice	150	35	150	150	30	200	100	30	240	.....	200
Onions	0	0	0	0	0	0	0	0	0	.....	0
Rice	[a]150	240	240	100	225	240	75	300	[c]35	.....	300
Bacon	50	50	50	50	50	50	50	50	50	.....	50

[a] Red rice substituted for white rice for next 20 days.

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 81.											
Rice	0	200	200	200	150	200	150	225	30	------	240
Bananas	100	100	100	100	100	100	100	100	100	------	100
Rice	200	200	150	150	265	225	240	300	300	------	240
Fish	30	30	30	30	30	30	30	30	30	------	30
Day 82.											
Rice	250	240	240	300	300	265	(a)	(a)	150	------	300
Fish	30	30	30	30	30	30	------	------	15	------	30
Rice	150	225	150	225	225	225	------	------	300	------	225
Potatoes	150	150	150	150	150	150	------	------	150	------	150
Bacon	50	50	0	0	50	50	------	------	0	------	50
Day 83.											
Rice Potatoes Bacon	No record kept.										
Rice	200	225	200	250	300	300	------	------	300	------	250
Fish	30	30	30	30	30	30	------	------	30	------	30
Day 84.											
Rice	0	225	40	200	225	150	------	------	300	------	150
Bananas	0	100	50	100	100	100	------	------	100	------	100
Rice	50	200	180	135	180	180	------	------	200	------	50
Bread	150	150	150	150	150	150	------	------	150	------	150
Bacon	30	30	30	30	30	30	------	------	30	------	30
Day 85.											
Rice	265	265	200	265	300	265	------	------	300	------	300
Fish	25	25	25	25	25	25	------	------	25	------	25
Potatoes	100	100	100	100	100	100	------	------	100	------	100
Rice	265	265	265	175	265	265	------	------	350	------	175
Onions	0	0	0	0	0	0	------	------	0	------	0
Day 86.											
Rice	300	300	250	300	300	275	------	------	300	------	300
Fish	40	40	40	40	40	40	------	------	40	------	40
Rice	225	265	225	150	40	225	------	------	300	------	265
Potatoes	100	100	100	100	100	100	------	------	100	------	100
Bacon	30	30	30	30	0	30	------	------	30	------	30
Day 87.											
Rice	240	265	225	225	240	225	------	------	240	------	150
Potatoes	100	100	100	100	100	100	------	------	100	------	100
Fish	30	30	30	30	30	30	------	------	30	------	30
Starch	10	10	10	10	10	10	------	------	10	------	10
Lard	15	15	15	15	15	15	------	------	15	------	15
Rice	225	150	75	75	75	225	------	------	300	------	75
Bacon	50	50	50	50	0	50	------	------	50	------	0
Day 88.											
Rice	300	250	200	300	150	300	------	------	300	------	150
Potatoes	100	100	100	100	100	100	------	------	100	------	100
Bacon	30	30	30	30	30	30	------	------	30	------	30
Rice	265	150	40	150	40	100	------	------	300	------	75
Bananas	150	150	50	150	50	50	------	------	150	------	150

[a] Diet discontinued.

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 89.											
Rice	265	240	225	300	150	240	.....	.....	300	.....	200
Fish	30	30	30	30	30	30	.....	.....	30	.....	30
Rice	300	225	150	150	75	150	.....	.....	300	.....	225
Potatoes	100	100	100	100	100	100	.....	.....	100	.....	100
Bacon	30	30	30	30	30	30	.....	.....	30	.....	30
Day 90.											
Rice	300	250	150	250	240	200	.....	.....	300	.....	300
Potatoes	100	100	100	100	100	100	.....	.....	100	.....	100
Fish	30	30	30	30	30	30	.....	.....	30	.....	30
Rice	305	230	45	175	115	115	.....	.....	350	.....	45
Bananas	150	150	0	150	150	150	.....	.....	150	.....	150
Sugar	75	0	0	0	taste	0	.....	.....	0	.....	0
Day 91.											
Rice	300	225	35	150	150	150	.....	.....	300	.....	225
Bacon	50	50	0	50	5	50	.....	.....	50	.....	0
Rice, Potatoes, Fish	No record kept.										
Day 92.											
Rice	300	0	0	300	300	0	.....	.....	300	.....	300
Bananas	100	0	0	100	100	0	.....	.....	100	.....	100
Sugar	25	0	0	25	25	0	.....	.....	25	.....	25
Rice	300	(a)	(a)	(a)	(a)	(a)	.....	.....	300	.....	(b)
Potatoes	100	.....	.....	.....	.....	.....	.....	.....	100	.....	.....
Bacon	30	.....	.....	.....	.....	.....	.....	.....	30	.....	.....
Day 93.											
Rice	300	.....	.....	.....	.....	.....	.....	.....	300	.....	.....
Fish	30	.....	.....	.....	.....	.....	.....	.....	30	.....	.....
Starch	15	.....	.....	.....	.....	.....	.....	.....	15	.....	.....
Lard	10	.....	.....	.....	.....	.....	.....	.....	10	.....	.....
Dinner	No record kept.										
Day 94.											
Rice	240	.....	.....	.....	.....	.....	.....	.....	300	.....	.....
Potatoes	100	.....	.....	.....	.....	.....	.....	.....	100	.....	.....
Bacon	30	.....	.....	.....	.....	.....	.....	.....	30	.....	.....
Rice	300	.....	.....	.....	.....	.....	.....	.....	300	.....	.....
Potatoes	100	.....	.....	.....	.....	.....	.....	.....	100	.....	.....
Day 95.											
Rice	300	.....	.....	.....	.....	.....	.....	.....	300	.....	.....
Bananas	150	.....	.....	.....	.....	.....	.....	.....	150	.....	.....
Sugar	25	.....	.....	.....	.....	.....	.....	.....	25	.....	.....
Rice	150	.....	.....	.....	.....	.....	.....	.....	300	.....	.....
Potatoes	100	.....	.....	.....	.....	.....	.....	.....	100	.....	.....
Bacon	30	.....	.....	.....	.....	.....	.....	.....	30	.....	.....
Day 96.											
Rice	300	.....	.....	.....	.....	.....	.....	.....	300	.....	.....
Fish	30	.....	.....	.....	.....	.....	.....	.....	30	.....	.....
Rice	300	.....	.....	.....	.....	.....	.....	.....	300	.....	.....

[a] Diet discontinued.

TABLE VI.—*Record of rations consumed by prisoners of Group IV*—Contd.

Diet.	Amount, in grams, consumed by prisoner number—										
	26	22	24	19	20	21	27	28	25	29	23
Day 96—Continued.											
Bananas	150								150		
Sugar	25								25		
Day 97.											
Rice	300								300		
Potatoes	100								100		
Fish	30								30		
Rice	300								300		
Bacon	50								50		
Day 98.											
Rice	300								300		
Potatoes	100								100		
Fish	30								30		
Rice	300								300		
Bananas	150								150		
Sugar	25								25		
Day 99.											
Rice	300								300		
Bacon	50								50		
Rice	300								300		
Fish	30								30		
Day 100.											
Rice	300								300		
Potatoes	100								100		
Bacon	30								30		
Rice	300								300		
Sugar	25								25		
Bananas	150								150		
Day 101.											
Rice	300								300		
Potatoes	100								100		
Fish	30								30		
Rice	300								300		
Bacon	50								50		
	End of experiment.										

TABLE VII.—*Regular prison diet for native and Asiatic prisoners.*

(Components and quantities of the ration.)

Components.	Quantities.						
	Sunday.	Monday.	Tuesday.	Wednesday.	Thursday.	Friday.	Saturday.
	Grams.	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*
Beef, forequarter	130			120			150
Pork, fresh		70			70		
Fish, dry			150			150	
Mongos	100	160		150	150		120
Potatoes		200	150	150	200	100	250
Camotes	500		150	200	200	150	
Onions		100	50	150		100	
Rice	400	400	400	400	400	400	400
Sugar	50	50	50	50	50	50	50
Salt	20	20	20	20	20		20
Tea	40	60				40	
Coffee			60		60		
Tomatoes			50			50	
Ginger-root				60			60
Vinegar					60		
Bread	166	166	166	166	166	166	166

TABLE VIII.—*Showing nature of the rice received by the different groups.*

Case No.	Group and rice received.	Total days.
	GROUP I.	
4	White rice + rice polishings for 13 days, followed by white rice + extract of rice polishings for 84 days.	97
2, 1, 6, 5, 8	White rice + rice polishings for 13 days, followed by white rice + extract of rice polishings for 95 days.	108
	GROUP II.	
7, 8	White rice for 97 days, followed by red rice for 20 days	117
11, 9	White rice	97
10, 12	White rice	108
	GROUP III.	
14	White rice + rice polishings for 17 days, followed by red rice for 80 days	97
16, 18, 13, 15, 17	White rice + rice polishings for 17 days, followed by red rice for 100 days	117
	GROUP IV.	
26, 25	White rice 81 days, followed by red rice for 20 days	101
22, 24, 19, 20, 21, 23	White rice	92
27, 28	White rice	82
29	White rice	75

SUMMARY OF THE RESULTS OF THE EXPERIMENTS.

If now we compare the results of the experiments in the different groups, it may be seen that in Group I, where the diet consisted largely of white rice together with extract of rice polishings, 4 of the 6 individuals comprising the group developed no symptoms of beriberi during the time of the experiment. One, No. 1, developed rather marked early symptoms of beriberi and one, No. 3, developed some of the early symptoms of this

disease. The symptoms of these cases did not improve until the monotony of the diet was varied by the addition of dried codfish and potatoes. Nos. 4 and 6 of this group suffered merely from erosions about the corners of the mouths during the experiment. It seems advisable to consider briefly the symptoms in the cases which suggested the diagnosis of beriberi. In case No. 1 the loss of weight was constant throughout the course of the experiment until the diet was changed, the individual losing in all 7.9 kilograms (17.5 pounds) in weight. From the time that fish and potatoes were added to the diet he began to gain slightly in weight and the unfavorable symptoms to improve. The striking symptoms suggestive of beriberi in this case were the slight increase of knee jerks noticed first on the eighty-first day of the experiment, pain in the abdomen, the huskiness and almost complete loss of the voice, the development of tachycardia, epigastric pulsation, slight œdema of the legs, and tenderness of the calves. These symptoms certainly were suggestive of beriberi. While it is an acknowledged fact that all cases of beriberi do not show loss of knee jerks and that usually, if perhaps not always, this symptom is a late one in the course of the disease, nevertheless in an experiment of this nature a definite diagnosis of beriberi was not made unless the loss of knee jerks had occurred in conjunction with the appearance of other symptoms of this disease. Also, it obviously is impossible to state whether, had the diet been continued for a longer period of time in this case, more definite symptoms of beriberi would have developed, but his condition and the progression of the symptoms certainly suggested such a course. In any case, a condition simulating beriberi was produced in this individual. In case No. 3 the patient lost in weight almost continuously up to the eighty-fourth day of the experiment, 4.5 kilograms (10 pounds) in all. The only symptoms of beriberi which were noted were the development of abdominal pain, visible epigastric pulsation, pain and tenderness in the calves of the legs, and huskiness of the voice. These symptoms improved upon the addition of dried codfish and potatoes to the diet, but the patient did not gain in weight until placed upon the regular prison ration. (See Table VII.) The dried codfish, as may be seen from Table II, contained 2.9 per cent phosphorus pentoxide,

but the potatoes only 0.25 per cent, which is less than the amount present in the white polished rice (0.37 per cent) employed in the experiments. The loss of weight in the subjects comprising this group, during the experiment, was as follows:

GROUP I.

Case.	Lost—		Then gained—	
	Kilograms.	Equivalent in pounds.	Kilograms.	Equivalent in pounds.
No. 1 [a]	7.9	17.5		
No. 2	2.9	6.5		
No. 3 [a]	4.5	10.0		
No. 4	2.04	4.5		
No. 5	2.04	4.5	2.9	6.5
No. 6	4.3	9.5		

[a] Developed symptoms of beriberi.

In none of the other cases of this group was the loss of weight so marked as in case No. 1, though case No. 6, in which no symptoms of beriberi developed, lost practically as much (4.3 kilograms or 9.5 pounds) as did case No. 3.

In Groups II and IV the diet consisted largely of white rice. In Group II, 4 of the 6 individuals comprising the experiment developed beriberi (Nos. 8, 9, 10, 11) and 2 (Nos. 7 and 12) early symptoms of the disease, while in Group IV, 4 of the 11 (Nos. 20, 26, 25, 29) developed beriberi, 2 (Nos. 19 and 22) developed early symptoms of the disease, 1 (No. 21) doubtful symptoms, and 3 (Nos. 24, 27, 28) showed no symptoms of beriberi throughout the experiment.

It is also advisable to examine into the symptoms of beriberi which developed in the individuals comprising these groups. In case No. 8 of Group II the most striking symptoms were the œdema of the legs and tenderness of the calf muscles, loss of knee jerks, and change in the position of the apex beat of the heart. In case No. 9, epigastric pain and pulsation, marked dyspnœa, paræsthesia and hyperæsthesia of areas of the skin, and hyperæsthesia of the muscles of the calves, together with loss of knee jerks. In case No. 10 the prominent symptoms were cardiac disturbances, hyperæsthesia of the calf muscles, and

loss of knee jerks, while in No. 11 paræsthesia, hyperæsthesia of the calf muscles, cardiac disturbances, loss of knee jerks, and development of foot drop occurred. In No. 7 the most striking symptoms suggesting the development of beriberi were anæsthesia and paræsthesia of areas of the skin, hyperæsthesia of the calf muscles, and cardiac disturbances. The knee jerks were absent before the experiment commenced and remained so. In No. 12, cardiac disturbances, pain and tenderness of the calf muscles, and œdema of the legs occurred.

The loss of weight in the subjects comprising this group during the experiment was as follows:

GROUP II.

Case.	Lost—	
	Kilograms.	Equivalent in pounds.
No. 7	6.1	13.5
No. 8[a]	4.5	10.0
No. 9[a]	6.1	13.5
No. 10[a]	2.7	6.0
No. 11[a]	3.6	8.0
No. 12	3.4	7.5

[a] Developed beriberi.

In considering the cases of Group IV, we find that in case No. 20 the most striking symptoms of beriberi which developed during the course of the experiment were cardiac disturbances, pain and tenderness in the calf muscles, and loss of knee jerks. In case No. 26 there occurred hyperæsthesia of the skin over the fingers and toes, loss of power of the grip of the hands, loss of knee jerks, and unsteadiness when standing with the eyes closed. In No. 25 the striking symptoms were weakness of the legs and tenderness in the calf muscles, and slight œdema of the legs, while in No. 29 marked œdema of the legs and face, epigastric pain, loss of knee jerks, cardiac disturbances, and collapse were the prominent symptoms. In case No. 19 the suggestive symptoms were pain in the legs and arms, the feebleness of the grip of the hands, paræsthesia and slight tenderness of the calves, and slight œdema over the tibiæ, while in No. 22

there was marked œdema of the legs and moderate tenderness of the calf muscles. In No. 21 slight cardiac disturbances, œdema of the legs, and hyperæsthesia of the muscles of the calves were present. The loss of weight in the subjects of this group during the course of the experiment was as follows:

GROUP IV.

Case.	Lost—		Then gained—	
	Kilograms.	Equivalent in pounds.	Kilograms.	Equivalent in pounds.
No. 19[a]	1.3	3.0	2.2	5.0
No. 20[b]	2.7	6.0		
No. 21	6.8	15.0	3.6	8.0
No. 26[b]	7.4	16.5		
No. 25[b]	3.6	8.0		
No. 22[a]	2.0	4.5		
No. 23	2.2	5.0	2.4	5.5
No. 24	2.9	6.5		
No. 27	4.5	10.0	1.3	3.0
No. 28	2.7	6.0	1.5	3.5
No. 29[b]	0.0	0.0		

[a] Developed symptoms of beriberi. [b] Developed beriberi.

In Group III, where the diet consisted largely of red rice, only 1 (No. 13) of the 6 developed rather marked symptoms of beriberi, while 1 (No. 18) developed only slight cardiac symptoms. In Nos. 14, 15, 16, and 17 no symptoms at all of the disease developed. In No. 13 the most striking symptoms suggestive of beriberi were pain and tenderness in the epigastrium, symptoms suggesting paræsthesia, epigastric pulsation, cardiac disturbances and dyspnœa, and marked diminution and almost disappearance of the knee jerks, so that it was very difficult or impossible at times to elicit them. The condition of this individual, at the time that his diet was changed, certainly led one to believe that had the diet been persisted with, a well-marked case of beriberi would have developed. In No. 18, epigastric pulsation and slight cardiac disturbances appeared, but these symptoms did not persist. In No. 15 erosions at the edges of the lips and conjunctivitis developed, and in No. 17 catarrhal conjunctivitis also occurred. The loss of weight in the subjects of this group during the experiment was as follows:

GROUP III.

Case.	Lost—		Then gained—	
	Kilograms.	Equivalent in pounds.	Kilograms.	Equivalent in pounds.
No. 13[a]	6.8	15.0		
No. 14	4.3	9.5		
No. 15	5.2	11.5		
No. 16	2.4	5.5	2.0	4.5
No. 17	3.6	8.0	2.0	4.5
No. 18[a]	2.4	5.5		

[a] Developed symptoms of beriberi.

From an examination of the tables showing the loss of weight in the patients in the four groups, it is seen that in some instances the loss of weight in those individuals who developed beriberi was marked, for example, No. 8, 4.5 kilograms (10 pounds); No. 9, 6.1 kilograms (13.5 pounds); and No. 26, 7.4 kilograms (16.5 pounds). In other cases, Nos. 10, 20, and 25, it was slight, 6, 6, and 8 kilograms, respectively, while in the most acute case, No. 29, there was no loss of weight at the end of sixty-one days when the patient died.

Cases Nos. 1 and 3 of Group I lost more in weight than any other members of the group, namely 7.9 and 4.5 kilograms (17.5 and 10 pounds), respectively, and were the only members of the group that developed symptoms suggestive of beriberi. No. 1 developed much more marked symptoms than No. 3. However, case No. 6 of the same group lost 4.3 kilograms (9.5 pounds) and developed no symptoms of the disease. Case No. 13 of Group III lost 6.8 kilograms (15 pounds) in weight, more than any other member of the group, and was the only one of the group to develop striking symptoms of beriberi. But case No. 7 of Group II developed no symptoms of beriberi and lost 6.1 kilograms (13.5 pounds), and case No. 21 of Group IV lost 6.8 kilograms (15 pounds) in the earlier part of the experiment, and also developed no symptoms of the disease. Apparently, therefore, the development of the symptoms of beriberi did not necessarily occur in at least all of these cases on account of the loss of weight, though it is certainly suggestive in cases No. 1 of Group I and No. 13 of Group III that there might be some connection between the loss of weight and the development of

the symptoms. We find no record in the literature as to whether during the incubation period of beriberi there is frequently or usually a loss in weight. All of our cases which developed beriberi showed a preliminary loss of weight, varying from 2.7 to 7.4 kilograms (6 to 16.5 pounds), with the exception of one case. In this one, death occurred from cardiac paralysis on the seventy-eighth day and there was no loss in weight up to the sixty-first day but rather marked œdema of the face and legs.

In none of the cases was the complete picture of beriberi obtained, except in those in which white polished rice formed the staple article of diet, but in one case fed upon red rice the diagnosis of beriberi was almost definite. Indeed, we believe that, had this case been encountered otherwise than in the course of this experiment, the diagnosis of beriberi would have been fully justified.

The occurrence of marked symptoms of beriberi in case No. 1 and early symptoms of the disease in No. 3, both fed upon white rice together with the alcoholic extract of rice polishings, requires some comment. The members of this group were given daily 40 cubic centimeters of the (unheated) alcoholic extract mixed with the rice after it was cooked; that is, they were given the amount of extract obtained from 320 grams of rice polishings or from the polishings obtained from approximately 3.2 kilograms of red rice. Even this amount, however, did not prevent some of the symptoms of beriberi from developing in two of the cases of this group. The result of the experiment, with this group, therefore, suggests that, whatever may be the results obtained with this extract in preventing polyneuritis in fowls and in curing this condition after it has developed, for the prevention of beriberi in adult man or the usual treatment of the disease,[78] some other substances, such, for example, as the mongo bean, *Phaseolus radiatus* Linn. (*katjang idjo*), or yeast are evidently far superior and much easier and cheaper to obtain.

However, Chamberlain and Vedder[79] have shown that it is possible to cure infants suffering with beriberi by means of this extract, and where the age of the child is such as to preclude the addition of the necessary nutritious articles to the diet or

[78] However, for the treatment of certain fulminating cases of beriberi the use of the protective substance in a more concentrated form, if it can be obtained, would appear desirable.

[79] *Bull. Manila Med. Soc.* (1912), 4, 26.

where milk is unobtainable, it would appear from their experiments that its use was advantageous.

Recently Tsuzuki [80] has claimed for a substance, which he calls *antiberiberin* and which consists of a concentrated alcoholic and ethereal extract of rice-bran, marked therapeutic properties for the cure of human beriberi. However, the strength of the extract employed and the details of the experiments are not given. Nevertheless, our experiment with Group I shows that some substance present in the rice polishings evidently has an effect in preventing the development of beriberi in adult men since 4 of the 6 subjects of the group developed no symptoms of the disease. It, however, also shows that the substance which seems necessary to prevent the symptoms from appearing is not contained in any large amount in this extract.

Our opinion in this respect in regard to the alcoholic extract, formed from the results of our experiments, is in accord with that of Cooper and Funk,[81] who state that "polishings appear to contain only a very small amount of the active substance," and of Funk [82] who believes "the substance is only present in small amounts, probably not more than 0.1 gram per kilogram of rice." Schaumann [83] claims that only 0.5 gram of the active substance which plays only a mediating part in the metabolism is present in the rice-bran and Simpson [84] states that extracts prepared by complicated methods can prolong the life of the animals, but do not restore them fully to health. In his experiments birds gained twice as much in weight in three days' treatment with yeast as in three weeks' treatment with large doses of the extract which Chamberlain and Vedder employed in their experiments.

Evidently, symptoms of beriberi may also sometimes occur in individuals (see Case No. 13) in which red rice forms the staple article of diet, when the diet is a very monotonous one comprising but few articles and is continued for long periods of time, and the appetite of the subject partaking of it becomes poor and he loses continually in weight.[85] The influence of work

[80] *Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* (1912), 16, 495.
[81] *Lancet* (1911), 2, 1266.
[82] *Journ. Physiol.* (1911), 43, 1400.
[83] *Arch. f. Schiffs- u, Trop.-Hyg.* (1912), 16, 357.
[84] *Trans. Soc. Trop. Med. & Hyg.* (1911), 5, 87.
[85] Obviously the food comprising our diets was not subjected to steaming or to prolonged high temperature in cooking as is frequently the case with tinned articles of food.

and exercise may also be a factor in such instances in preserving the appetite. None of the subjects in our experiments did any work or practically took any exercise. However, the diet in which red rice formed the staple article was obviously the most favorable one. The diet which consisted largely of extract of rice polishings mixed with the white rice was the next most favorable, while that one in which white rice formed the staple article of diet was the least favorable of all. It is evident from our experiments that beriberi may be produced by the prolonged consumption of a diet in which white rice constitutes the staple article of diet. Of the 17 individuals fed upon such a diet, 8 developed beriberi, and the stage of the disease was well advanced before the close of the experiment. All of these cases had distinct loss of the knee jerk, in addition to other well-marked symptoms of the disease. Symptoms of the disease appeared in some cases in from sixty-one to seventy-five days from the commencement of the diet, and the diagnosis was definite and the knee jerks gone in one case as early as the sixty-third day of the diet. In another case the knee jerks disappeared by the one hundred fifth day of diet.

In Fraser and Stanton's experiments no case of beriberi occurred in less than eighty-seven days, and the majority of the cases occurred at a considerably later period, in from one hundred twenty to one hundred sixty days. However, the individuals in their experiments were engaged in hard labor in the open country. From their experiments and our own it would appear that the incubation period of beriberi is not less than sixty days. Undoubtedly, the incubation period varies with the character of the diet. None of the individuals in our experiments developed symptoms suggesting scurvy.

CONCLUSIONS.

It is evident that among the individuals comprising our experiments beriberi was produced only by means of the diet, and that the disease has, therefore, a true dietetic causation. It is further evident from our experiments that beriberi develops owing to the absence of some substance or substances in the diet necessary for the normal physiological processes of the body. Without the supply of such substances in the food, beriberi results. Such a substance or such substances are evidently present in red rice and in rice polishings and also in small amount in the alcoholic extract of rice polishings, and when these articles are added to what would appear to be an otherwise phys-

iologically proper diet, they usually prevent the development of the symptoms of the disease. In some instances, however, even when these substances are constituents of the diet, when the diet is without variation and composed of very few articles, and the individual suffers from loss of appetite and the assimilative functions appear to be poor and he loses markedly in weight, symptoms of beriberi may develop in such individuals. However, such symptoms may be dispersed by causing a variation in the diet by the addition of other nutritious substances to it. It is also evident from our experiments that the disease is certainly not an infectious one in the sense which we usually employ this term. The rigid isolation of the prisoners undergoing the test would seem to exclude the possibility of the introduction of an infectious agent through any other individual or by the introduction of any article. And although the individuals of Groups I, II, and III all mingled freely together, there was no tendency of the disease to spread in Groups I and III. It is also noteworthy that the cases of beriberi developed under the most favorable hygienic conditions with exception in regard to diet. It is not probable that the infection could have been introduced with the food, since this was all freshly cooked, and at a temperature at which only a spore-bearing organism would survive. The food was also eaten a very short time after being cooked. Moreover, if the infection had been introduced with the food, the incidence of the disease should have been the same in all of the groups, which it was not. No fermentation of the rice employed occurred either before or after it was cooked, so that it would appear that the action of such bacteria as have been described by Kohlbrügge [86] and by Bréaudat [87] could be excluded. It has been suggested that a diet of white rice predisposes to the disease, since it furnishes a better medium for the development of the specific organism which resides in the intestine of the host, and that the red rice or extract of polishings forms a preventive for the development of such a specific organism. There is no definite evidence of such an hypothesis and, moreover, the results obtained in our experiment would argue against it, since in two instances, at least (Nos. 1 and 13), distinct symptoms of beriberi were present in individuals who had received these substances in the diet. It can not be claimed with reason that the resistance of the individuals having been lowered by weakness and loss of weight, the specific organism residing in the intestine of the individual was able to

[86] *Loc. cit.* [87] *Loc. cit.*

increase and multiply and produce the disease; for in several instances where the loss of weight of the individuals was marked and their general condition poor, as was manifested by the occurrence of erosions about the corners of the mouth, sore mouth and tongue, and conjunctivitis, no symptoms of beriberi developed. Indeed, from our experiments there is no evidence of any nature which suggests that beriberi is an infectious disease, and on the contrary the evidence is definite that beriberi in the Philippine Islands is due to the prolonged consumption of a diet which lacks certain substances necessary for the normal physiological needs of the human body. That the disease encountered was true beriberi was confirmed definitely by the lesions encountered in the pathological study. As to the definite chemical nature of the substance or substances in the food whose presence prevents the development of beriberi further investigations are necessary, but from a practical standpoint as we are cognizant of the etiology of the disease, its cure and prevention is a simple problem. For the prevention and cure of beriberi in man all that is necessary is that he shall be supplied with a liberal and nutritious diet suitable to the physiological needs of the body. The recent researches of Schaumann,[88] of Chamberlain, Vedder, and Williams,[89] of Funk,[90] of Axelholst,[91] and of Simpson [92] have thrown much light upon the question of the nature of the protective substance in the diet. Nevertheless, the opinions are not yet in accord in regard to its exact chemical nature which still appears to be unknown.

Fraser and Stanton [93] have repeatedly called attention to the fact that the phosphorus content of the rice serves as an indication of the extent to which the rice has been polished and have suggested that any rice which contains 0.4 per cent or more of phosphorus pentoxide might be regarded as safe for a staple article of diet in preventing polyneuritis gallinarum in fowls and, hence, beriberi in man. They state—"None of the rices connected with outbreaks of beriberi yielded more than 0.26 per cent of phosphorus pentoxide. The rices substituted for these and which were effective in preventing the continuance of

[88] *Arch. f. Schiffs- u. Trop.-Hyg.* (1912), 16, 28. This article also gives the references to this author's earlier publications on this subject.

[89] *This Journal, Sec. B* (1912), 7, 39. This article also gives the references to the earlier publications of these authors.

[90] *Journ. Physiol.* (1911), 43, 395.

[91] *Trans. Soc. Trop. Med. & Hyg.* (1911), 5, 76.

[92] *Ibid.*, 87.

[93] *Loc. cit.* and also *Lancet* (1911), 2, 1159.

the outbreaks yielded not less than 0.4 per cent of that substance." More recently Heiser[94] advocates for the prevention of beriberi the passage of a law placing a tax upon rice which contains less than 0.4 per cent of phosphorus pentoxide, such rice being regarded legally as polished rice, and no tax on rice which contains 0.4 per cent or more of phosphorus pentoxide, such rice being regarded legally as an unpolished rice. Although it seems quite definite that a rice containing this amount of phosphorus will prevent the appearance of polyneuritis in fowls, nevertheless, from our experiments it is evident that beriberi in man may be produced by rice containing 0.37 per cent of phosphorus pentoxide when it forms the staple article of a little varied diet. Therefore the question arises as to whether the margin of safety is sufficient between such a rice and that containing only 0.4 per cent of this substance. Since it has been generally admitted that the higher the phosphorus content of rice the less is the liability of that rice to produce beriberi and since Fraser and Stanton found as an average result of all their examinations that unpolished rice contained 0.54 per cent of phosphorus pentoxide and Aron[95] found that unpolished rice in the Philippine Islands contains 0.557 per cent of phosphorus pentoxide and freshly husked rice 0.455 per cent, before legislation is enacted it would seem to be advisable to consider carefully the question of the amount of phosphorus pentoxide which a rice should legally be required to contain in order for it to be regarded as an unpolished rice and to be exempt from taxation in the Philippine Islands.

[94] *Journ. Trop. Med. & Hyg.* (1912), 15, 124.
[95] *This Journal, Sec. B* (1910), 5, 81, 98.

ILLUSTRATIONS.

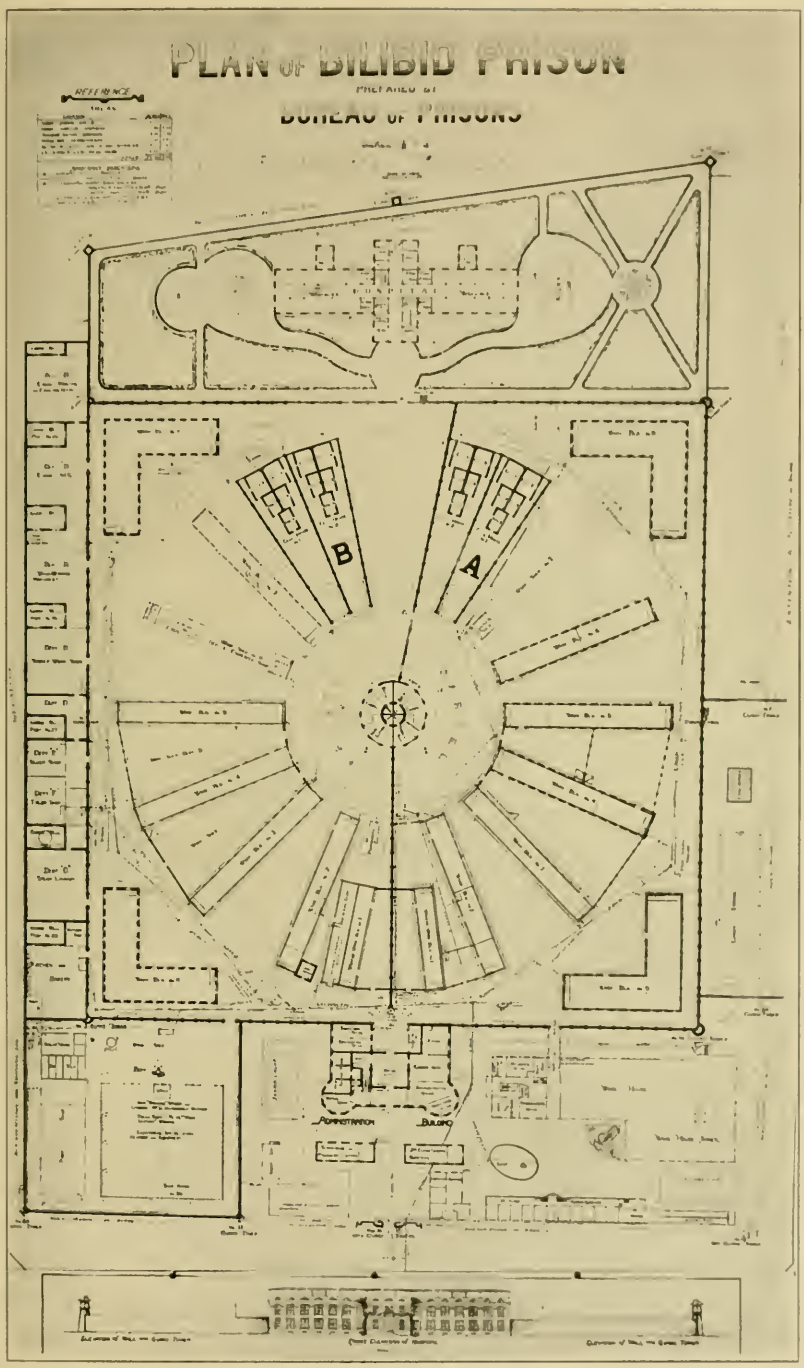


PLATE I. PLAN OF BILIBID PRISON.

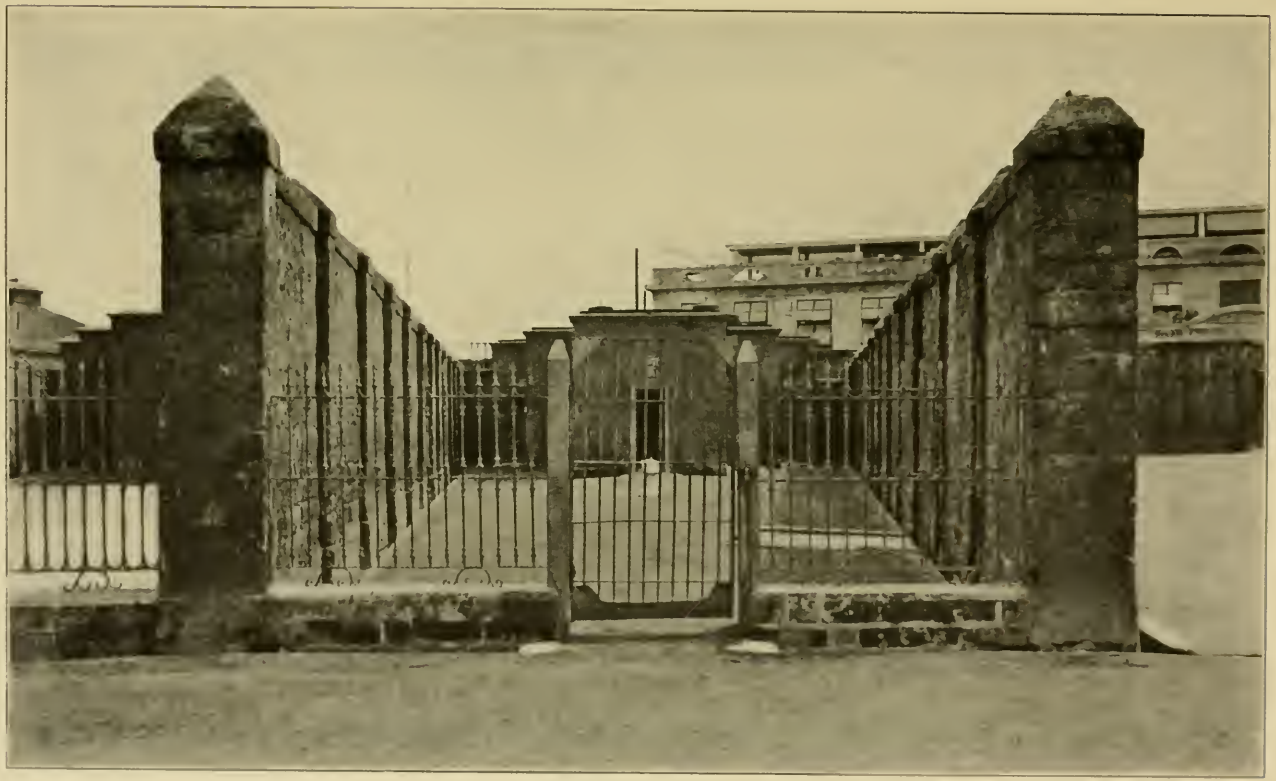


PLATE II. BARTOLINA AND CELL HOUSE.

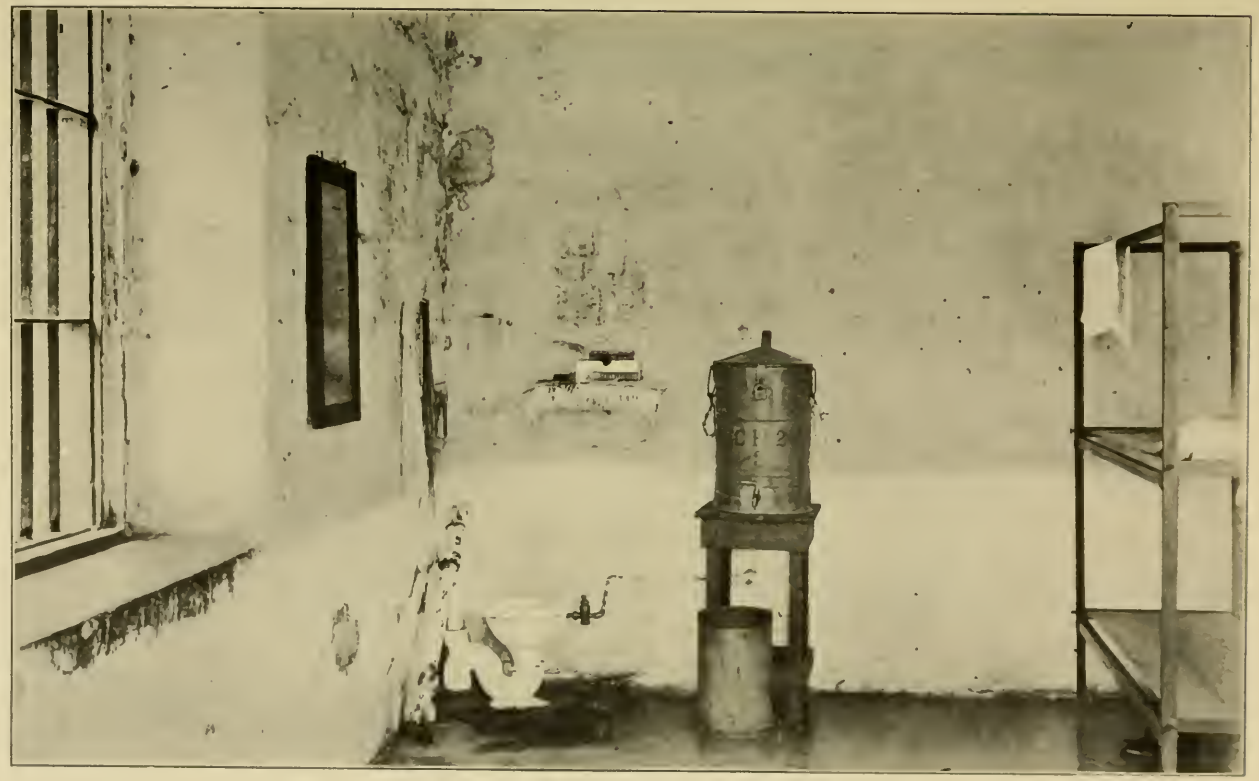


PLATE III. INTERIOR OF CELL HOUSE.

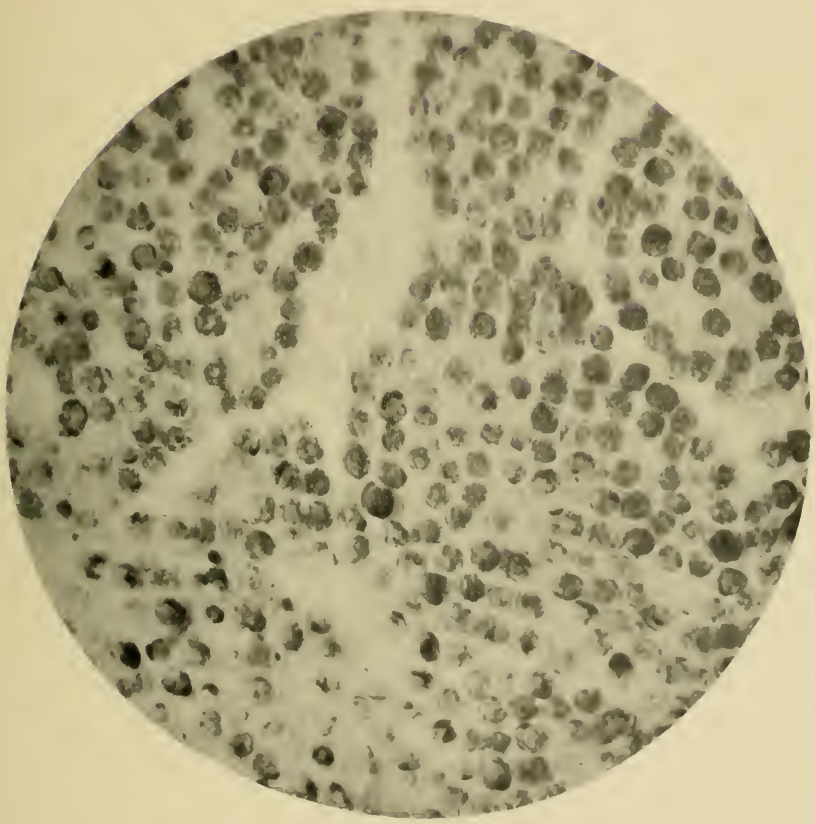


PLATE IV. TRANSVERSE SECTION OF SCIATIC NERVE.

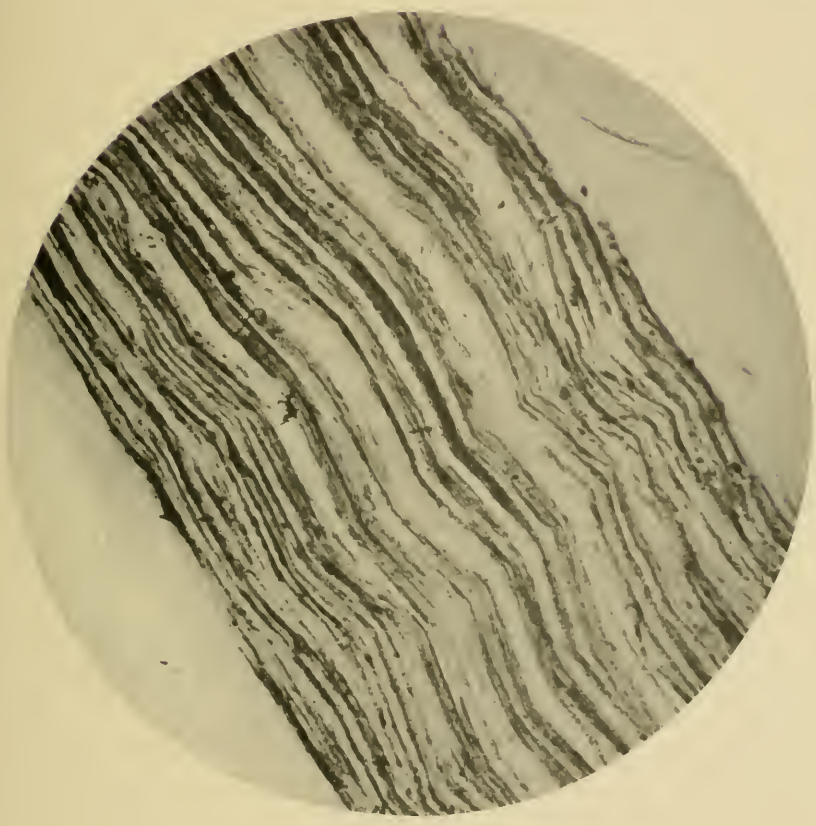


PLATE V. LONGITUDINAL SECTION OF VAGUS NERVE.

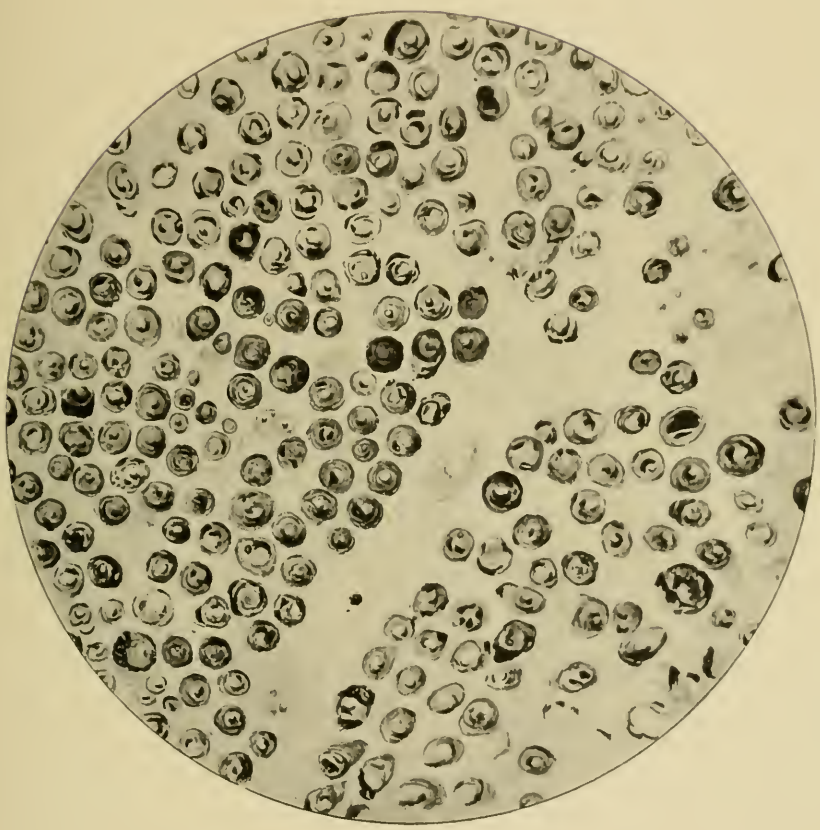


PLATE VI. TRANSVERSE SECTION OF SCIATIC NERVE.

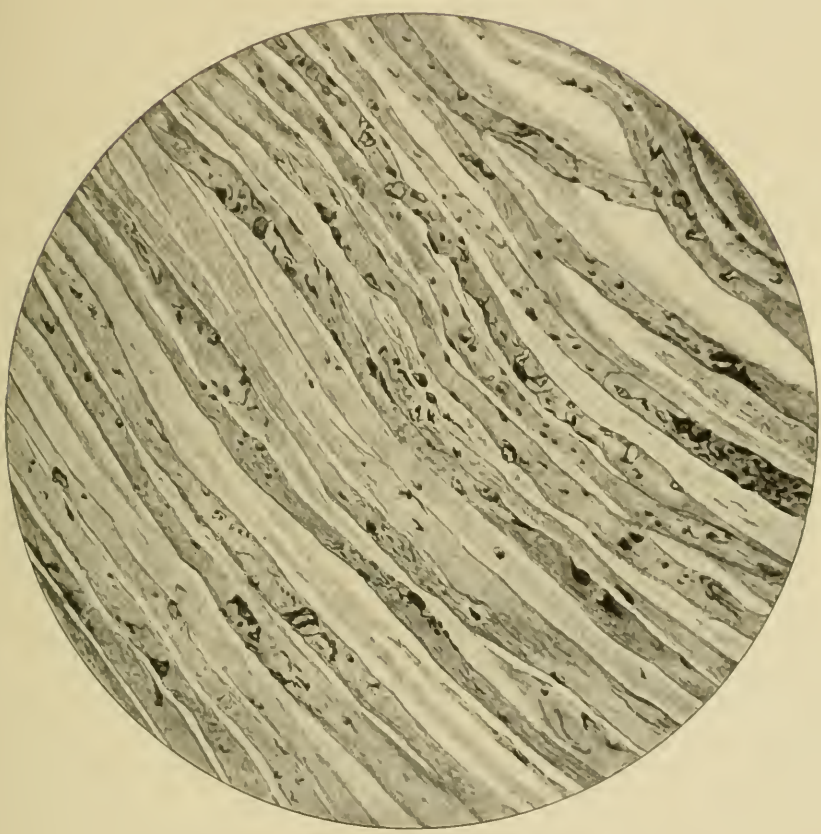


PLATE VII. LONGITUDINAL SECTION OF VAGUS NERVE.

A FOURTH CONTRIBUTION TO THE ETIOLOGY OF BERIBERI.[1]

By EDWARD B. VEDDER.[2]

(From the United States Army Board for the Study of Tropical Diseases.)

Soon after our last paper(1) was submitted for publication, our attention was attracted by the work of Funk.(2) This investigator claims that the neuritis-preventing substance which is absent in polished rice and is contained in rice polishings is an organic base which is completely precipitated by phosphotungstic acid. It will be remembered that we had failed to precipitate the neuritis-preventing substance with phosphotungstic acid, but that we had used basic lead acetate as a reagent before employing phosphotungstic acid. This suggested the possibility that we had failed to precipitate the desired compound with phosphotungstic acid because it had been previously destroyed by the basic lead acetate.

Experiment 22.—A portion of extract of rice polishings prepared as described previously was, therefore, treated with a sufficient quantity of a saturated solution of phosphotungstic acid to produce complete precipitation. This precipitate was filtered off and the remaining filtrate was tested as follows:

Four fowls were fed on polished rice with a daily addition of 10 cubic centimeters of this filtrate which contained that portion of the extract of rice polishings that was not precipitated by phosphotungstic acid.

One case of neuritis appeared after twenty-eight days when this experiment was discontinued.

The precipitate obtained from the extract when treated with phosphotungstic acid was then ground in a mortar with freshly slaked lime and baryta according to the method we had previously employed. Calcium phosphotungstate was then filtered off, and the remaining filtrate, which should contain any organic

[1] Published with permission of the Chief Surgeon, Philippine Division.

[2] Captain, Medical Corps, United States Army, member of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

113145—10

bases precipitated by the phosphotungstic acid, was rendered slightly acid with H_2SO_4. The barium sulphate was filtered off, and the remaining filtrate diluted with distilled water in such proportion that each cubic centimeter of this fluid represented the substances obtained by this method from 1 gram of the polishings.

Four fowls were fed on polished rice with a daily addition of 10 cubic centimeters of this fluid containing the substances precipitated from the extract of rice polishings by phosphotungstic acid.

One case of neuritis appeared after twenty-five days when this experiment was discontinued. As a control 4 fowls were fed on polished rice with a daily addition of 10 cubic centimeters of untreated extract of rice polishings. These fowls remained well for sixty days, when they were released.

This failure to obtain the neuritis-preventing substance in the phosphotungstic acid precipitate confirms our previous work. But while we have thus far been unable to confirm Funk's statement that this substance is precipitated by phosphotungstic acid, neither do we regard our work as disproving this statement, since the method we used differed slightly from that used by Funk. It is plain, however, since both filtrate and precipitate from phosphotungstic acid were ineffective, that either the neuritis-preventing substance was destroyed by the phosphotungstic acid, or else that it was precipitated by that reagent and was subsequently destroyed by the slaked lime and baryta used. In either case it is evident that this neuritis-preventing substance is a most delicate compound and that chemical manipulations with this substance must take place only under certain as yet undetermined conditions if they are to be successful. Further experiments will be continued along this line.

In pursuing investigations into the cause of beriberi it is by no means uncommon to find instances where beriberi has developed in spite of the fact that the patients had received what was supposed to be a tolerably well-balanced ration in addition to the staple article of rice. This observation has been frequently urged as an insuperable objection to the theory that beriberi is caused by a rice diet. It is apparent, however, that the neuritis-preventing substance is not present in all articles of food. Thus in a previous paper, we showed that polyneuritis was not prevented in fowls by giving them an extract of onions. It was

now thought desirable to ascertain whether polyneuritis would develop in fowls fed on a balanced ration consisting of foodstuffs which did not contain this principle. To achieve this purpose, it was first necessary to test these food principles separately.

Experiment 23.—Cottonseed oil was chosen as a digestible and readily obtainable fat. Four fowls were fed on polished rice and were given a daily addition of 5 cubic centimeters of cottonseed oil.

All 4 fowls developed neuritis in twenty-two, twenty-six, twenty-seven, and thirty-four days respectively.

Egg albumin was chosen to represent the proteid element to be added to the rice. Four fowls were fed on polished rice and given a daily addition of 1 cubic centimeter of egg albumin taken from fresh eggs.

Three fowls developed neuritis after twenty-three, twenty-five, and thirty-five days respectively.

Sugar, asparagin, and inorganic salts had already been tested in experiments previously reported. Having completed these preliminary experiments, 4 fowls were fed on a diet consisting of the following components which were given daily: 100 grams of polished rice, 5 cubic centimeters of cottonseed oil, 1 cubic centimeter of egg albumin, and 10 cubic centimeters of a solution which was prepared as follows: twenty grams of saccharose, 5 grams of sodium chloride, 5 grams of potassium phosphate, and 5 grams of asparagin were dissolved in 1,000 cubic centimeters of distilled water. Five grams of magnesium phosphate were added to this solution which was well shaken before administration.

All 4 fowls developed polyneuritis after twenty-three, twenty-six, twenty-eight, and twenty-nine days respectively.

Before any conclusions can be drawn from this experiment, it is necessary to determine whether this was a balanced ration. Voit's standard for a man of 150 pounds was 118 grams of proteid, 56 grams of fat, 500 grams of carbohydrate, producing 3,054 calories. Chittenden thought that equilibrium of metabolism was maintained on a diet containing only 60 grams of proteid with fats and carbohydrates sufficient to produce 2,800 calories. The fowls on which we experimented averaged 3 pounds in weight. Let us assume that their food requirements are, proportionately to their weight, the same as that of a man.

Wiley's figures representing the composition of polished rice are as follows.

Constituent.	Per cent.
Moisture	12.40
Proteids	7.50
Ether extract	0.40
Crude fiber	0.40
Starch	78.80
Ash	0.50
	100.00

Therefore, these fowls, receiving 100 grams of polished rice daily, received 78.8 grams of starch which is equivalent to 3,940 grams for a man of 150 pounds. This is more than seven times the amount required according to Voit's standard. They received 7.50 grams of proteid in this rice, equivalent to 375 grams for a man, in addition to which they received 1 cubic centimeter of egg albumin equivalent to 50 grams for a man. Therefore, they received proteid far in excess of Voit's standard. The 5 cubic centimeters of fat which were administered are equivalent to 250 cubic centimeters of fat for a man as compared with Voit's requirement of 56 grams. The diet which these fowls received was, therefore, not balanced in the sense that the food principles were administered in exactly correct proportions, but it is plain that this diet contained an ample sufficiency of all the food elements. They received a great excess of proteids, carbohydrates, and fats, and by the addition of egg albumin and saccharose a certain amount of variety of proteid and carbohydrate food was provided. In addition to the 0.5 gram of inorganic salts contained in the rice, they received the salts given in the solution described above.

From this experiment it appears to be conclusively shown that polyneuritis gallinarum does not result because of any deficiency in the ordinary food elements, and assuming that beriberi in man is a similar disease, it is apparent that beriberi may develop in men who are receiving what is supposed to be a balanced ration, provided that none of the components of that ration contain the neuritis-preventing principle. It has been shown that onions, egg albumin, and cottonseed oil are lacking in this important principle, and it appears quite possible that many other articles of food are similarly deficient. This point must be considered in the future in determining the components of a ration, particularly when that ration is intended for natives using rice as a staple.

It has been known for a long time that the efficacy of an extract of rice polishings is destroyed by heating at 120° C. or even by prolonged boiling. It has been generally assumed that the neuritis-preventing principle was destroyed by this heat, but there remained the distinct possibility that this substance might be volatile and thus be lost although not actually destroyed.

Experiment 24.—In order to test this possibility, a quantity of extract of rice polishings, prepared as described in previous papers, was tested on fowls and found to prevent polyneuritis. The extract was then placed in a flask and distilled, the process being continued until practically the entire quantity of extract had been obtained in the distillate and nothing remained in the flask but a thick syrupy mass. The distillate and the residue were each diluted with distilled water until 1 cubic centimeter was equivalent to 1 gram of polishings.

Four fowls were fed on polished rice with a daily addition of 10 cubic centimeters of the distillate from the extract of rice polishings.

All 4 fowls developed neuritis in twenty-three, twenty-four, twenty-eight, and twenty-nine days respectively.

Four fowls were fed on polished rice with a daily addition of 10 cubic centimeters of the residue remaining after distillation.

All 4 fowls developed neuritis in nineteen, twenty-three, twenty-six, and twenty-nine days respectively. Therefore, it appears that the neuritis-preventing principle is not volatile, but is actually destroyed by heat.

The possibility that this substance was an alkaloid was next considered. Its powerful action and the minute quantities in which it is present in the rice polishings suggest this possibility, but an ethereal extract of rice polishings had already been shown to be ineffective. However, the previous ether extract was slightly acid in reaction and some alkaloids can not be extracted in an acid solution.

Experiment 25.—A portion of extract of rice polishings was rendered very slightly alkaline with sodium hydroxide and was then extracted by shaking with successive portions of ether. The ether was then evaporated by means of an electric fan and the residue so obtained was rendered slightly acid with hydrochloric acid and diluted with distilled water to the original bulk of the extract. The extract remaining after treatment with ether was then extracted with chloroform, by shaking with successive portions of chloroform until nothing further could be extracted. This chloroform was then evaporated off by means

of an electric fan, and the residue diluted with distilled water to the original bulk of the extract.

Four fowls were fed on polished rice plus a daily addition of 10 cubic centimeters of the ethereal extract.

Three fowls developed neuritis in twenty-three, twenty-nine, and thirty-six days respectively.

Four fowls were fed on polished rice plus a daily addition of 10 cubic centimeters of the chloroform extract. One fowl died in thirteen days as the result of an injury received, and 2 fowls developed neuritis on the twenty-eighth and thirty-ninth day respectively.

The extract of rice polishings remaining after extraction with ether and chloroform was given to 4 fowls fed on polished rice, and these 4 fowls remained well for fifty days when this control experiment was discontinued. It is plain that the neuritis-preventing substance still remained in this extract and was, therefore, insoluble in ether whether acid or alkaline in reaction and was also insoluble in chloroform. It is, therefore, probable that the neuritis-preventing substance is not an alkaloid.

Iodine is present in small amounts in the human body. Thus it is an important constituent of the thyroid secretion and is also found in smaller amounts in milk. The presence of iodine in the thyroid extract indicates that this element is of the greatest physiologic importance to the organism, but we are entirely ignorant of its mode of action and the reason for its importance. Therefore, it was considered desirable to determine whether polyneuritis gallinarum is caused by the deficiency of this element.

Experiment 26.—(a) Four fowls were fed on polished rice and given an additional daily dose of 10 cubic centimeters of a solution prepared by dissolving 10 grams of potassium iodide in 1 liter of distilled water.

All 4 fowls developed neuritis in twenty, twenty-three, twenty-six, and twenty-eight days respectively.

(b) Four fowls were fed on polished rice and given an additional daily dose of 5 drops of syrup of the iodine of iron U. S. P.

Two fowls developed neuritis on the twenty-eighth and thirty-sixth day respectively.

(c) Four fowls were fed on polished rice and given an additional daily dose of 1 grain of thyroid extract (tablet of Burroughs Wellcome and Company).

All 4 fowls developed neuritis in twenty-two, twenty-three, twenty-four, and twenty-five days respectively. From this ex-

periment it will be seen that the addition of iodine to the diet of polished rice failed to prevent the development of polyneuritis, whether added in organic or inorganic combination.

Osborne and Mendel (3) in performing feeding experiments with isolated food substances found that they could maintain life on a diet in which the inorganic salts were supplied by Röhmann's salt mixture. It seemed, therefore, that, if fowls were fed on polished rice and given this salt mixture and if polyneuritis still developed, the inorganic salts could be finally excluded from further consideration in the search for the neuritis-preventing substance.

Experiment 27.—Röhmann's salt mixture was prepared as follows:

Constituent.	Grams.
$Ca_3(PO_4)_2$	10
K_2HPO_4	37
NaCl	20
Sodium citrate	15
Magnesium citrate	8
Calcium lactate	8
Ferric citrate	2
Distilled water q. s. ad, 1,000 cubic centimeters.	

Four fowls were fed on polished rice and given an additional daily dose of 10 cubic centimeters of this salt mixture.

Three fowls developed neuritis in twenty-two, twenty-five, and thirty-five days, respectively.

Taking into consideration the large number of inorganic salts which we have now tried with negative results as reported in preceding papers, it seems evident that polyneuritis gallinarum is not caused by the deficiency of an inorganic element in the diet.

It has been suggested by several writers that polyneuritis gallinarum is caused by the alcohol generated through the fermentation of the excessive amount of starch. While not attaching any importance to this speculation, it seemed desirable to determine whether fowls would develop neuritis when given considerable quantities of alcohol.

Experiment 28.—Four fowls were fed on unpolished rice and given a daily dose of 4 cubic centimeters of 95-per-cent alcohol diluted to 10 cubic centimeters with distilled water. This was continued for forty-five days when the experiment was interrupted because it became necessary to leave Manila. No neuritis had developed in any of these fowls, and they appeared to be in good health although they had been receiving daily an amount

of alcohol equivalent to 200 cubic centimeters for a man weighing 150 pounds. This is approximately the amount of alcohol that would be contained in 400 cubic centimeters of brandy. It is clear, therefore, that if neuritis can be produced at all in fowls by the administration of alcohol, it can only be accomplished by using very large amounts of alcohol over a period much longer than the incubation period of polyneuritis gallinarum.

While the above experiments are all negative in result, it is believed they are worthy of being recorded since each additional experiment affords confirmation of the belief that there is a certain definite substance which is capable of preventing polyneuritis gallinarum. Moreover, apparently this substance alone possesses such power, and every element that is excluded simplifies the task of identifying this substance.

CONCLUSIONS.

1. The administration of large amounts of alcohol has failed to produce neuritis in fowls.

2. Fowls develop polyneuritis when fed on a diet containing a sufficiency of all the alimentary principles, providing no one of the ingredients of this diet contains the neuritis-preventing substance.

3. The neuritis-preventing substance is not volatile, but is destroyed by heat.

4. The neuritis-preventing substance is not an inorganic salt.

5. The neuritis-preventing substance is probably not an alkaloid.

6. Since it has been shown that this substance is not a fat, proteid, inorganic salt, or alkaloid, it seems probable that it is an organic base as claimed by Funk, but we have been unable as yet to confirm his work.

REFERENCES.

(1) CHAMBERLAIN, VEDDER, and WILLIAMS. A Third Contribution to the Etiology of Beriberi. *Phil. Journ. Sci., Sec. B* (1912), 7, 39.

(2) FUNK. On the Chemical Nature of the Substance which Cures Polyneuritis in Birds Induced by a Diet of Polished Rice. *Journ. Physiol.* (1911), 43, No. 5.

(3) OSBORNE and MENDEL. Feeding Experiments with Isolated Food Substances. *Pub. Carnegie Inst. Washington* (1911), No. 156, Parts I and II.

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

THE SUBANUNS OF SINDANGAN BAY.

By EMERSON B. CHRISTIE.

121 pages, 1 map, 29 plates.

Order No. 410. Paper, $1.25 United States currency, postpaid.

Sindangan Bay is situated on the northern coast of Zamboanga Peninsula. The Subanuns of this region were studied by Mr. Christie during two periods of five and six weeks, respectively.

The following is an abstract from the contents of Mr. Christie's report on the Subanuns: Habitat and history; relations with the Moros; material culture; houses; industries; trade; agriculture; family life; social customs; administration of justice; religion; the medicine man; ceremonies; tales; word-lists; physical measurements.

The 29 plates illustrate the Subanuns at work and at play; their industries, houses, altars, and implements; and the people themselves.

THE HISTORY OF SULU.

By NAJEEB M. SALEEBY.

275 pages, 4 maps, 2 diagrams.

Order No. 406. Paper, $0.75 United States currency, postpaid.

In the preparation of his manuscript for The History of Sulu Doctor Saleeby spent much time and effort in gaining access to documents in the possession of the Sultan of Sulu. It is fortunate that these records have now been translated and preserved in permanent form. This book is a history of the Moros in the Philippines from the earliest times to the American occupation.

STUDIES IN MORO HISTORY, LAW, AND RELIGION.

By NAJEEB M. SALEEBY.

107 pages, 16 plates, 5 diagrams.

Order No. [illegible] Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

This volume deals with the earliest written records of the Moros in Mindanao. Doctor Saleeby was fortunately able to obtain exact copies of carefully preserved early records written in the Magindanao dialect with Arabic characters. The author presents translations of these as well as 16 half-tone illustrations of certain pages from the originals. The names of the rulers of Magindanao are recorded in five folding diagrams.

NEGRITOS OF ZAMBALES.

By WILLIAM ALLAN REED.

83 pages, 62 plates.

Order No. 402. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

The introductory chapter deals with the general distribution of Negritos and with the distribution of the Philippine branch of the race. The succeeding chapters deal with the various industries, amusements, and social relations of these little men.

Plates from photographs, the greater part of which was taken for this publication, show ornaments, houses, men making fire with bamboo, bows and arrows, dances, and various types of the people themselves.

CONTENTS.

The "Philippine Journal of Science" is issued as follows:	U. S. currency
Section A, Chemical and Geological Sciences and the Industries	$2.00
Section B, The Philippine Journal of Tropical Medicine	3.00
Section C, Botany	2.00
Section D, General Biology, Ethnology and Anthropology (Section D began with Volume V)	2.00
Entire Journal, Volume II, III, IV, or V	5.00
Entire Journal, beginning with Volume VI	7.00
Single numbers	.50
Volume I, 1906 (not divided into sections)	10.00
Supplement to Volume I (botany)	3.50
Volume I (without supplement)	6.50

Each section is separately paged and indexed.

Publications sent in exchange for the Philippine Journal of Science should be addressed: Library, Bureau of Science, Manila, P. I.

Subscriptions may be sent to the BUSINESS MANAGER, Philippine Journal of Science, Bureau of Science, Manila, P. I., or to any of the agents listed below:

AGENTS.

The Macmillan Company, 64–66 Fifth Avenue, New York City, U. S. A.
Wm. Wesley & Son, 28 Essex Street, Strand, London, W. C., England.
Martinus Nijhoff, Nobelstraat 18, The Hague, Holland.
Mayer & Müller, Prinz Louis Ferdinandstrasse 2, Berlin, N.W., Germany.
Kelley & Walsh, Limited, 32 Raffles Place, Singapore, Straits Settlements.
A. M. & J. Ferguson, 19 Baillie Street, Colombo, Ceylon.
Thacker, Spink & Co., P. O. Box 34, Calcutta, India.

Entered at the post-office at Manila, P. I., as second-class matter.

VOL. VII, SEC. B, NO. 5 OCTOBER, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

ALVIN J. COX, M. A., PH. D.
GENERAL EDITOR

SECTION B

THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

MANILA
BUREAU OF PRINTING
1912

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

REPORT OF THE INTERNATIONAL PLAGUE CONFERENCE.

Held at Mukden, April, 1911, under the auspices of the Chinese Government.

Edited by ERICH MARTINI, G. F. PETRIE, ARTHUR STANLEY, AND RICHARD P. STRONG.

483 pages, 18 plates (2 colored, 4 half-tones, 12 charts and maps).

Order No. 416. Cloth, $3.50; paper, $2.50 United States currency, postpaid.

The proceedings of this International Conference and information gained therefrom, together with the results of certain bacteriological investigations, constitute the present report.

Nothing hitherto has been published which gives such a complete and comprehensive account of the entire subject of pneumonic plague.

Delegates from America (United States of), Austria-Hungary, France, Germany, Great Britain, Italy, Japan, Mexico, the Netherlands, Russia, and China attended the Conference.

The Bureau of Science of the Government of the Philippine Islands has been appointed sole agent for the distribution of the printed proceedings of the International Plague Conference.

THE SUGAR INDUSTRY IN THE ISLAND OF NEGROS.

By HERBERT S. WALKER.

145 pages, 10 plates, 1 map.

Order No. 412. Paper, $1.25 United States currency, postpaid.

Considered from the viewpoint of practical utility, Mr. Walker's Sugar Industry in the Island of Negros is one of the most important papers published by the Bureau of Science. This volume is a real contribution to the subject; it is not a mere compilation, for the author was in the field and understands the conditions of which he writes. The following is a brief synopsis of the contents:

Tables of soil analyses, both chemical and physical; analyses of the cane, juice and bagasse; estimates based on actual information as to the costs of production and of cultivation; and estimates of the cost and location of possible central factories. The island is considered by sugar-producing districts; the area of cultivation and the production per hectare are given, and the possibility for future expansion discussed.

The plates illustrate various phases of sugar industry from the cultivation of the field to the transportation of sugar in native sailboats.

A MANUAL OF PHILIPPINE SILK CULTURE.

By CHARLES S. BANKS.

53 pages, 20 plates.

Order No. 413. Paper, $0.75 United States currency, postpaid.

The silk industry is particularly adapted to be undertaken by persons with small capital, and like the making of hats in the Philippine Islands it should thrive with a little encouragement.

In A Manual of Philippine Silk Culture we have presented the results of several years' actual work with silk-producing larvæ together with a description of the new Philippine race. Half-tone plates illustrate in natural size silkworms in different stages of development, pupæ, adult moths, samples of cloth made from eri silk, hand reel, and silk house. Other plates illustrate the various appliances used in raising silkworms and in spinning silk; hand and power reels are illustrated; working drawings are given for a silk house and for a hand reel.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

VOL. VII OCTOBER, 1912 No. 5

A STUDY OF POLYNEURITIS GALLINARUM.[1] A FIFTH CONTRIBUTION TO THE ETIOLOGY OF BERIBERI.

By EDWARD B. VEDDER and ELBERT CLARK.[2]

CONTENTS.[3]

Since Eijkman (1) first described polyneuritis gallinarum a large number of investigators have studied this disease. At the present time there is general agreement among these investigators that the disease is produced by an exclusive diet of polished rice and may be prevented and cured by the addition of rice polishings or various extracts of rice polishings to the diet. Some of these investigators (2) (3) (4) described briefly the symptomatology and pathology of the disease, but the majority have confined themselves to the study of its etiology.

[1] Read before the Philippine Islands Medical Association, November, 1912, and published with permission of the Chief Surgeon, Philippine Division.

[2] Edward B. Vedder, captain, Medical Corps, United States Army, member of the United States Army Board for the Study of Tropical Diseases as they Exist in the Philippine Islands.

Elbert Clark, associate professor of anatomy, University of the Philippines.

[3] The experimental work is by Vedder; the microscopic work by Clark.

In a series of experiments lasting for several years and reported elsewhere,(5) (6) (7) (8) we have had an excellent opportunity to study polyneuritis gallinarum and therefore believe that our observations on its symptomatology and pathology may be of value. In addition, we have made observations which throw an entirely new light on the pathology of this interesting disease.

I. OBSERVATIONS ON SYMPTOMATOLOGY.

Incubation period.—Observers agree that, when fowls are fed exclusively on polished rice, the symptoms of polyneuritis appear in from twenty to thirty days. We have a record of 124 fowls in which the conditions of the experiment were such as to permit an accurate observation of the period of incubation. The average incubation period of the disease in these fowls was 26.86 days. The shortest incubation period observed was seventeen days, but a number of cases occurred in eighteen and nineteen days. On the other hand, in a number of cases the disease only appeared after forty days. These fowls were all fed on polished rice. However, if fowls are fed on a diet of polished rice, but receive in addition small amounts of other foodstuffs, or an amount of extract of rice polishings which is insufficient to afford complete protection, they suffer from the disease in its typical form, but only after a greatly prolonged incubation period. Thus, some of our fowls on such a diet have developed neuritis after ninety days' feeding, and Eijkman records a case where neuritis appeared only after a year's feeding.

Percentage of fowls affected.—Of 211 fowls on an exclusive diet of polished rice, 154, or 73 per cent, have developed polyneuritis while 57, or 27 per cent, have not shown any symptoms of the disease. The experiments from which this observation is made continued for only sixty days. It is, of course, probable that a higher percentage of fowls would have succumbed if the experiments had been extended over a longer period.

Course of the disease.—A typical case of the disease may be described as follows. Careful observation during the incubation period will reveal nothing abnormal, except that the fowl may be noticed standing bunched up with ruffled feathers and the comb may become blue. The first symptom noticed is a weakness of the legs, so that the fowl is unable to walk well, and as he steps there is a tendency for the joint formed by the tibio-tarsus and the tarso-metatarsus to give way, causing the fowl to sink to the ground. This is due to beginning paralysis of the extensor muscles of the leg which, it will be remembered, are the first

muscles to be affected in men suffering from beriberi. A peculiarity in the gait may be recognized before the legs become completely paralyzed. This is a tendency to raise the feet high in the air and thrust forward with them as though the fowl were attempting to brush away something. This high-stepping gait has never been seen in any condition affecting fowls other than polyneuritis. The fowl may show a tendency to teeter forward on its toes, and may stumble when hurried. From the time when paralysis first appears the disease progresses with great rapidity, and as a rule by the second day the fowl will be unable to stand. The position assumed by the bird in this condition is very characteristic. Usually it sits quite still upon its flexed tarso-metatarsus, but occasionally a bird of more vigor attempts to walk about the cage. However, as the extensor muscles are completely paralyzed, it can not walk upon its feet, but shuffles along upon its flexed tarso-metatarsus. The paralysis now extends rapidly cephalad affecting the muscles of the wings, the neck, and the body, usually in the order named. As a result, the bird is soon unable to sit up, but lies upon its side. There seems, however, to be a general weakness or debility associated with this paralysis. At any rate, the fowl becomes prostrated rather more rapidly than one would expect as a result of mere muscular paralysis. Most of the fowls affected in this way die very promptly, and it is by no means unusual to find the bird dead within two or three days after the first onset of the disease. Some fowls live longer, but almost none survive for a week after the paralysis has set in.

Wing drop.—Many of the birds present this symptom, which consists in inability to hold the wings in the accustomed position close to the body. They droop in some cases until the wing feathers trail on the ground. This symptom, which is probably due to the paralysis of the wing muscles referred to above, does not occur in all cases and comes on later than the leg symptom. It will be remembered that beriberi in man almost always commences by affecting the muscles of the legs, and if the arms are affected this is almost always during a later stage of the disease.

Spasticity.—This occurs in rare instances during the development of the disease, but more often during recovery. A fowl that has developed this spastic gait stands and walks with the knees stiff, leaning forward on the tips of the toes so that the ball of the foot scarcely touches the ground. In the effort to maintain its balance, short rapid steps are taken as though the body were so far forward that the feet have to hurry to keep up. During walking the feet frequently strike together and,

when the spasticity is severe, the fowl topples forward as the result of this interference of the legs.

Retraction of the head.—This is a frequent symptom in the later stage of the disease. The anterior groups of muscles in the neck become paralyzed, and the continued action of the posterior groups retracts the head far backward. This overbalances the fowl so that it is unable to sit upon its paralyzed legs. If a fowl in this condition is placed upon its legs in a squatting position, it makes several spasmodic efforts to retain its equilibrium, and finally topples over backward. Such a fowl is unable to rise without help.

Dysphagia.—After the fowl becomes so paralyzed that it is unable to arise, dysphagia almost always sets in. The fowl appears to be totally unable to swallow normally, and when water or medicines are administered they run out of the mouth when the bird is laid down, unless care is exercised to prevent this. It is also very easy to choke such a bird by attempting to revive it by hand feeding.

Respiration.—The respiration of the fowl suffering from an advanced stage of the disease is slower and deeper than normal. As the bird lies on its side, its abdomen may be observed to expand and contract slowly almost like a pair of bellows.

Sensory symptoms.—It is somewhat difficult to obtain accurate information with regard to the sensory changes. But by tapping, pinching, and pricking the legs, and comparing the reaction with that obtained in normal fowls, it is apparent that sensation is much reduced in the legs of birds suffering from polyneuritis, and it is believed that this loss of sensation precedes slightly the motor paralysis. It is possible that the peculiar high-stepping gait described above may be the result of sensory disturbance.

Loss of weight.—Progressive loss of weight was an almost constant symptom. Thus of 20 fowls fed on polished rice, whose weights were carefully recorded, the average weight at the beginning of the experiment was 3.15 pounds. The average weight of these same fowls taken on the date when the first symptoms of polyneuritis appeared was 2.45 pounds. This represents an average loss of 0.7 pound, or 22 per cent, of their original body weight. A few fowls, however, developed neuritis although they lost comparatively little weight. Thus one fowl whose original weight was 3 pounds 1 ounce developed neuritis after a loss of only 3 ounces, and several fowls lost only 5 ounces.

This loss of weight is such a constant observation, that the view has been held that polyneuritis of fowls is simply the result of inanition which is expressed by this loss of weight. That this

is not the case is shown by the fact that fowls fed on polished rice and protected by an extract of rice polishings also lose weight but do not develop neuritis. Thus 25 fowls fed in this way, of an average original weight of 3.08 pounds, weighed 2.68 pounds at the conclusion of the experiments which lasted ninety days. They thus lost an average of 0.4 pound, or 13 per cent, of their original weight as compared with the 22 per cent lost by the fowls on the same diet but which received no protection. Moreover, several fowls in this group ended the experiment with no loss of weight, and one or two fowls actually gained a few ounces.

Fulminating cases.—While the disease, as described above, appears to be the usual form, a certain percentage of cases present marked variations. Some of the cases are even more rapid in their course, and for lack of a better name may be called fulminating cases. During the incubation period they may lose considerable weight and may appear to be in poor health, but they rarely show any paralysis of the legs. They will be seen in this condition on one day, and the next day will be found lying on the side completely prostrated, often with the neck retracted, and exhibiting the characteristic breathing already described. Death follows within a few hours. The course of the disease in these cases is therefore much more rapid, and is marked by much greater muscular wasting and general prostration than usual.

In a still smaller percentage of cases, paralysis of the legs occurs suddenly as already described, but the bird remains in good general health. The comb is red, the appetite remains good, and the fowls lose little weight. We have had several fowls that lived in this paralyzed state, but in good health otherwise, for a month while still subsisting upon polished rice.

Treatment.—Fowls affected with any of these forms of polyneuritis can rarely be saved by feeding an ordinary mixed diet. Almost all die in spite of efforts to save them by hand feeding. But if they are given an extract of rice polishings, the majority of them can be saved. A great difference, however, has been observed in the manner in which fowls respond to this treatment. Thus birds affected with the form of the disease described as fulminating have been observed that appeared moribund, but recovered almost completely after the administration of this extract, so that they were able to walk about within a few days. This result has not been obtained with fowls suffering from marked paralysis. If birds of this latter group are given this extract, they improve in general health, but the paralysis remains, and it is usually only after several months of treatment that they recover complete control of their legs.

The relation between the amount of polished rice eaten and the development of neuritis.—It has been generally observed that the great majority of the fowls fed on polished rice usually lose their appetites after about a week on this diet, and thereafter eat only small amounts of rice. There are always a few fowls, however, which eat greedily up to the very last, and will eat far greater amounts than the usual ration allowed (120 grams). Several deductions have been drawn from this fact with regard to the development of neuritis. Some observers have thought that those fowls that have eaten well throughout the experiment have been protected from the development of the disease by this increased consumption of rice and, therefore, have been inclined to regard polyneuritis as the result of simple inanition. On the other hand, other observers have thought that those fowls that ate the most rice developed the disease soonest, and have regarded this as an argument in favor of the theory that polyneuritis is caused by some toxin contained in the polished rice. We have observed fowls that always ate well, and yet developed neuritis sooner than usual; we have observed other fowls that ate large quantities of rice throughout the experiment, but whose incubation period was longer than normal. Again, some of the fowls that have eaten poorly have developed neuritis promptly, while others have not developed the disease at all. Therefore, it is believed that the amount of rice eaten has little to do with the development of the disease, which depends rather on the idiosyncrasy of the fowl with regard to the amount of neuritis-preventing substance required.

II. OBSERVATIONS ON PATHOLOGY.

Eijkman, Fraser and Stanton, Chamberlain and Vedder, and others have described degeneration in the sciatic nerves of the domestic fowl after a prolonged diet on polished rice. The questions as to whether the condition is a general nervous affection or a peripheral neuritis, as to the extent of the degenerative changes, the selective localization of the affection, the place of onset of the neuritis and regeneration have led us, in addition to what has been said above, into a study of the minute anatomical changes which may take place in the nervous system in such fowls.

A microscopic study was first made of those nervous elements in which the degenerative changes are probably first manifested and in which these changes are most apparent, that is, the peripheral nerves. This, as might well be expected, increased our interest in the more obscure changes.

In considering in this connection the general question of polyneuritis, it is natural to inquire whether the neuritis is peripheral or involves the entire nervous system. The neuritis produced in fowls by a prolonged diet of polished rice is, so far as the best evidence indicates, a neuritis due to a deficiency of some food constituent or constituents necessary for the maintenance of the metabolic and functional activity of the nervous system. The numerous feeding experiments noted above and the experience and results of Eijkman, Fraser and Stanton, Chamberlain and Vedder, and others well-nigh place this hypothesis beyond the pale of doubt. This being granted, it is probable that the neuritis is, in a greater or lesser degree, a general systematic affection—greater or lesser, because one would not expect different animals to react similarly to any given etiological factor.

The observation that some of our fowls show prostration without showing any well-marked symptoms of peripheral neuritis is evidence favoring the theory of a general nervous affection. This prostration comes on suddenly. It is extremely difficult to bring about recovery after the severest prostration. On the other hand, fowls show varying degrees of peripheral neuritis in the legs while maintaining otherwise good systemic conditions. As many cases come under this latter class, and as the affection often appears to be distinctly limited to the legs in these fowls, we are justified in saying that, whatever the state of the general nervous system, the disease shows a great tendency to involve the peripheral nerves. However, certain observations on the ganglia cells, the nerve cells of the lumbosacral cord, and the anatomical changes in the fiber tracts of the cord and the brain stem itself have convinced us that the central nervous system is much more involved than has been generally thought.

In those cases where the affection is selective enough to be termed peripheral neuritis, one naturally inquires whether it is a primary or a secondary affection; that is, whether the degeneration of the fibers of the peripheral nerve precedes or follows changes in the nerve cells of these fibers. From our present knowledge of the degeneration of nerves, there is little difficulty in supposing that the degeneration in the fibers may be primary, secondary to, or simultaneous with, degenerative changes in their nerve cell. For we know on the Wallerian theory that a fiber severed from its cell or deprived of the "tropic" influence of the cell undergoes degeneration. And, on the other hand, in a cell thus separated from its nerve fiber, atrophic changes occur from disuse.

Some claim that degeneration in the sciatic nerve in beriberi begins in the most peripheral rami, in the smaller branches of the lower part of the leg and foot, and proceeds centrally. These observers claim that the large sciatic nerve shows degeneration at a later period than its peripheral and smaller rami and that at any given time the degeneration in a small peripheral ramus is relatively greater and further advanced than in the fibers of the sciatic in the upper thigh region and precedes any changes in the nerve cells. Were these observations confirmed and proved beyond doubt for polyneuritis in the fowl, the question of the primary affection would be settled. On such a theory of peripheral neuritis we would not expect to find degenerative changes in fiber tracts of the cord and the higher nerve centers. At most, degenerative changes in the fiber tracts of the cord would follow only after atrophic changes in the cells of the dorsal root ganglia and of the ventral horn of gray matter had advanced to a considerable degree. Since, as Engelmann(9) has shown, in a sectioned nerve "in the central stump, despite its functional inactivity, no further changes (*i. e.*, beyond the first node of Ranvier) occurred for months," we should scarcely expect to find degenerative changes in the fiber tracts of the cord (aside from those fibers running between the nerve cells and the periphery of the cord) during at least the first two months of the experiment. This, however, does not agree with our observations which show degenerative changes in the fiber tracts of the cord and changes in its nerve cells. In view of the fact that fowls die shortly after symptoms of neuritis manifest themselves, which circumstance occurs in most cases before the thirtieth day of the experiment and rarely later than forty days, it would seem that degeneration in the cord—on the above hypothesis, a degeneration of disuse—would not be expected. We were not able to confirm the assumption, as will be shown, that degeneration begins in and is more extensive in the most peripheral fibers.

Our microscopic study comprises:

A. Pathology.
   1. Changes in the heart.
   2. Degenerative changes in the peripheral nerves including the vagus.
   3. Degenerative changes in the nerve roots.
   4. Changes within the fiber tracts of the cord and brain.
   5. Changes in the nerve cells of the cord and dorsal root ganglia.
   6. Regeneration.

B. Time of onset of degeneration in peripheral nerves.

Changes in the heart.—Following our own observations that in those fowls showing symptoms of peripheral neuritis or prostration the vagus showed a greater or less degree of degenerative change, an examination was made of the heart. In the gross, the heart showed little or no change from normal. Hypertrophy was not observed. There was an absence or diminution of fat beneath the pericardium. In most cases the myocardium was of a lighter hue than normal. Pericardial fluid was never present in great excess. Aside from those cases of extreme prostration before death, œdema was not noticed. In some of these latter cases a slight œdema was observed beneath the pericardium at the base of the heart. Microscopically, in the hearts of those fowls dead after prostration there was little to be observed which would indicate a pathological change in the musculature. A few fibers here and there were seen in the myocardium of the ventricles in which the cross striation was more or less obscure and which stained poorly. An apparent increase in pigment was also noted in several hearts. At most, we would hesitate to claim any changes further than those which would indicate beginning parenchymatous or mucoid degeneration. In those fowls which presented chiefly the symptoms of peripheral neuritis it was even more difficult to observe changes which could be considered pathological, and in some cases no change whatever was to be noted.

Degeneration in the peripheral nerves. The vagus.—Degenerative changes, as shown by the Marchi method, were observed in all the cases examined. Plate III, figs. 5 and 6, illustrates high- and low-power photomicrographs of a vagus nerve showing degeneration stained by Marchi's method. Unlike the sciatic nerve, however, the extent and degree of degeneration in the vagus did not always correspond to the severity of the symptoms before death, nor was the most extensive degeneration to be seen in the vagus nerve of those cases which showed prostration. Fowls in good general condition sometimes showed extensive degeneration in the vagus. Likewise, we were not able to establish an interrelation between the severity of the degeneration in the vagus and the amount of pathologic change in the heart.

That there may be no interrelation between the severity of nervous symptoms and the systemic condition of the animal before death on the one hand and the degree or extent of degeneration found in the vagus nerve on the other is well shown by the following four cases:

Fowl 3 showed symptoms of very little peripheral neuritis

(slight indications of paralysis), but became suddenly prostrated. The vagus nerve showed almost no degeneration.

Fowl 5 showed extreme peripheral neuritis, no prostration, and little degeneration in vagus.

Fowl 6 showed marked peripheral neuritis, no prostration, and extensive degeneration in vagus.

Fowl 8 showed marked peripheral neuritis, extreme prostration, and extensive and advanced degeneration in vagus.

The vagus nerve of fowl 13 (Plate III, fig. 5) shows the extent to which degeneration may progress in the vagus, and in our series is relatively advanced degeneration for the vagus. In the teased preparations of the vagus nerve of this fowl no single nerve fiber could be found which did not show areas of blackening along its course. This was found to obtain in the vagus of most of the cases; that is, that somewhere along its course in segments of the nerve from 2 to 5 millimeters long, each fiber showed one or more areas of blackening with the osmic acid of Marchi solution. At the periphery of this illustration single fibers may be seen showing frequent globules of fat along their course. In those vagi showing little degeneration the blackened areas are not so numerous.

Plate III, fig. 6, is a high-power view of a teased preparation of the same nerve. In this there will be seen rather large globules of degenerated myelin. This stage is about as far advanced as has been observed by us. It will be noted that, while there is a distinct globular arrangement of degenerated myelin, there is no vacuolation of either degenerated myelin or of the medullary sheath. In no case has there been observed a vacuolation of the medullary sheath nor a collection of degenerated myelin into very large globules as is found in the sciatic nerve or as is very characteristic in peripheral nerves which show Wallerian degeneration after section. There has not been observed a breaking up of the axis cylinder of the fibers of the vagus. These observations lead us to believe that, although in polyneuritis in fowls each nerve fiber of the vagus may, and usually does, show degenerative changes by the Marchi method, this degeneration never progresses far enough before the death of the fowl to bring about the destruction of the axis cylinder.

Cervical ganglion and its pre- and postganglionic fibers.—The superior and inferior cervical ganglia from several cases were examined by the Marchi method for degeneration. Very small droplets of fat, approximately one-half micron in diameter, were observed in many of the ganglia cells. However, these were by no means numerous, ranging from 4 or 5 to 20 or 30 in a cell,

but not in more than one-third of the cells. In the medullated pre- and postganglionic fibers larger, though fewer, globules of fat were seen. It was found very difficult to tease the ganglia, and sections after paraffine embedding were made. It is thus quite possible that the degeneration here observed does not represent the full extent to which degeneration had progressed in these fibers. In the nonmedullated fibers no multiplication of the nuclei of the neurilemma was observed. Thus, while there are indications of degeneration in the sympathetic ganglia (that is, cervical ganglia) and their fibers, this degeneration is slight, and a careful search must be made to detect it.

The sciatic and its peripheral branches.—Most of the investigators who have undertaken a study of polyneuritis in fowls have taken the sciatic as a basis for their anatomical study, and have confined themselves to the Marchi stain. In most cases all that was desired was to know if degeneration had or had not taken place. Thus far the Marchi method is an excellent one and well adapted for the purpose. On the other hand, to obtain an opinion as to the extent of degeneration, an indication of the probable changes which have occurred within the nerve, including the condition of the axis cylinder and nuclei of the neurilemma sheath, the Marchi method must be supplemented by other staining methods. In our study of the degenerative changes occurring in the sciatic nerve we have employed the Marchi; the Weigert stain for myelin sheath; the Altmann, the Benda, and the Meves mitochondria methods; the Golgi, Cajal, Mallory, fuchsin, and safranin methods for the axis cylinder; and hæmatoxylin methods for the nuclei of the neurilemma sheath.

As in the case of the vagus, in those sciatic nerves in which degenerative changes are apparent by the Marchi method, practically every fiber shows some indication of degeneration within short limits of its course (2 to 5 millimeters). The degenerative appearances, however, vary within the widest limits in the various fibers of the same nerve. In nerves from well-marked cases many fibers show only slight changes—small black droplets or a localized slight blackening—here and there at relatively wide intervals, from 100 to 500 microns along their course. Other fibers, and these form the majority of the fibers, show more extensive change—larger and more frequent droplets of degenerated myelin. A certain proportion of the fibers from well-marked cases of neuritis show advanced degenerative changes. These make up from 10 to 15 per cent of the fibers. Whether the other fibers show advanced degeneration at other places we could not prove beyond doubt, but regeneration experiments,

which are usually characterized by the rapid recovery of the fowl, indicate that they do not. These fibers showing advanced degeneration are marked by the accumulation of myelin in large globules and droplets, a swelling and bulging of the nerve sheath at these points, and a disintegration of the axis cylinder. The largest globules usually appear vesicular and, in their center, segments or fragments of the axis cylinder are frequently to be seen. In these larger and some of the smaller globules the stainable material is found at the periphery and appears laminated. This laminated appearance is very characteristic in Weigert preparations and is the rule in the larger globules. Usually 3 distinct layers are clearly visible of which the outer is the thickest. Other incomplete layers and fragments are seen centrally. The larger globules of degenerated myelin are not in proximity with one another; they are separated by at least many microns. The space between contains a few small droplets of degenerated myelin. It seems otherwise almost or quite devoid of structural contents. In other fibers the change appears just as complete and the segments and globules of the degenerated myelin are just as evident, but the globules are uniformly smaller. The same fiber may and probably does show both conditions at different places along its course.

Plate II, fig. 3, *b*, shows a nerve fiber in which degenerative changes are well marked. None of the largest globules are shown. Small droplets are seen between the larger globules in the otherwise apparently empty space. In this fiber the change of myelin into fat seems complete, while in fiber, *c*, the myelin seems intact and quite normal in appearance. It will be noted that here and there the degenerated myelin fails to fill the neurilemma sheath. Thus an apparently empty space is left between the latter and the degenerated myelin. This is in contrast to the condition found in those fibers containing the largest globules. Here the globule fills and distends the neurilemma.

In addition to the appearance just noted, other fibers were seen, in the nerves where degeneration was most marked, in which the degenerated myelin was confined to small droplets which failed still further of filling up the neurilemma sheath. Here segments of the axis cylinder were less frequent, but the more or less indistinct granules which were taken to be fragments of the axis cylinder were more numerous. In others the neurilemma sheath appeared much shrunken or collapsed, and a few small droplets of degenerated myelin were contained within.

A careful study of all these fibers has convinced us that the successive stages of myelin degeneration correspond pretty well with the order just described. The earliest stage made apparent by the Marchi method consists of a slight swelling of the medullary sheath, which shows a diffused blackening with the osmic acid and slight tendency toward segmentation at the circumference. Plate II, fig. 3, *a*, and Plate IV, fig. 7, show such fibers.[4]

Then follows the stage in which the largest globules distending the nerve are seen. Next is the stage in which the globules are much smaller, though quite black and discrete, and which only partly fill the sheath of Schwann. In the succeeding stage, the globules are very small but numerous. Then follows a stage where the shrunken neurilemma contains only a few scattered droplets of fat.

The neuraxis.—As stated above, the axis cylinder in those nerve fibers which show marked degeneration usually appears broken up. In the larger globules of myelin and at other places, segments of the axis cylinder were to be seen. Plate V, fig. 9, shows such a fiber. The granular appearance of the axis cylinder as is shown in this figure is quite typical for axis cylinders in fibers of this type. The segments enclosed within the globules of myelin which are usually curved or somewhat S-shaped also show this granulation when stained in certain dyes; carmine, acid fuchsin, Mallory's phosphomolybdic acid, hæmatoxylin, etc.

It might be remarked in this connection that many authors hold the view that the axis cylinder contains many neurofibrillæ along whose course many fine granules or enlargements are scattered. In those fibers in which the degeneration is further advanced, the remains of the axis cylinder is seen; not as a segmented, but rather as a fragmented structure. The fragments appear rather indistinct and diffuse and contain small obscure granules. The appearance somewhat simulates in section coagulated exudate or serum. Plate V, fig. 10, *a*, illustrates the appearance of a fragmented axis cylinder after staining with hæmatoxylin and acid fuchsin. In each fiber showing advanced myelin degeneration the axis cylinder was broken up. Segments of the axis cylinder are to be seen in all the large globules if properly stained. Whether the breaking up of the axis cylinder precedes or follows the formation of the large

[4] A diffuse blackening of the myelin, however, may be obtained even in a normal nerve by too short a mordanting in the Müller's fluid or by prolonged staining in Marchi's mixture. The tendency to segmentation though is absent.

globules must remain more or less a matter of speculation. Our observations lead us to believe that they occur somewhere near the same time.

Certain nerve fibers observed by us from nerves showing marked myelin degeneration gave indications of a segmentation of the myelin sheath and a disappearance of myelin with a persistence of the axis cylinder. This, however, has not been sufficiently confirmed to claim it as a possible type of degeneration in polyneuritis.

The neurilemma.—The neurilemma persists throughout all degenerative stages and in all fibers. No fiber was seen in which the neurilemma could not be easily distinguished. In Plate II, fig. 4, showing well-marked degeneration in a fiber of the sciatic nerve, the typical appearance of the neurilemma is well illustrated. Here the sheath of Schwann does not appear hypertrophied nor is there present an increase in the number of nuclei.

Degeneration in the proximal part of the sciatic and in its peripheral rami.—All phases of the degeneration described above for the fibers of the sciatic were to be seen in its peripheral branches and no additional type was seen. On the theory that the affection begins in the peripheral branches and progresses toward the spinal cord, one would expect to find in preparations from a given fowl more advanced and more extensive degeneration in the peripheral rami than near the spinal cord. Further, that degeneration might be found in the peripheral nerves—those supplying the foot and lower part of the leg—and not be apparent in the sciatic. Our observations do not warrant either assumption. In two teased preparations from a given nerve stained by the Marchi method, it is impossible to distinguish which is peripheral and which central. In both cases all fibers show some degeneration. As stated above, in preparations from fowls presenting well-marked symptoms of peripheral neuritis, 10 to 15 per cent of the fibers show well-marked degeneration. These are clearly differentiated from the remainder of the fibers. The number of these fibers showing marked degeneration has always been found practically the same near the cord and in the peripheral branches; thus in fowl 37, suffering from marked peripheral neuritis, in 500 fibers from different portions of the central end of the sciatic, 51, or 10.2 per cent, showed well-marked degeneration. One of the finer peripheral rami taken from near the foot contained 535 fibers of which 58, or 10.8 per cent, showed marked degeneration.

In cross sections of nerves of other fowls we found, respectively, fibers in advanced degeneration as follows:

a. Four in a total of 208 fibers in a peripheral nerve and 5 in 285 of the sciatic.

b. Five in a total of 193 fibers in a peripheral nerve and 7 in 421 of the sciatic.

c. Four in a total of 154 fibers in a peripheral nerve and 10 in 368 of the sciatic.

These figures represent advanced degeneration in one plane, and as noted above do not include all the fibers showing advanced degeneration.

We are then unable to distinguish any anatomical difference in degeneration in the central portion of the sciatic and its peripheral branches as to extent, degree, or time of onset. Thus we are of the opinion that degeneration progresses uniformly throughout the course of the fibers as has been shown to be the case in the peripheral portion of a sectioned nerve. Nor should we expect, either from the symptoms of neuritis shown by the fowl before death or from our knowledge of experimental degeneration of nerves, that in the present case degeneration would begin at the periphery and progress centrally. Within a few hours after showing the first symptoms of neuritis the fowl usually "comes down" and is unable to walk. The proximal portion of the sciatic in these fowls shows advanced degeneration.

We know from curare experiments, fatigue experiments, cold block, etc., that when a motor nerve ending is placed out of commission, the nerve itself is of no more service than if it were completely degenerated or sectioned. Stimulation by any means whatsoever produces absolutely no effect on the muscle which it supplies. Now, in polyneuritis in fowls on a polished rice diet, should degeneration progress from the periphery, the fowl would show paralysis just as soon as degeneration in the peripheral rami or in their end organs had progressed to a certain extent. This in all cases would be before degeneration to a similar degree or extent occurred in the sciatic (from which the peripheral nerves arise), and we should expect to find fowls that had just developed paralysis, in which the peripheral nerves showed advanced degeneration and whose sciatic showed only the earlier stages or none whatever. As stated above, we have not observed this condition in a single fowl. On the contrary, there are proportionately just as many nerves showing a breaking up of the axis cylinder in the sciatic as in its more peripheral rami. This, indeed, is the exact parallel of the condition in peripheral nerves showing degeneration after section as was shown by Monakow.(10)

According to this observer, degeneration in a sectioned nerve progresses uniformly throughout the peripheral part. Thus the only condition in which we should expect to find more degenerated fibers in the peripheral nerves than in the sciatic would be in the case of those fibers which branch as the periphery is approached, both rami showing degeneration.

Nerve roots.—The nerve roots in several cases were examined after staining by the Marchi as well as by the Weigert and mitochondria methods. Degeneration was observed in both ventral and dorsal roots by all these methods. However, degeneration was more frequent and much more pronounced in the ventral than dorsal roots.

Ventral roots.—Degeneration in the ventral nerve roots of the sciatic was pronounced in those cases in which degeneration in the sciatic was marked and degeneration in the two (*i. e.*, sciatic and nerve roots) was parallel and comparable; in fact, teased preparations from the ventral nerve roots resembled very closely teased preparations from the sciatic. In the ventral nerve roots degeneration was easily demonstrated by all the methods mentioned above.

Dorsal nerve roots.—In those cases in which degeneration was far advanced in the fibers of the sciatic, degeneration was demonstrated in the dorsal nerve roots. In other cases it was more difficult to demonstrate or was absent altogether. In only the most advanced cases was degeneration to be seen after the Marchi method. In other cases it required the mitochondria method to bring out the changes. Owing to the difficulty in teasing, the section method was frequently employed. The changes in the dorsal nerve roots resembled more nearly the earlier stages of degeneration in the fibers of the sciatic. Few cases were seen where advanced degeneration was present.

The spinal cord.—Degeneration within the spinal cord was observed in the fiber tracts of all columns, and changes were observed in the nerve cells of both ventral and dorsal horns.

The fiber tracts.—When a specimen of the spinal cord from a normal fowl is treated by the Marchi method, it shows in both sectioned and teased preparations numerous small black areas. In teased preparations (which are very difficult to obtain) and in cross sections of the cord, these small black areas, which are about the size of the smaller globules in a degenerated nerve, are seen in close relation with the fibers in the cord. It is sometimes difficult to tell whether a given globule is within the fiber or in apposition to it. Naturally then other methods must also be employed to confirm any suspected degeneration within the

cord. All the methods enumerated above (the Weigert and mitochondria methods) for the myelin sheath and others for the neuraxis were made use of to this end.

Plate I, fig. 2, is a photomicrograph from the anterior lateral portion of the white matter of the cord of a normal fowl after Marchi method. The black areas shown at *a* are the globules referred to, which stain black in the Marchi fluid. A careful inspection will show that these are not within the fibers, but are in close proximity to them. What these structures represent we have not determined. At *b* two fibers show enclosures which resemble very much the small droplets of myelin in a degenerated nerve fiber. These we have noted occasionally here and there, but have not interpreted them. However, despite these resemblances to degeneration of fibers in the normal cord, the picture presented by a section or a teased preparation from the cord of a fowl with well-marked paralysis is easily distinguishable as one showing degeneration.

In studying degeneration in the fibers of the spinal cord, sections and teased preparations were made from the thoracic cord. Since, as has been pointed out, the nerve roots of the sciatic group show degeneration, a preparation from the lumbosacral cord showing degeneration might indicate nothing more than degeneration in the fibers of the roots passing up or down the cord for a short distance. True degeneration in the columns of the cord would be equally apparent in the thoracic region where primary fibers of the sciatic group are absent.

Plate VI, figs. 11 and 12, and Plate VII, fig. 13, are from the thoracic cord of fowls with marked degeneration in the sciatic nerve. Fig. 13 is low-power magnification of the lateral column of the cord (as near the pyramidal tract as we could determine) of a fowl whose sciatic showed marked degeneration. At *a*, *a'*, *a''*, and *a' ''* appearances strongly suggestive of degeneration within the fibers are seen. Owing to the fact that the fibers of the cord do not run a straight nor parallel course, it is extremely difficult, and much a matter of chance, to get a longitudinal section which shows the course of a fiber except for a short distance. Plate VI, fig. 11, a low-power magnification of the dorsomesial (Goll's) columns of the cord of another fowl with marked degeneration in the sciatic, shows at *a*, *a'*, *a''*, etc., undoubted enclosures of degenerated myelin within the fibers. Plate VI, fig. 12, is a higher magnification of a small area of the same. Whatever the other dark areas may mean, there can be little doubt that at *a* and *a'* two fibers are seen which contain

globules of degenerated myelin. This is especially evident at *a*, which gives the appearance of a globule from which much of the fat has been dissolved by the clearing agent.

It might be claimed that, since the spinal cord gives off two spinal nerves at each segment of the vertebral column, the fibers described above might represent primary fibers from the nerve roots of these spinal nerves. We recognize this as a possibility in many cases. However, it must not be forgotten that the fibers of Goll's column (ascending) are secondary neuraxes of sensory fibers which enter the cord in the lumbosacral region; that is, that they are axis-cylinder processes of cells situated in this portion of the cord. It might be further pointed out that the more mesial fibers arise from cells in the lower segments of the cord. Now, since fibers *a* and *a'*, fig. 11, are such mesial fibers, it follows that they can not be fibers of the nerve roots of the thoracic spinal nerves, but are fibers of Goll's column showing degeneration.

If the medullary sheath of the fibers within the cord shows myelin degeneration, it is natural to inquire into the state of the axis cylinder. Longitudinal and transverse sections of the thoracic region of the cord have been examined after staining by the various methods noted above for the axis cylinder. Appearances of degeneration similar to those described for the axis cylinder of certain fibers of the sciatic have been noted in the fibers of all columns of the cord. These changes consist in segmentation and fragmentation which are evident only in longitudinal sections of the cord and granulation which is best seen in transverse section. We were unable to determine whether relatively more fibers show a breaking up of the axis cylinder in one column than in another. This is due to several reasons. We have no stain distinctly specific for the axis cylinder. The Golgi, Cajal, and other metallic methods besides bringing out other structures can not be relied upon to impregnate every axis cylinder; it is very difficult to stain a degenerating axis cylinder, and small corpora amylacea and neuroglia cells with their small amount of surrounding connective tissue might easily be mistaken for cross section of such a fiber.

Plate V, fig. 10, which is from the posterior lateral column of the thoracic cord of a fowl with well-marked neuritis, shows at *a* and *a'* two fibers with degenerating axis cylinders. The axis cylinder shows a granular or somewhat flocculent appearance, and probably represents an advanced stage of degeneration. As the columns of the cord are not well demarcated, we

are not able to say whether these fibers are ascending or descending; that is, sensory or motor. The number of fibers of the cord which show undoubted degeneration in either the axis cylinder or the medullary sheath was in no case great—much less than we had expected to find. The number of the former scarcely make up 0.25 per cent of the total fibers in *a given cross section,* while the latter are approximately 1 per cent in the most advanced cases. These observations lead us to believe that in fowls showing well-marked neuritis there is degeneration in a very small percentage of the fibers of all columns of the spinal cord.

Changes in the brain.—Similar observations in Marchi preparations were made on the fiber tracts of the medulla, pons, midbrain, and internal capsule of fowl 72. Degenerated fibers were found in each one of these brain divisions comparable to those found in the cord, Plate V, fig. 23.

Changes in the nerve cells. Cells of the cord.—One would expect that degeneration in the fibers of all columns of the cord and in the peripheral nerves would be accompanied by changes in the nerve cells themselves. Our attention has been confined chiefly to a study of the cells of the lumbosacral cord. From what has been said above relative to degeneration in the peripheral nerves and in the fiber tracts of the cord, it is evident that the most marked changes in the nerve cells of the cord would be found in the lumbosacral region. For a study of these changes we have employed the Nissl method, Giemsa's blood stain after alcohol fixation, and the mitochrondria methods.

Plate X, fig. 19, shows a nerve cell from the anterior horn of the thoracic region of a normal fowl stained by Nissl's method. No nerve processes are shown. Plate X, fig. 20, is a similar nerve cell stained by Giemsa's blood stain. In both cells the tigroid substance is well shown.

In the spinal cord of the fowls showing well-marked degeneration in the sciatic, we have never been able to find a nerve cell in the lumbosacral portion, in which the tigroid substance shows as clear distinct areas like those in figs. 19 and 20. The stainable substance shows a marked tendency to diffusion throughout the cell. Cells from these cords, however, were observed in which the tigroid bodies appeared as definite though indistinct globules or areas. The usual appearance of the large cells of the anterior horn and of the large cells of the posterior horn was a diffusion of the stainable material and a collection of it at one side of the cell. The stainable material which is granular in

appearance shows a tendency to group itself around the base of one of the processes of the cell (Plate X, figs. 21 and 22), but whether this process is usually the axon as shown in fig. 22, *a*, we are not able to say. This figure shows the typical appearance of the large nerve cells of the ventrolateral horn, from which the fibers of the ventral root arise, and of the large cells of the posterior horn around which the terminations of the sensory neuraxes from the dorsal root ganglia arborize. Its granular appearance is suggestive of a disintegration rather than a solution of the tigroid substance. The cells of the other parts of the gray matter of the cord do not show this change to such an extent. They stain poorly, the stain is easily differentiated out, and the cell has a pale appearance. The stainable portions are arranged in a coarse reticular network. The appearance is that of a cell in which the tigroid substance is wanting. Cells of somewhat similar appearance are also seen in sections of the normal cord, but are not so numerous here. A comparison between the large cells of the anterior and posterior horns of the normal and neuritic fowl, noted above, is best made by a study of figs. 19 and 20 and of figs. 21 and 22. Fig. 22 gives the appearance of rather advanced retrogressive changes. The stainable material is collected at one point of the cell and causes a bulging here. The nucleus also suggests degenerative changes. This has been noted in very few cells, and the picture is the most suggestive of degeneration in the nerve cells of any we have seen.

Since marked changes in the tigroid substance of the nerve cells of the spinal cord can be brought about, as Nissl(11) and others have shown, by fatigue, direct electrical stimulation in excess, toxemia, and other factors, it is impossible to say that the changes noted in the nerve cells of the neuritic fowls represent degenerative changes or changes due to other causes. We have thus employed other methods in studying these cells. By the Marchi method a few very fine, intensely black granules can be seen here and there within the nerve cell. These, however, are so scarce that their pathologic significance is probably very small. A study of the mitochondria of the nerve cells was next made.

Of recent years a great deal of work has been devoted to the study of mitochondria and their significance. Mitochondria occur as numerous rods and granules in all the various types of cells of the embryo (Bensley,(12) Meves,(13) and others) and in practically all types of cells of the adult, which have an active metabolism or which are actively engaged in secretion, as the

numerous researches of Meves, Benda,(14) Bensley, Regaud,(15) Renaut, and others have shown. For the great advance which has been made in our knowledge of this subject, we are probably justified in saying that mitochondria are identical with the "Filarmasse" of Flemming, the "Bioblasts" of Altmann,(16) (Meves, Bensley, and others), and are necessary for the metabolic and functional activity of the cell. Regaud and others have shown that mitochondria occur in normal nerve cells and Cowdry(17) and others have shown that they are distinct from the tigroid substance and that the two occur simultaneously in the same normal nerve cell. One of us (Clark) has not been able to demonstrate them in certain pathologic cells (pancreas). An examination of the nerve cells of the spinal cord of the fowls with marked degeneration in the sciatic nerve by the mitochondria method shows rods and granules in cells of the type which show such marked changes by the Nissl method. In the cells of the thoracic cord it was practically impossible to distinguish between the cells from the normal and from the neuritic fowl as regards mitochondria. The rods and granules were perhaps a little less numerous in the latter cells, but this is far from being definite. A cell with no mitochondria was not observed in the lumbosacral cord of the more advanced cases.

We are thus of the opinion that, along with degeneration in the peripheral nerves and in the fiber tracts of the cord, there occur changes in certain nerve cells of the anterior and posterior horns of the spinal cord, which may or may not signify degenerative changes, but which probably never progress to any great extent before death of the fowl.

Regeneration.—In the numerous experiments to bring about recovery after prostration or after pronounced symptoms of peripheral neuritis had manifested themselves, we have found that fowls show as much individual variation here as they do in developing the affection. Of fowls in which the symptoms were distinctly those of peripheral neuritis (severe in nearly all), recovery was accomplished in almost every case.

The nerves from fowls, carried toward recovery by feeding for sixty days and which were apparently well, were examined for degeneration. In a majority of the fibers only very small blackened areas (Marchi's method) were to be seen. From 10 to 15 per cent of the fibers, however, showed segmentation and globular arrangement of the myelin and no axis cylinder. The globules were never large at this period, and the core of the fiber within the neurilemma sheath contained relatively large amounts

of apparently empty space. This appearance is strongly suggestive of a partial absorption of the large globules of degenerated myelin seen in the nerves of fowls with marked peripheral neuritis. These observations make it probable that regeneration in those nerves showing advanced degeneration is very slow or doubtful, that recovery after neuritis means a recovery of those nerve fibers which do not show advanced degenerative processes, and that in recovery after peripheral neuritis the fowl is able to do without the 10 or 15 per cent of the fibers which are the slowest to regenerate. Rapid regeneration after prostration alone confirms the anatomical findings that degeneration is further advanced in the nerves of those fowls showing symptoms of peripheral neuritis than prostration without peripheral neuritis.

III. OBSERVATIONS ON THE EARLIEST DEGENERATIVE CHANGES IN THE NERVES.

Time of onset of degenerative changes in the fibers of the sciatic nerve.—Finding that degenerative changes were to be observed in the sciatic nerve of all those fowls which had been on a polished rice diet for thirty-five days or more, even though symptoms of neuritis did not manifest themselves (Plate XI, fig. 24), we sought to determine when the first changes are to be detected. From the advanced degeneration occurring in some fibers of such nerves, it became evident that degenerative changes took place long before signs of neuritis were evident. It became an interesting point to determine at what period these degenerative changes are first to be detected. Accordingly 12 fowls were fed polished rice and killed at varying intervals of time, ranging from seven to twenty-three days. Thus Nos. 24 and 25 were killed after seven days on polished rice; Nos. 26 and 27, after eleven days; Nos. 28 and 29, after fourteen days; No. 30, after sixteen days; No. 31, after seventeen days; No. 32, after eighteen days; No. 33, after nineteen days; No. 35, after twenty-two, and No. 36, after twenty-three days on polished rice. None of these fowls showed symptoms of peripheral neuritis and, with the exception of Nos. 35 and 36 (somewhat droopy), all were lively and apparently normal. As controls 4 normal fowls were used. The mitochondria methods proved to be the most delicate and serviceable in this series, and the methods of Benda, Meves, Bensley, and Regaud were employed as checks on each other. It was found that after prolonged fixation in Müller's fluid (two weeks or more in 2 or 3 changes), each of the above methods gave excellent results. As the iron-

hæmatoxylin method (Meves, Regaud, Rubaschkin,[18] and others) gives the most permanent preparations and is easy of application, it was most frequently employed.[5]

In good preparations of a normal nerve stained by this and the other mitochondria methods, the medullary sheath is seen to contain innumerable little bacilli-like rods. When seen from above, the fiber gives the appearance of containing both rods and granules, but in a fiber which has been split down the middle in sectioning, so that the medullary sheath is seen only on either side of the axis cylinder and not above, only rods are to be observed. These rods arrange themselves in a general radial direction around the axis cylinder, but at places show a more or less X-like crossing. From this it is apparent that the granular appearance is due to an end view of the radially arranged rods. These appearances are identical to similar structures and arrangements described and illustrated by Nageotte[19] in the cauda equina of the guinea pig and termed by him mitochondria. Plate VII, fig. 14, is a photomicrograph of an iron-hæmatoxylin preparation, and illustrates the arrangement and number of these rods in a normal nerve. At *a*, *a'*, and *a''*, the radial arrangement of the rods is shown. This picture is typical of all preparations from the nerves of the 4 normal fowls stained by each of the mitochondria methods mentioned above.

Fowls 24 and 25, fed for seven days on polished rice, are the earliest on which examinations were made in this series. Fowls were not killed at an earlier period than this, because it was thought that several days must elapse before the normal metabolic balance of the fowl would be disturbed. Thus in these 2 fowls, which serve as a check on each other, we did not expect

[5] The iron-hæmatoxylin method for staining mitochondria is very simple, easy of application, and well adapted for nerve tissue. It has the further advantage of being permanent and it brings out the rods in sharp contrast. Small pieces are fixed and mordanted in Müller's fluid two weeks or longer, washed in water (twelve hours), and embedded in paraffine through xylol. Sections, not over 5 microns thick, are mordanted (twelve to twenty-four hours) in 2 per cent iron ammonia alum, washed in water, and stained in Weigert's hæmatoxylin (for myelin sheath), eight to twenty-four hours in this climate. Differentiate in iron ammonia alum (1 or 2 per cent). Sections sometimes give clearer pictures if immediately before staining they are treated one or two minutes in 0.25 per cent potassium permanganate, washed in water, and placed for one or two minutes in Pahl's solution of 0.5 per cent potassium sulphite and 0.5 per cent acid oxalic. For further details on staining mitochondria and other methods, see Altmann,[16] Bensley,[12] Benda,[14] Meves,[13] Regaud,[15] and Rubaschkin.[18]

to find any demonstrable change from the normal. Much to our surprise, however, nearly all the rods had disappeared from practically every fiber of the sciatic shown in a longitudinal section through the middle of the nerve. In the smallest fibers a few rods were to be seen, but they were extremely scarce in the large fibers. This condition obtained in the sciatic of both fowls. The stainable material of the medullary sheath which demonstrated itself in the form of rods in the normal fiber here took on quite a different and surprising appearance. In the 7-day fowls it was seen as smaller, or larger, irregular, branched, and anastomosing globules. A few fibers showed an apparent swelling here and there and a more or less distinct network. Plate VIII, fig. 15, is taken from the sciatic of fowl 24, and is more or less typical for both birds. The globular arrangement is well demonstrated—*b* is a fiber showing the swelling and network arrangement. This was confirmed by the other methods. This change in so short a time was so pronounced and remarkable that with a little skepticism the normal nerves were again worked over. These confirmed in every particular our first preparations. With considerable enthusiasm, the remainder of the series of fowls was examined, and a routine examination of all the previous fowls was begun. The results were well worth the trouble, for in none of these preparations was it possible to find a single fiber which even approached in appearance that of the normal fiber. It was the rarest instance that a single rod could be found.

Changes in the fibers from the remainder of the series (that is, fowls fed for more than seven days on polished rice) were not so pronounced over the 7-day preparations as this was over the normal. In fact the 11-day preparation resembles very closely the 7-day, and it is practically impossible to distinguish the 11- or 14-day from an 18-day preparation. Later changes are shown in Plate VIII, fig. 16, and Plate IX, fig. 17. In these latter subjects, most of the fibers show little advance over the 7-day or over the next preceding stage. There is, however, to be observed a general tendency toward segmentation of the myelin in the 11-day, 14-day, *et seq.* A few fibers here and there, on the other hand, show progressive change. The stainable substance collects in larger irregular globules and skeins, the remainder of the medullary sheath being remarkably clear. (Plate VIII, fig. 16, fibers *a, b, c. d.*) In fowls which have been fed for a longer period, a few fibers show a still more pronounced collection of the stainable material into large irregular masses and segments. Plate IX, fig. 17 *b*, is characteristic of such a fiber. The other and great

majority of the fibers show little or no advance over the preceding stage. In those fibers from fowls which present symptoms of neuritis and whose nerves show pronounced degeneration, the stainable material takes on a more diffuse and somewhat homogeneous appearance in a majority of the fibers. Other fibers are seen (10 to 15 per cent) which show an exaggeration of the globular arrangement. These globules are more regular in shape and oval in contour, and the stainable material shows a preference for the periphery. These resemble very much the fibers which show advanced degeneration by the Marchi method and are probably identical with them. (Plate IX, fig. 18, fiber *a*.) Thus it is evident that the fibers of the peripheral nerves of fowls on a polished rice diet show an early (7-day or somewhat earlier) change in their medullary sheath, and that in a varying percentage (10 to 15) this change is progressive and leads to the condition ordinarily termed degeneration. This can easily be followed in Plate VIII, figs. 15 and 16, and Plate IX, figs. 17 and 18.

IV. THE INFLUENCE OF VARIOUS ARTICLES OF FOOD ON THE PRODUCTION OF POLYNEURITIS GALLINARUM.

In pursuing investigations into the cause of beriberi it has been by no means uncommon to find instances in both experience and the literature where beriberi has developed in spite of the fact that the patients had received what was supposed to be a fairly well-balanced ration containing rice as the staple article of diet. This observation has been frequently urged as an insuperable objection to the theory that beriberi is caused by rice diet. In a previous paper(8) one of us has shown that fowls likewise develop polyneuritis when fed on diet containing a sufficiency of all the alimentary principles, provided no one of the ingredients of this diet contains the neuritis-preventing substance. It is apparent that the neuritis-preventing substance is not present in all articles of food, and that, in those articles in which it is present, it occurs in very variable amounts. It was, therefore, considered desirable to test certain articles that are usually included in an ordinary diet, in order to determine just what degree of protection they would afford when combined with a staple of polished rice.

The following experiments were performed for this purpose:

Experiment 29.—Four fowls were fed on polished rice, and in addition were given daily 10 grams of raw potatoes. One fowl developed neuritis in thirty-two days, 1 in thirty-eight days, and the other 2 fowls remained well after sixty-three days, when the experiment was discontinued.

Experiment 30.—Four fowls were fed on polished rice, and in addition

were given daily 10 grams of boiled potatoes. One fowl developed neuritis after twenty-five days' feeding, 1 fowl developed neuritis after fifty-nine days, and 2 fowls remained well after sixty-three days, when the experiment was discontinued.

Experiment 31.—Four fowls were fed on polished rice, and in addition were given daily 10 grams of white wheat bread such as is issued to troops. One fowl developed typical neuritis in twenty-six days, 1 in twenty-seven days, and 1 in thirty-two days. One fowl remained well after forty-eight days, when the experiment was discontinued.

Experiment 32.—Four fowls were fed on polished rice, and in addition were given daily 10 grams of raw beef. One fowl developed neuritis in nineteen days, 1 in forty-eight days, and 1 in fifty-seven days, while 1 fowl remained well after sixty-three days, when the experiment was discontinued.

Experiment 33.—Four fowls were fed on polished rice, and in addition were given daily 10 grams of boiled beef. One fowl developed neuritis in twenty-five days, while the other 3 fowls remained well after sixty-three days, when the experiment was discontinued.

Experiment 34.—Four fowls were fed on polished rice, and in addition were given daily 10 grams of dried peas. All 4 fowls remained in perfect health when the experiment was discontinued after sixty-three days' feeding.

Experiment 35.—Four fowls were fed on polished rice, and in addition were given daily 5 cubic centimeters of canned milk (Highland Cream). One fowl developed neuritis in nineteen days, 1 in twenty-three days, and 1 in thirty-two days. One fowl remained well after sixty-three days' feeding.

Experiment 36.—Four fowls were fed on polished rice, and in addition were given daily 5 cubic centimeters of fresh cow's milk. One fowl developed neuritis in twenty-three days, 1 in thirty-one days, and 2 fowls remained well after sixty-three days.

Experiment 37.—Four fowls were fed on polished rice, and in addition were given daily 10 grams of unroasted peanuts. One fowl died of avian diphtheria after twenty-eight days' feeding without developing neuritis, and the other 3 fowls remained well after sixty days' feeding.

It should be noted that in all of these experiments the birds were fed these different articles of diet by hand, so that there can be no doubt as to what they actually received. It is a striking fact that the only two of these groups that received complete protection were those in which the fowls were given a daily addition of 10 grams of dried peas and 10 grams of peanuts.

V. SUMMARY.

1. There appear to be three types of polyneuritis gallinarum:

(a) A form in which the symptoms of neuritis and those of general prostration are combined. This is the usual form. When these birds are given an extract of rice polishing, they improve at once in general condition, but the symptoms of neuritis only disappear after several months of treatment..

(b) A form in which there is pronounced neuritis, but the fowl remains in good general health. These fowls will also recover from the neuritis after several months' treatment with the extract of rice polishings.

(c) A form described above as fulminating cases, in which the symptoms of neuritis are absent, but in which greater general prostration occurs. These fowls recover speedily when given extract of rice polishings.

2. In polyneuritis gallinarum developing after a prolonged diet of polished rice the heart may show no microscopic change. In other cases the heart may show slight œdema, a slight increase in pigment, or an appearance of beginning mucoid or parenchymatous degeneration.

3. While in marked cases of neuritis every fiber of the vagus may and usually does show degenerative changes, as indicated by the Marchi method, no fiber has been observed in which the change was far advanced. We have not been able to correlate the extent of degeneration in the vagus with the change in the heart nor with the severity of the symptoms before death.

4. No marked changes suggestive of degeneration have been observed in the cervical sympathetic ganglia nor in the post- or preganglionic fibers.

5. In every one of the 56 fowls which had been fed thirty-five days or more on polished rice, changes indicative of degeneration (Marchi method) were seen in the fibers of the sciatic nerve, regardless of whether symptoms of neuritis had or had not manifested themselves before death. (Plate II, fig. 3, and Plate XI, fig. 24.)

6. Advanced degeneration in the peripheral nerve fibers manifests itself by a change in both myelin sheath and in the axis cylinder. The myelin sheath breaks up into globules and droplets, which stain black in the Marchi solution—indicative of fatty degeneration. The axis cylinder breaks up into segments or disintegrates in all those fibers showing advanced degeneration in the medullary sheath. (Plate V, fig. 9.)

7. The degree of degeneration in the sciatic nerve corresponds closely with the extent of the paralysis of the legs. Advanced degeneration was observed in only 10 to 15 per cent of the fibers of the sciatic nerve of fowls showing pronounced symptoms of leg paralysis. In the remaining fibers the change was not advanced.

8. We could detect no difference in the degeneration in the sciatic and its peripheral branches either as regards extent or time of onset.

9. Degeneration was observed in both dorsal and ventral nerve roots, being most pronounced in the latter.

10. Degenerative changes in both axis cylinder and medullary sheath were seen in fibers of all columns of the thoracic spinal cord. (Plate V, fig. 10, Plate VI, figs. 11 and 12, Plate VII, fig. 13.)

11. Changes were observed (Nissl method) in certain large cells of both ventral and dorsal horns of the gray substance of the lumbosacral cord. In the cells of both horns, the tigroid bodies were not visible, and the stainable material was collected at one side of the cell around the base of one of the processes. Cells were occasionally seen whose nuclei stained very poorly. (Plate X, fig. 22.)

12. Mitochondria were observed in the nerve cells of the lumbosacral cord, even though there was a pronounced alteration of the tigroid bodies. The mitochondria here were of similar appearance and almost or quite as numerous as in corresponding cells of the normal cord.

13. In the medullary sheath of fibers of the sciatic nerve of normal fowls numerous small, bacilli-like rods, arranged radially around the axis cylinder, were made apparent by the various mitochondria methods. These structures are probably mitochondria. (Plate VII, fig. 14.)

14. Fowls show alteration in the medullary sheath of the sciatic fibers after only seven days on a polished rice diet. In the sciatic fibers of fowls fed for seven days on polished rice alone, the rods are scarcely to be observed. Instead, the stainable material shows remarkable alterations and occurs in the form of irregular, branched, and anastomosing masses. (Plate VIII, fig. 15.)

15. In fowls fed for a longer period, these masses show, in a certain percentage of the fibers, progressive changes which manifest themselves in the form of more definite skeins and segmentations and larger masses and globules of stainable material. In fibers showing marked degeneration by the Marchi method these occur as larger or smaller vesicular, oval globules and correspond to the black globules shown by the Marchi preparations. Plate VIII, fig. 16, and Plate IX, figs. 17 and 18 illustrate these changes.

16. When fowls are fed on polished rice and in addition given some protective substance, such as is contained in extract of rice polishings or in various foods, but in insufficient quantity to confer complete protection, the disease appears in its char-

acteristic form and with all the evidences of nerve degeneration, but after a prolonged incubation period—forty-five to ninety days, or even after one year of such feeding (Eijkman).

17. When fowls are fed on polished rice and in addition receive daily 10 grams of white wheat bread or 5 cubic centimeters of canned milk, they receive little or no protection from polyneuritis gallinarum.

18. When fowls are fed on polished rice and in addition receive daily 10 grams of meat cooked or uncooked, 10 grams of potatoes cooked or uncooked, or 5 cubic centimeters of fresh cow's milk, they receive partial protection as indicated by the prolongation of the incubation period.

19. When fowls are fed on polished rice and in addition receive daily 10 grams of dried peas or 10 grams of peanuts, they receive complete protection for at least sixty days.

VI. CONCLUSIONS AND DISCUSSION.

CONCLUSIONS.

1. In addition to the changes demonstrated above, Funk(22) has shown that chemical changes take place in the brains of fowls suffering from polyneuritis gallinarum. It therefore appears that the disease is not simply a peripheral neuritis as has been generally supposed. On the contrary, the entire nervous system is affected.

2. The symptoms of the disease are not chiefly referable to degeneration of the peripheral nerves, since the degeneration occurs before symptoms arise, and because advanced degeneration may be present accompanied by no symptoms at all, and because degeneration of the nerves remains after recovery has occurred.

DISCUSSION.

It is apparent from this study that the symptomatology and pathology of polyneuritis gallinarum can not be regarded as identical with that of beriberi in man. We have never observed any œdema in fowls at all comparable to wet beriberi in man, and while there are undoubtedly slight changes in the heart of fowls suffering from polyneuritis, there is none of the hypertrophy which is such a characteristic finding in human beriberi. In spite of these facts, however, there is more similarity than difference between the two diseases.

When we consider the etiology of the two diseases, the case is different. The experiments of Fraser and Stanton(23) and of

Strong and Crowell(24) prove beyond the shadow of a doubt that beriberi in man is the result of a too nearly exclusive diet of polished rice, or of other foods lacking in the neuritis-preventing substance. It has been proved beyond question that polyneuritis of fowls is due to a similar diet. The cause of the two diseases is therefore the same. Therefore, the conclusion already published by Chamberlain and Vedder(6) "that the two conditions are due to the same pathological process causing slightly different manifestations in diverse species" is abundantly justified. Since this is the case, it is evident that we may deduce some important facts concerning the relation between diet and beriberi from the above feeding experiments on fowls.

Both meat and potatoes contain a certain, but relatively small, amount of the neuritis-preventing substance. This explains the immunity from beriberi of those races whose main articles of diet are meat and potatoes. On the other hand, the man who eats a pound of polished rice daily with a small or occasional addition of meat will not receive complete protection from beriberi, although the onset of the disease may be delayed by the meat thus eaten. Eijkman showed that fowls fed entirely on potato starch did not develop polyneuritis. This confirms our observation that potatoes contain the neuritis-preventing substance. If men live chiefly on potatoes, as many Irish peasants have often done, they will be protected from beriberi, but a diet of polished rice with a small addition of potatoes would result in the production of beriberi.

Our observation that ordinary white bread is quite lacking in the neuritis-preventing substance is also interesting. This confirms the observation of Holst(25) that animals fed on wheat bread developed neuritis while those fed on rye bread did not. Beriberi began to appear on Norwegian sailing ships in 1894, when the diet of the sailors was changed. Prior to that date they ate largely rye bread. Subsequently they received wheat bread and developed beriberi. The occurrence of ship beriberi among sailors who live chiefly on bread or hardtack made of white or overmilled wheat flour is thus explained.

Little(26) has also recently reported the occurrence of beriberi in Labrador and Newfoundland among a native population living during certain seasons almost exclusively on white wheat flour. This has been taken in some quarters as throwing doubt upon the theory that beriberi is produced by a diet of polished rice. However, since polished rice only produces beriberi because of its deficiency in the neuritis-preventing substance and since

wheat flour is shown to be similarly deficient,[6] this observation is a strong confirmation of that theory. It is evident that we can not prevent beriberi by adding bread to the ration.

The experiments show that peas and peanuts possess the property of preventing the disease equally with beans or mongos (katjang idjo). It is probable that most leguminous seeds possess this property. This is of practical importance since it indicates that peas will be equally as efficacious as beans in preventing beriberi when added to a ration for use on shipboard or for natives subsisting chiefly upon rice.

It will be noted that both meat and potatoes when cooked appeared to afford more protection than when eaten raw. It had been expected that the reverse would be the case, since it was supposed that some of the protective substance might be destroyed by cooking. We are at present unable to account for the fact that the cooked food appeared to afford greater protection than raw food. These experiments, however, dispose of the objection so often raised against the deficiency theory that men who eat various quantities of other food in addition to the staple diet of rice may nevertheless develop beriberi. It is clearly shown that most articles of diet contain only small amounts of the protective substance, and that when even moderate quantities of many foods are added to a staple of rice, which practically contains none at all, the deficiency still exists.

Funk(27) has apparently isolated the neuritis-preventing substance from rice polishings and other foodstuffs, and has shown that it is an organic base probably belonging to the pyramidine group having a formula of $C_{17}H_{20}N_2O_7$ and a melting point of 233° C. This base, or vitamine as Funk calls it, was precipitated by phosphotungstic acid. Chamberlain, Vedder, and Williams(7) had already tried this method unsuccessfully, but they do not regard their failure as disproving Funk's results, owing to the fact that their extract was prepared in a slightly different manner from that used by Funk.

Accepting Funk's discovery as correct, from the above conclusions we deduce the following: The organic base or vitamine, which prevents the development of polyneuritis gallinarum and which is present in varying amounts in different foodstuffs, is a building stone which is essential for the normal metabolism

[6] Little also showed that the disease in Labrador could be prevented and cured by the use of bran or polishings from wheat, thus clearly demonstrating that the disease in this case was also due to a food deficiency.

of nervous tissue. Moreover, a certain amount of this vitamine is necessary for each fowl constantly as is shown by the fact that degeneration of the nerves may be demonstrated within seven days after the supply of this vitamine is cut down by a polished rice diet. The amount necessary, however, varies for different fowls according to their individual idiosyncrasy, because, as has been shown, some fowls are more susceptible to this deficiency than others. If the supply of vitamine is cut down by feeding on polished rice, or any other dietary which contains an insufficient amount of this substance, the normal metabolism of the nervous system at once suffers. Should this faulty diet be continued, the degeneration of the nervous system progresses steadily, until a point is finally reached when the symptoms of polyneuritis appear. Even though the amount of this necessary substance is reduced only very slightly below the quantity essential for a given fowl, degeneration occurs though more slowly, and the symptoms of neuritis will appear if the reduction be continued for a sufficient length of time.

The question naturally arises if this vitamine is essential to normal nervous metabolism, why are any fowls on a polished rice diet protected from polyneuritis gallinarum and any men from beriberi? This is probably due to the fact that the metabolic processes are much more active in some individuals than in others. Those fowls whose metabolic processes are very active require larger amounts of vitamine, and succumb most promptly on a diet of polished rice. In those fowls whose metabolic processes are more sluggish, the incubation period is longer. It is probable that even polished rice contains a trifling quantity of this vitamine in comparison with other food. Therefore, some fowls whose metabolism is exceptionally sluggish may be able to subsist for some time on this polished rice without developing neuritis. However, in most cases this protection is not complete as is shown by the fact that degeneration may be demonstrated in their nerves, although they are apparently in good health. Probably in most instances the protection apparently enjoyed by some fowls on polished rice is only partial, and if the diet be continued long enough practically all will succumb. The interesting case related by Eijkman where the fowl developed neuritis only after a year's feeding is a case in point. The same explanation will account for the fact that some men are more susceptible to beriberi than others and that some are apparently exempt. From the fact that the incubation period in man averages three or four months as compared with only twenty-six days in the fowl,

we may infer that the amount of vitamine required by man is much less proportionately than that required by the fowl.

The question of loss of weight also requires some elucidation. It is quite apparent that if the metabolism of the entire nervous system suffers from the loss of this vitamine, the rest of the body tissues will also waste away as a result and there will be great loss of weight. But how account for the loss of weight that occurs in fowls fed on polished rice, but which have received this substance in extract of rice polishings? It is believed that the loss of weight in these cases may be due to the fact that the fowl living on this diet is not in equilibrium of metabolism with regard to other substances. For instance, it is quite possible that it is suffering from a deficiency of fat, of phosphorus, of potassium, and of other substances that are deficient in polished rice. This is quite enough to account for the loss of weight in these cases.

The cause of the great prostration in this disease should also be considered. Some birds present this symptom while others do not. We have seen that the degree of degeneration of the vagus bears no relation to the degree of prostration of the fowl, and that there is not sufficient change in the heart to account for the sudden death. It is highly improbable that the prostration is due to the peripheral neuritis. There are several possible explanations of this phenomenon. Since the entire nervous system is probably affected in this disease, we can easily suppose that this general prostration occurs when the higher nerve centers either in the brain or the cord are affected by the degenerative process.

On the other hand, a most attractive hypothesis presents itself to account for this condition. Let us suppose that rice polishings and other foods contain two substances or vitamines that are essential for proper metabolism. One of these is the neuritis-preventing substance, and the other a substance that prevents general prostration, cardiac failure, etc. This hypothesis would account for the three classes of symptoms observed in fowls suffering from polyneuritis. Those cases belonging to class 1 evidently suffer from the deprivation of both vitamines. The cases in class 2 suffer from deprivation of the neuritis-preventing vitamine, but have received sufficient of the second vitamine to prevent the occurrence of prostration; while those fowls in class 3 have received sufficient of the neuritis-preventing vitamine to defer at least the symptoms of nerve degeneration, but not enough of the second vitamine to prevent their dying of general prostration. This supposition would account for the three types

of beriberi in the same way. It would also offer a rational explanation for the confusing fact observed in ship beriberi, that neuritis is sometimes apparently entirely absent, and is usually slight, while in other cases the neuritis is pronounced. On account of this fact, many observers such as Nocht have not been willing to accept ship beriberi as true beriberi. If this explanation were correct, this difficulty would disappear, for it would evidently be possible for the symptoms of wet beriberi and the symptoms of polyneuritis to be mixed in all sorts of forms depending upon the proportions of these two essential vitamines that were present in the diet consumed in each case. Moreover, this hypothesis might account for the existence of the disease epidemic dropsy which some observers have thought to be a form of beriberi while others have denied this. Epidemic dropsy according to this theory would be caused by the lack of this second vitamine. There are many indications that this hypothesis may be the correct one, but at present experimental evidence is lacking to prove its validity. Experiments are being continued by Vedder and Williams.

The degeneration found in the cord presents another field for speculation. It is generally believed by physiologists that the fibers of the cord are incapable of regeneration. Yet here we have an instance where degeneration has undoubtedly occurred and where apparently complete recovery also takes place. Can this recovery occur without regeneration of these fibers of the cord by the process of training other fibers to assume the function of those that have been destroyed, or does regeneration of these fibers actually occur?

In order to study regeneration of the nerves, several fowls suffering from pronounced polyneuritis were saved by administration of extract of rice polishings. It was observed that after a few days a pronounced spasticity, similar to that observed when the symptoms of neuritis were first manifested and described above, set in. This spastic condition remained for two months after daily administration of extract of rice polishings was commenced, without apparent improvement. *It then suddenly disappeared in a single day.* On one day, the fowl was hardly able to totter about on its toes, and on the next day it was walking about like a normal fowl. Nor was this an isolated observation. Two questions are suggested. What is the cause of this spasticity, and what causes it to disappear suddenly? In this connection we may recollect that the symptoms of paralysis also often appeared in a single day, although the degeneration of the nerves

was very gradual. The sudden appearance of the paralysis and the immediate cures reported by Funk after administration of the vitamine could be explained if this vitamine constitutes an essential element for the metabolism of the nerve cells. The changes found by us in the nerve cells of the cord appear to lend support to this view. These changes are probably not a true degeneration, since similar changes have been observed in nerve cells after fatigue. The paralysis, therefore, may appear suddenly when the nerve cells become exhausted from the lack of this vitamine essential to their metabolism, and disappear equally promptly when this substance is supplied in sufficient quantity.

A definite answer to all of these questions is manifestly beyond the scope of this paper. However, the questions which have been raised by this study make it certain that this interesting disease of fowls deserves further investigation, and we may expect our knowledge of the metabolism and pathology of the nervous system to be greatly extended by such work.

REFERENCES.

(1) Eijkman. Eine beriberiähnliche Krankheit *Virchow's Arch.* (1897), **168**, 523.
(2) Maurer. Polyneuritis der Hühner und Beriberi *Münch. Med. Wochenschr.* (1907), **54**, 131.
(3) Fraser and Stanton. The etiology of beriberi. Studies from Institute for Medical Research. Federated Malay States (1911), No. 12.
(4) Shiga and Kusama. Über die kakke- (beriberi-) ähnliche Krankheit der Tiere. *Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* (1911), **15**, 59.
(5) Chamberlain and Vedder. A contribution to the etiology of beriberi. *Phil. Journ. Sci.* (1911), **6**, 251.
(6) Idem. A second contribution to the etiology of beriberi. *Ibid.* (1911), **6**, 395.
(7) Chamberlain, Vedder, and Williams. A third contribution to the etiology of beriberi. *Ibid.* (1912), **7**, 39.
(8) Vedder. A fourth contribution to the etiology of beriberi. *Ibid.* (1912), **7**, 415.
(9) Engelmann. *Pflüger's Arch.* (1876) **13**, 474.
(10) Monakow. Cited by Obersteiner. The anatomy of the central nervous organs. Translated by Alexander Hill. London (1900), 139.
(11) Nissl. *Centralbl. f. Nervenh. u. Psychiat.* (1894), **17**, 337; *Neurol. Centralbl.* (1896), **15**, 9.
(12) Bensley. *Am. Journ. Anat.* (1911), **12**, 297.
(13) Meves. *Arch. f. mikros. Anat. u. Entw.* (1908), **71**, 573.
(14) Benda. Verh. der Anat. Gesellsch. Bonn (1901).
(15) Regaud. *Compt. rend Soc. biol.* (1908), **65**, 660.
(16) Altmann. Die Elementarorganismen und ihre Beziehungen zu den Zellen. 2. Auflage. Leipzig (1894).

(17) COWDRY. *Anat. Record.* (1912), 6, 33.
(18) RUBASCHKIN. *Anat. Hefte.* 1st Abt. (1910), 41, 399.
(19) NAGEOTTE. *Arch. f. mikros. Anat.* Abt. 1 (1911), 77, 245.
(20) MANN. *Journ. Anat. & Phys.* (1895), 29, 100.
(21) HODGE. *Journ. Morph.* (1892), 7, 1.
(22) FUNK. The effect of a diet of polished rice on the nitrogen and phosphorus of the brain. *Journ. Physiol.* (1912), 44, 50.
(23) FRASER AND STANTON. Studies from Institute for Medical Research. Federated Malay States (1909), No. 10; *Lancet* (1909), 1, 451.
(24) STRONG AND CROWELL. *Phil. Journ. Sci.* (1912), 7, 271.
(25) HOLST. *Trans. Soc. Trop. Med. & Hyg.* (1911), 5, 76.
(26) LITTLE. Beriberi caused by fine white flour. *Journ. Am. Med. Assoc.* (1912), 58, 2029.
(27) FUNK. The preparation from yeast and certain foodstuffs of the substance the deficiency of which in diet occasions polyneuritis in birds. *Journ. Physiol.* (1912), 45, 75.

ILLUSTRATIONS.

Photomicrographs by Martin and Cortes. Camera lucida outlines were used in the preparation of all the drawings.

Plate I.

Fig. 1. Photomicrograph of a teased preparation of sciatic nerve from a normal fowl. (Marchi method.) Zeiss 4 × 4 mm.

2. Transverse section of lateral fiber column of thoracic spinal cord of normal fowl. (Marchi method.) At (*a*) blackened masses are seen in close proximity to the fibers. At (*b*) the black globules appear to be within the fiber.

Plate II.

Fig. 3. Photomicrograph of a teased preparation of the sciatic nerve of fowl 6. (Marchi method.) For two days this fowl had been unable to stand, but appeared to be in good condition otherwise. Different stages of degeneration are here illustrated. Note occasional globules of degenerated myelin in some fibers (*a*), a diffuse blackening of the medullary sheath with indications of segmentation in fiber (*b*), and large globules of degenerated myelin in fiber (*c*). Zeiss 4 × 4 mm.

4. Fiber from sciatic nerve of fowl 6, showing advanced degeneration. (Marchi method.) Note large globules and small droplets of degenerated myelin and clear spaces between. The neurilemma sheath is well shown. Zeiss 4 × 4 mm.

Plate III.

Fig. 5. Teased preparation of vagus of fowl 13 (good general condition, but unable to walk since three days). (Marchi method.) This figure shows relatively advanced degeneration (for our series). Numerous large globules of degenerated myelin are seen here and there. At the periphery where the individual fibers are best seen, globules are to be observed at frequent intervals in every fiber. Zeiss 4 × AA.

6. High-power magnification of an area of the same preparation.

Plate IV.

Fig. 7. Drawing of a nerve fiber from the sciatic to show early stage of myelin degeneration. (Marchi method.) Note diffuse blackening, tendency to segmentation (*s*), and beginning globular arrangement of the myelin (*G*); (*n*) is nucleus of neurilemma sheath. Zeiss 4 × 4 mm. Apochomatic (?).

8. From a transverse section of a sciatic nerve showing marked degeneration, to illustrate the percentage of fibers showing varying degrees of degeneration in a given plane. A majority of the fibers show blackening to some extent. *a*, *b*, *c*, etc., are cross sections of the larger globules of degenerated myelin. Zeiss 2 × 4 mm. Apochomatic.

PLATE V.

FIG. 9. Advanced degeneration in a nerve fiber from the sciatic, showing also segmentation of the axis cylinder. Swelling of the medullary sheath and the granular appearance of the axis cylinder are well shown: *a*, axis cylinder; *n*, node of Ranvier. Hæmatoxylin and acid fuchsin. Zeiss 3 × 1/12 oil immersion. Reduced one-half.

10. Cross section of fibers of the ventromarginal column of the thoracic cord from fowl 14, showing pronounced symptoms of peripheral neuritis and marked degeneration in the sciatic nerve. At *a* and *a'* two fibers are seen in which the axis cylinder has undergone fragmentation and granulation. Hæmatoxylin and acid fuchsin. Zeiss 4 × 1/12 oil immersion.

23. Fiber from the ventral portion of the midbrain of fowl 72 with pronounced neuritis. Small globules of degenerated myelin are clearly seen. Marchi method. Leitz 3 × 6.

PLATE VI.

FIG. 11. Transverse section of the posterior columns of the thoracic cord of fowl 14, showing pronounced symptoms of peripheral neuritis and marked degeneration in the sciatic. At *a*, *a'* and *a''*, three fibers are seen which undoubtedly contain globules of degenerated myelin. Marchi method. Zeiss 4 × AA. apr.

12. High-power illustration of same preparation as fig. 11—dorsomarginal (Gall's) column. Degenerated areas within the fibers are clearly seen at *a* and *a'*. Marchi method. Zeiss 4 × 4 apcr.

PLATE VII.

FIG. 13. Longitudinal section of lateral column of thoracic cord of fowl 15, showing pronounced symptoms of peripheral neuritis and marked degeneration in the sciatic nerve. At *a*, *a'*, *a''*, and *a'''*, fibers are seen containing globules and droplets of degenerated myelin. Marchi method. Zeiss 4 × AA. apcr.

14. Longitudinal section of the sciatic nerve of a normal fowl stained by the mitochondria (iron-hæmatoxylin) method. The stainable substance is seen in the form of little rods arranged radially around the axis cylinder. Note fibers *a*, *a'*, and *a''*. At *a* the rods show a tendency to cross. Zeiss 4 × 4 apcr.

PLATE VIII.

FIG. 15. Longitudinal section of the sciatic nerve of a fowl fed for seven days on polished rice to illustrate the changes in the medullary sheath. The stainable substance is seen as larger or smaller irregular and branched masses. In fiber *b* a network formation is seen. Mitochondria (iron-hæmatoxylin) method. Zeiss 4 × 4 apcr.

16. Same, from a fowl fed for eleven days on polished rice. The segmentation is a little more pronounced and in some fibers the masses are larger. Note fibers *a*, *b*, *c*, and *d*. Zeiss 4 × 4 mm. apcr.

Plate IX.

Fig. 17. Longitudinal section of the sciatic nerve of a fowl fed for eighteen days on polished rice. In fiber *b*, the stainable material has collected into larger masses which in places coalesce into globules, *b*. Mitochondria (iron-hæmatoxylin) method. Zeiss 4 × 4 mm. apcr.

18. Longitudinal section of the sciatic nerve of fowl 14, showing pronounced symptoms of peripheral neuritis and marked degeneration in the sciatic. Globules are more discreet than in fig. 17, and the stainable material is for the most part at the contoured periphery of the globules, *a*. The other fibers show a diffusion of the stainable material. Mitochondria (iron-hæmatoxylin) method. Zeiss 4 × 4 mm. apcr.

Plate X.

Fig. 19. Nerve cell from spinal cord of normal fowl. Nissl stain. Zeiss 4 × 4 mm.

20. Same. Giemsa blood stain.

21. Nerve cell from ventrolateral group of the lumbosacral cord of a fowl (No. 48, twenty-four days on polished rice) with marked paralysis of the legs and marked degeneration in the sciatic. The tigroid bodies are no longer apparent. The stainable material which appears granular has collected at one side of the cell around the implantation cone (*a*) of the axis cylinder. Giemsa blood stain. Zeiss 4 × D.

22. Nerve cell from same preparation as fig. 21, same group. Note bulging of cell at *a* where the stainable material is collected in one mass. The nucleus, *n*, shows degenerative changes. Zeiss 4 × 1/12 oil immersion. Camera lucida, reduced ½.

Plate XI.

Fig. 24. Teased preparation (Marchi method) of the sciatic nerve of fowl 16 which was fed for thirty-five days on polished rice without showing any symptoms of neuritis. At *a*, a fiber is seen showing advanced degeneration. Other fibers show less marked change. Zeiss 4 × 4 mm.

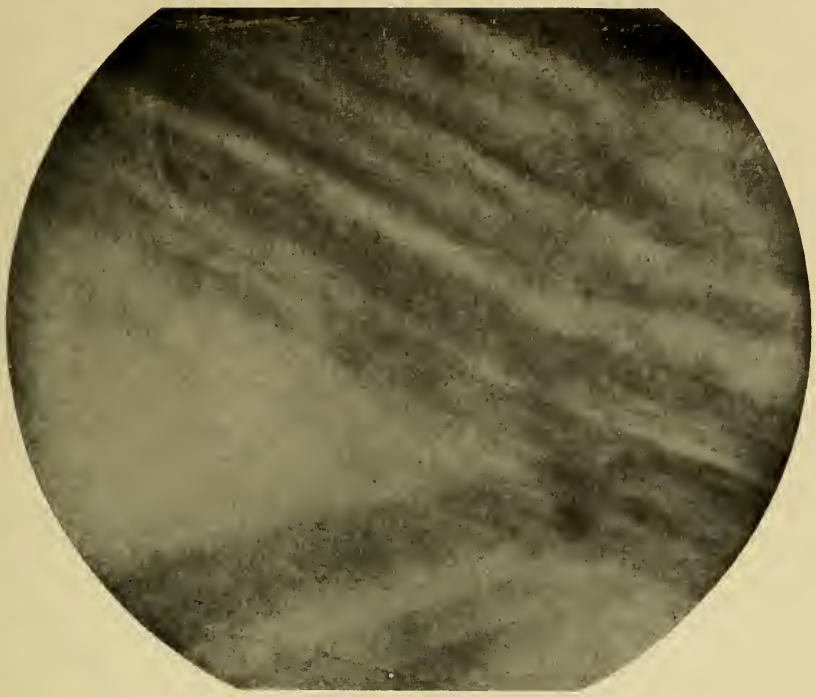


Fig. 1.

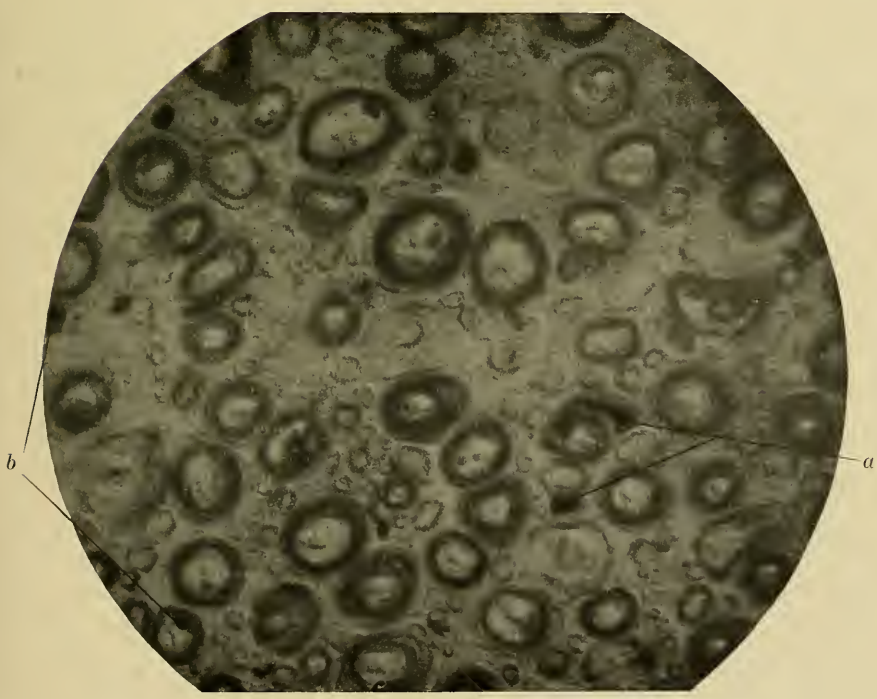


Fig. 2.

PLATE I.

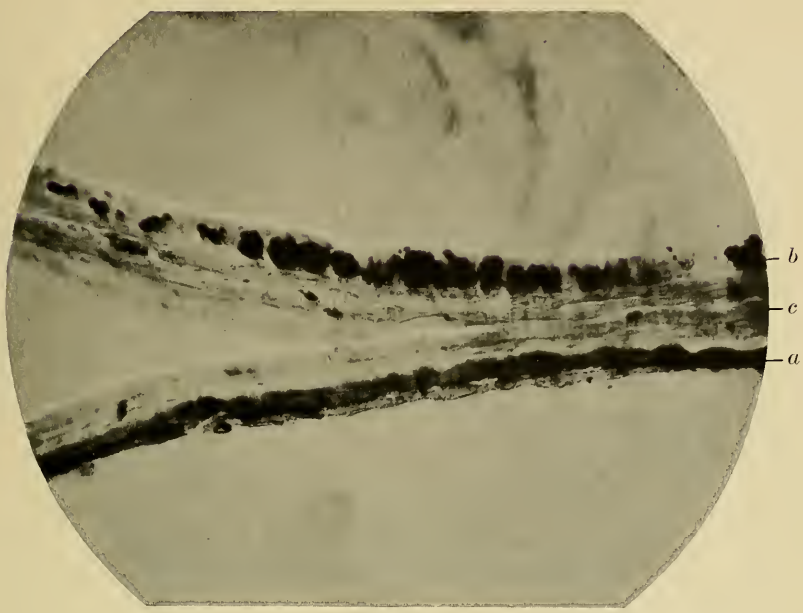


Fig. 3.

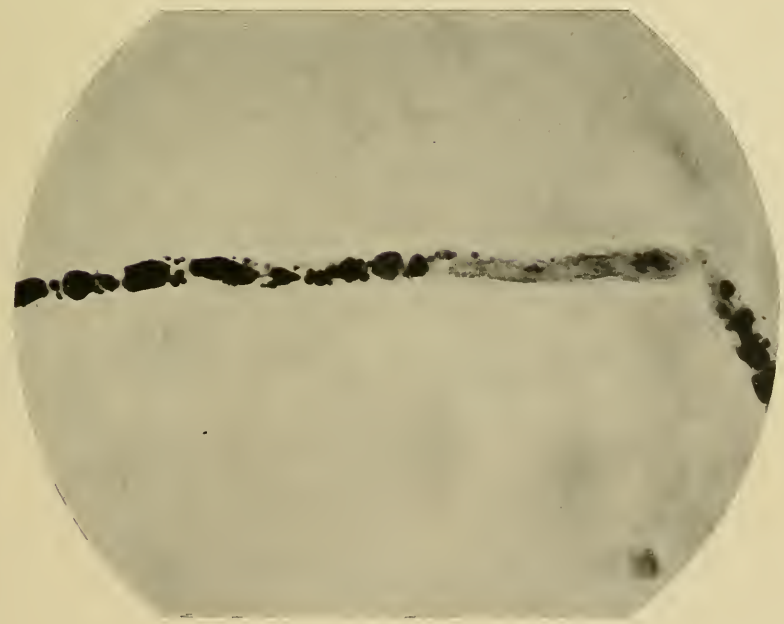


Fig. 4.

PLATE II.

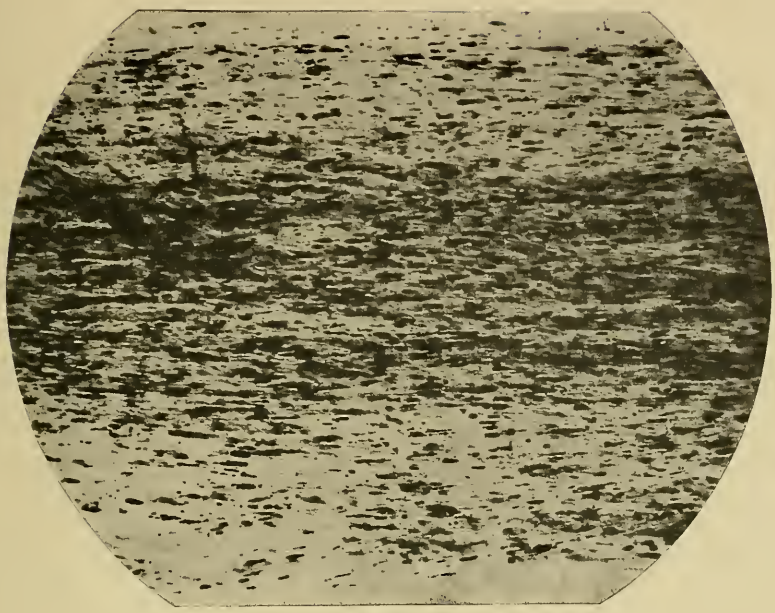


Fig. 5.

Fig. 6.

PLATE III.

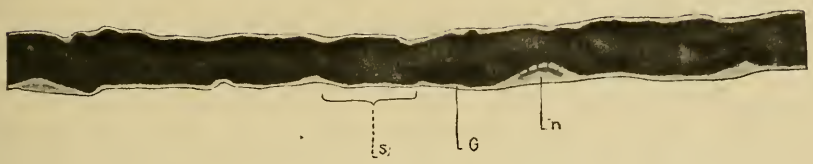


Fig. 7.

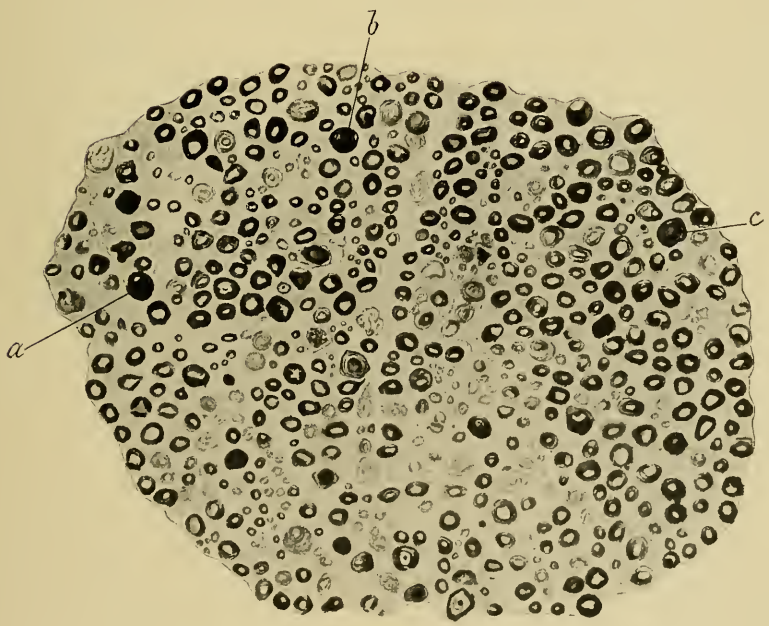


Fig. 8.

PLATE IV.

Fig. 9.

Fig. 23.

Fig. 10.

PLATE V.

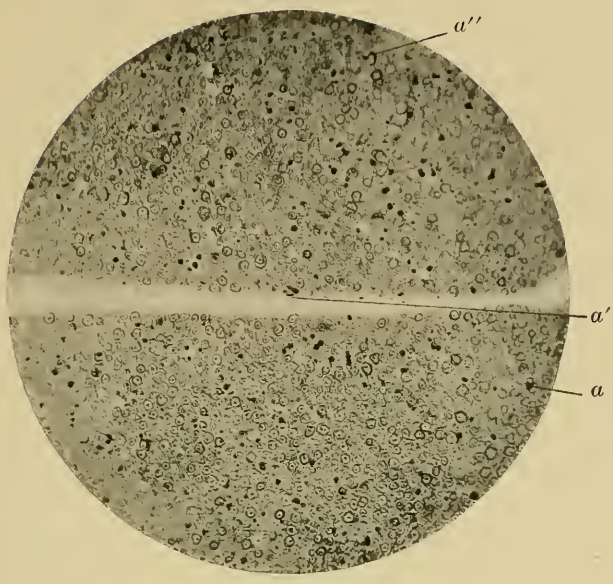


Fig. 11.

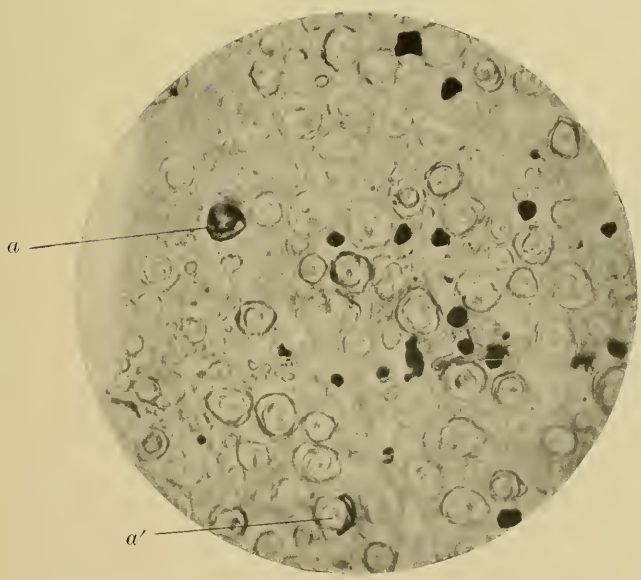


Fig. 12.

PLATE VI.

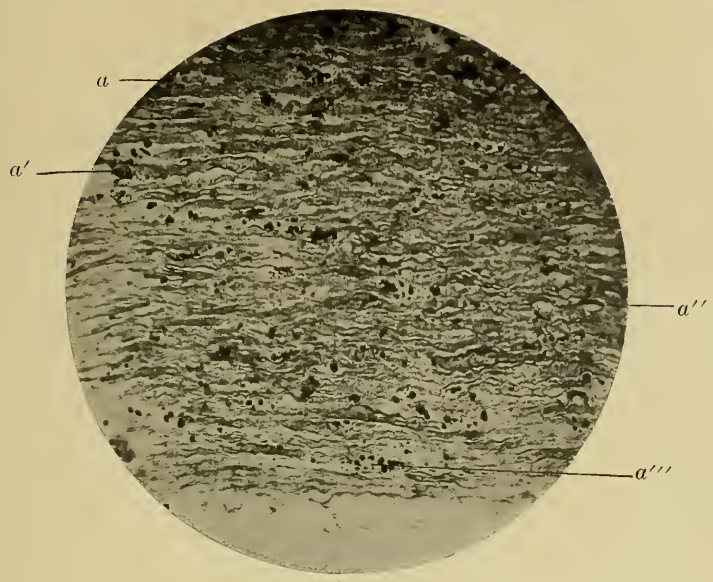


Fig. 13.

Fig. 14.

PLATE VII.

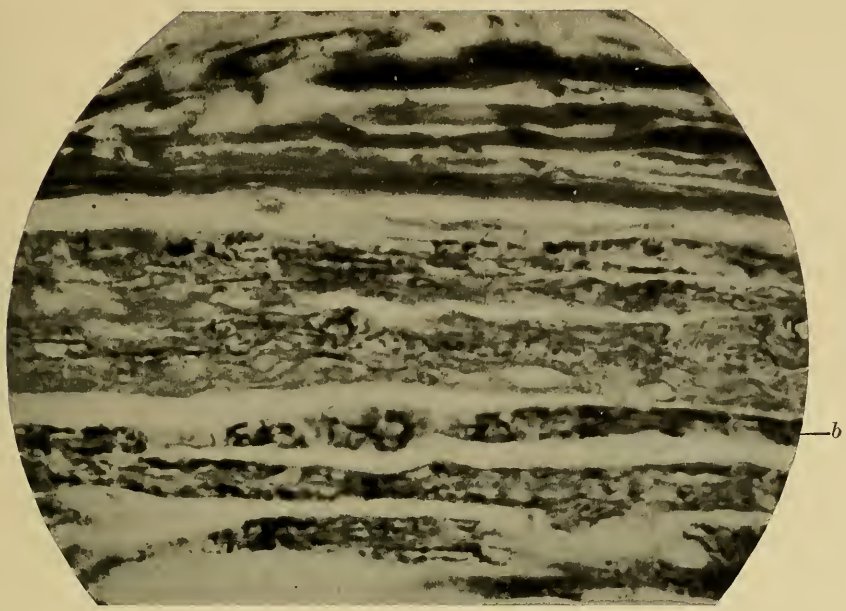


Fig. 15.

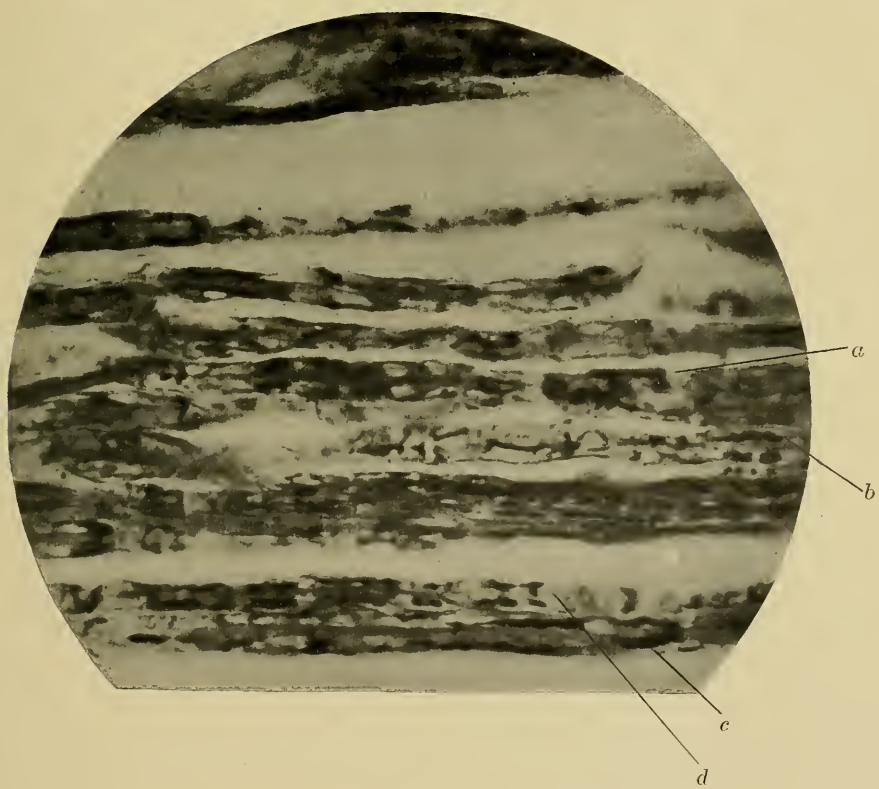


Fig. 16.

PLATE VIII.

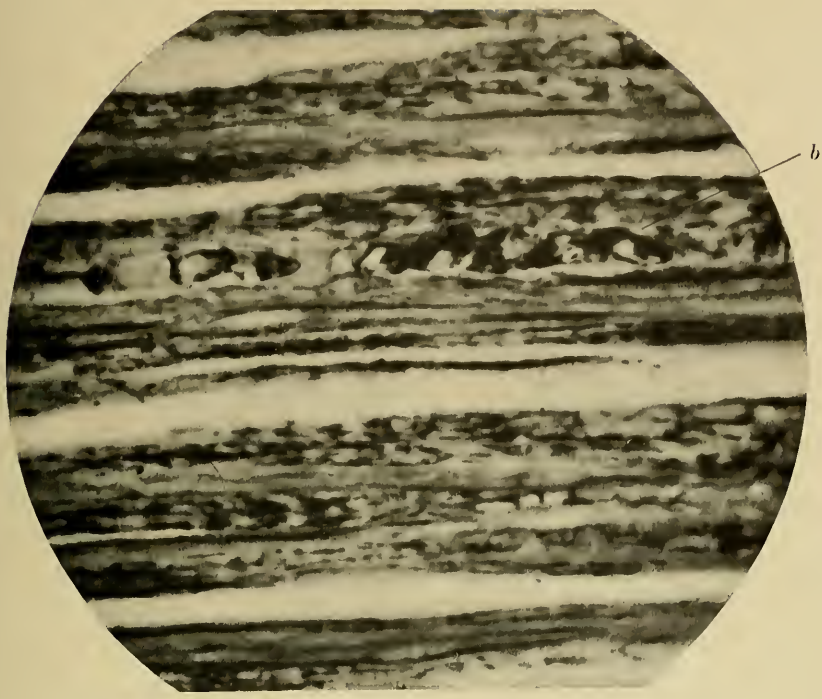


Fig. 17.

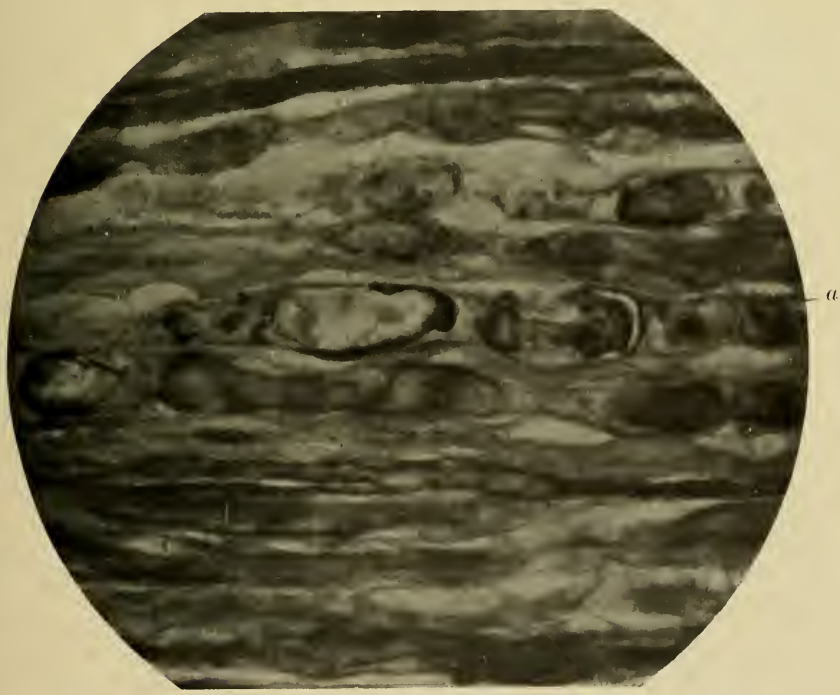


Fig. 18.

PLATE IX.

Fig. 19.

Fig. 20.

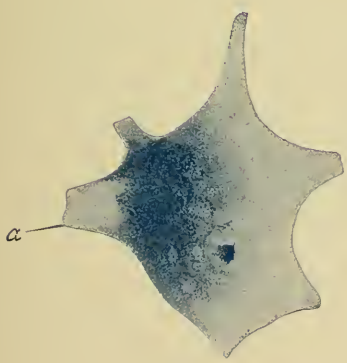


Fig. 21.

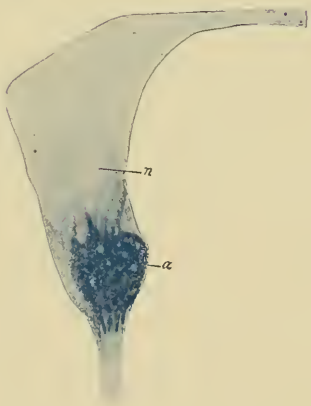


Fig. 22.

PLATE X.

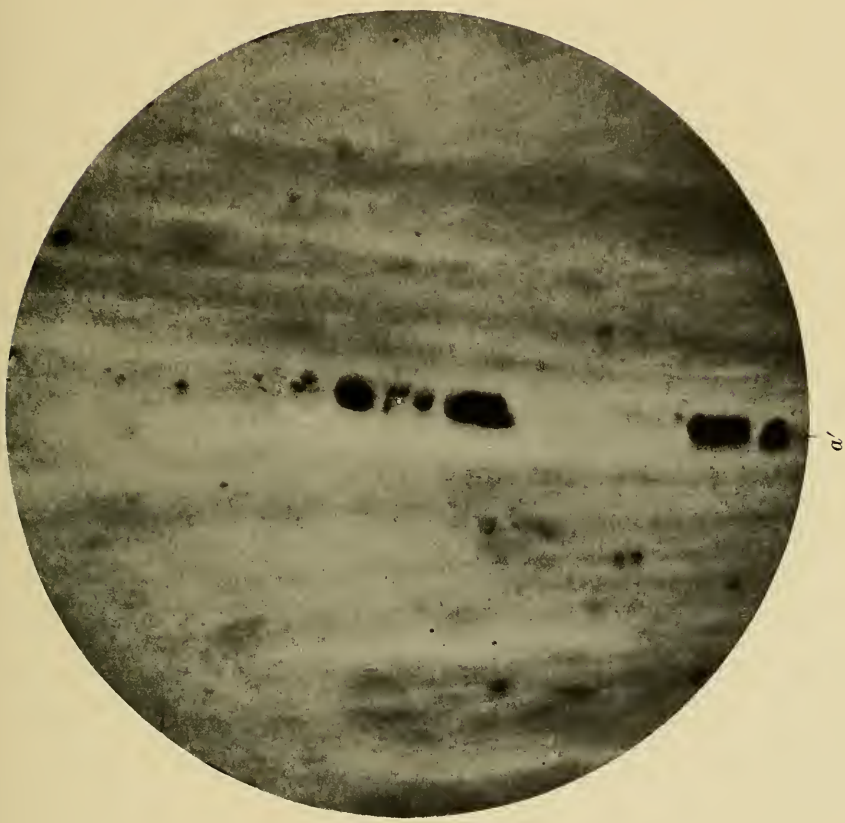


Fig. 24.

PLATE XI.

REPORT OF THE PATHOLOGICAL EXAMINATIONS FOR ONE YEAR FROM THE SURGICAL CLINIC OF THE PHILIPPINE GENERAL HOSPITAL.

By P. K. Gilman

(From the Philippine General Hospital and the College of Medicine and Surgery, University of the Philippines.)

and

B. C. Crowell.

(From the Biological Laboratory, Bureau of Science, and the College of Medicine and Surgery, University of the Philippines.)

During the year from July 1, 1911, to June 30, 1912, the specimens from the operating rooms of the Philippine General Hospital have been examined by the authors, who were detailed to the work by the late director of the Bureau of Science. Within this period, the first attempt at complete organization of this work was made, with the result that during the latter part of the year all of the specimens from the operating rooms have been examined and complete records have been filed. While it is true that during the latter part of the year routine examination of all specimens was made, no selection of the material to be examined during the earlier part was exercised, those being examined for which time was available.

The following is a statistical survey of the material:

Four hundred forty-eight specimens derived from 415 cases were examined as follows:

Gynæcological specimens	233 or 52 per cent.	General surgical specimens	174 or 38.9 per cent.
Genito-urinary specimens	41 or 9.1 per cent.		

GYNÆCOLOGICAL SPECIMENS.

Uterine scrapings	122	Ovaries	42
Cervices, sections of	32	Fallopian tubes	13
Uteri	24		

GENITO-URINARY SPECIMENS.

Male genitalia	30	Kidneys	4
Female genitalia	7		

GENERAL SURGICAL SPECIMENS.

Appendices	75	Liver	1
Breasts	17	Pancreas	1
Lymphatic glands	32	Eye	2
Stomach and intestines	9	Nerves	4
Thyroids	13	Skin, muscles, and bone	39
Salivary glands	2		
Tumors of neck, origin undetermined	8		

In detail, these were as follows:

GYNÆCOLOGICAL.

Uterine scrapings	122	Uterine scrapings—Continued.	
Acute catarrhal endometritis	8	Chronic interstitial endometritis	91
Subacute or congestive endometritis	7	Chronic glandular endometritis	10
Pregnancy	6		

CERVICES.

Acute cervicitis	2	Carcinoma	1
Chronic cervicitis	22	Polypi	2
Hypertrophic cervicitis	5		

UTERI.

Fibromyoma	13	Endometritis (chronic)	3
Carcinoma (cervix)	3	Cervicitis (chronic)	3
Carcinoma (fundus)	1	Perimetritis (chronic)	1

OVARIES.

Cysts.

Simple—		Dermoid, small	4
Small	12	Dermoid, large	2
Large	5	Dermoid, bilateral	1
Multilocular, large	3	Oöphoritis (chronic)	9
Papillary, large	5	Carcinoma	1

FALLOPIAN TUBES.

Salpingitis, acute	1	Tubal pregnancies	3
Salpingitis, chronic	9		

GENITO-URINARY.

FEMALE.

Urethra—			
Papilloma	2	Vagina (chronic vaginitis)	1
Carcinoma	1	Vulva (condyloma)	1
Chronic inflammation	2		

MALE.

Penis (epithelioma)	4	Epididymo-orchitis (chronic)	2
Tunica of testis—		Vesical calculus	11
Sarcoma	2	Ulcerating granuloma of pudendum	1
Hydrocele (chronic)	4	Kidney—	
Testes—		Chronic glomerulo-nephritis	1
Epithelioma (secondary)	1	Laceration	1
Cryptorchid	1	Perinephric tuberculosis	1
Cord, spermatic—		Perinephritis (chronic inflammatory	1
Chronic inflammation	2		
Cysts	2		

GENERAL SURGICAL.

APPENDICES.

Appendicitis—		Appendicitis—Continued.	
Acute catarrhal	10	Chronic atrophic	6
Acute gangrenous	1	Chronic tuberculous	2
Acute suppurative	1	Chronic, containing ascaris	1
Chronic catarrhal	27	Chronic perityphlitis	2
Chronic obliterative	5	Routine appendices (some of these included in the above)	19
Chronic, with diverticula	1		

BREASTS.

Fibro-adenoma	5	Intracanalicular adenofibroma	1
Fibroma	1	Carcinoma (adenocarcinoma)	7
Fibro-adenocystoma (bilateral)	1	Carcinoma (scirrhous carcinoma)	2

LYMPHATIC GLANDS.

Cervical—		Inguinal—	
Tuberculosis	17	Chronic adenitis	3
Endothelioma	1	Acute adenitis	2
Sarcoma	1	Mesenteric	4
Epithelioma (metastatic)	2	Tuberculosis	2
Carcinoma (metastatic)	1	Syphilis	1
Axillary, carcinoma (metastatic)	1	Sarcoma	1

STOMACH AND INTESTINE.

Gastritis, chronic	1	Rectum, carcinoma	1
Small intestine—		Anus, condylomata	1
Sarcoma	1	Cæcum, carcinoma (colloid)	1
Chronic inflammatory	1	Mesentery, necrotic tissue	1
Rectum, hæmorrhoids	2		

THYROID GLAND.

Simple colloid struma	8	Adenoma	1
Calcified colloid struma	1	Carcinoma	2
Colloid cyst	1		

SALIVARY GLANDS.

Submaxillary, sarcoma	1	Parotid, mixed tumor	1

TUMORS OF NECK, UNKNOWN ORIGIN.

Carcinoma	6	Thyroglossal cyst, early malignancy	1
Sarcoma	1		

LIVER.

Carcinoma	1

PANCREAS.

Cyst	1

ORBIT.

Hæmangioma orbit	1	Leiomyoma orbit	1

NERVES.

Neurofibroma	2	Chronic interstitial neuritis	1
Lymphangioma (optic)	1		

SKIN, MUSCLES, BONES.

Forehead—		Abdominal wall, sarcoma	1
Inflammatory tissue	1	Thigh—	
Fibrolipoma	1	Sarcoma	2
Nose, inflammatory tissue	1	Scar tissue	1
Scalp—		Pudendum, ulcerating granuloma	1
Dermoid cyst	1	Lower extremity—	
Wart	1	Crushed	1
Epithelioma	1	Sarcoma	1
Face, carcinoma	2	Knee—	
Maxilla—		Tuberculous arthritis	1
Osteoma	1	Chronic synovitis	1
Fibrosarcoma	1	Ankle, tenosynovitis	1
Carcinoma	1	Foot—	
Gum, sarcoma	2	Epithelioma	1
Neck, fibroma	1	Mycetoma	1
Shoulder—		Tuberculosis	1
Lipoma	1	Toe—	
Chronic myositis	1	Granuloma	1
Gumma	1	Chronic inflammation	1
Arm, crushed	1	Back—	
Finger—		Hæmangioma hyperplasticum	1
Wart	1	Abscess	1
Scar tissue	1	Papilloma	1
Hand, fibroma	1		

In these figures are included some examinations of tissues removed during the course of operations for diseases of other viscera, and, on the other hand, there are not included numerous tissues that were secondarily the seat of disease. An example of the former is the removal of the appendix during a gynæcological operation, and of the latter ovaries and tubes removed in a panhysterectomy.

It is of interest to note the frequency and distribution of tuberculosis and neoplasms. The relative infrequence of lesions recognizably syphilitic is noteworthy, and may possibly be accounted for by the improved diagnostic methods for this disease.

Tuberculous lesions.

Perinephric abscess	1
Ulcers of the vermiform appendix	2
Lymphadenitis	19
Arthritis, knee	1
Cutaneous, foot	1
Total	24

The infrequence of tuberculous disease of bone is noteworthy.

Of the 81 specimens of new growths, 33 were benign and 40 malignant.

Benign tumors.

Papilloma	2
Adenoma	1
Fibroma	2
Neurofibroma	2
Fibromyoma	13
Lipoma	1
Fibrolipoma	1
Fibro-adenoma	5
Fibro-adenocystoma	1
Intracanalicular adenofibroma	1
Osteoma	7
Lymphangioma	1
Hæmangioma	2

Malignant tumors.

Carcinoma	37
Sarcoma	9
Endothelioma	1
Mixed parotid	1

The hospital from which this material was derived admits only selected early cases of tuberculosis and none of the contagious diseases.

REVIEWS.

Laboratory Studies in Tropical Medicine. By C. W. Daniels, M. B. Camb., M. R. C. P. Lond., and H. B. Newham, M. R. C. S. Eng., L. R. C. P. Lond., D. P. H. Camb., D. T. M. and H. Camb. Third revised edition. Philadelphia, P. Blakiston's Son and Co. 1911. Pp. 535. Cloth. Price $4 net.

This is the third edition of Daniels and Newham's well-known "Laboratory Studies in Tropical Medicine" which has been revised and brought up to date. The plan and scope of the book remain unchanged. It is intended to serve as a laboratory reference book for the physician and investigator in the Tropics. General pathological and histological technique and the clinical examination of blood, sputum, urine, and fæces are fully considered. A brief but comprehensive description is given of the morphology, development, and classification of the protozoan and metazoan parasites of man and some of the more important parasites of animals. Considerable space is devoted to the insect and arachnoid carriers of infectious diseases, including methods of collecting, rearing, and studying these animals. The chapter on bacteriology is necessarily brief, owing to the limits of the volume, but it is comprehensive and practical and can be supplemented by reference to any standard text-book on the subject. This edition continues to be the only complete laboratory reference book on tropical medicine. It is unfortunate that a book which is intended to be subjected to constant usage should have been so poorly and unsubstantially bound.

E. L. W.

The American Illustrated Medical Dictionary. By W. A. Dorland, A. M., M. D. Sixth edition, revised and enlarged. Philadelphia and London, W. B. Saunders Company. 1911. Pp. 986. Limp leather.

The completeness and up-to-dateness of a medical dictionary can be pretty accurately measured by the fulness of its vocabulary in the newer medical sciences, such as immunology, protozoölogy, and chemotherapy. Judged by this standard, the new edition of Dorland's Medical Dictionary leaves nothing to be desired.

The definitions, while concise, are comprehensive, and the correct pronunciation, the capitalization, and the derivation of the words are given. By the use of thin but opaque paper and small but clear-cut type, compactness is secured without sacrificing completeness or legibility, while reference is facilitated by printing the words in heavy type and making them project beyond the line of the paragraph. The work is supplemented by many anatomical, clinical, posological, and therapeutical tables and by a large number of good plates, many of which are colored. The book is well and attractively bound in limp red leather.

E. L. W.

Contributions to Medical Science by Howard Taylor Ricketts 1870–1910. Published as a Tribute to his Memory by his Colleagues under the Auspices of the Chicago Pathological Society. The University of Chicago Press. Chicago, Illinois. 1911. Pp. 497. Cloth.

This volume, in which are collected all of the original papers of investigations published by Doctor Ricketts and his pupils, forms a worthy memorial to this brillant young man who had accomplished so much, who gave such promise for the future, and who sacrificed his life to science. A statement by the Committee of the Chicago Pathological Society appointed to prepare a suitable memorial and a short biography of Doctor Ricketts by Ludvig Hektoen forms a suitable introduction to the volume. The earlier papers on blastomycosis and imamunology are important contributions to medical science, but it is the work on Rocky Mountain spotted fever and typhus fever that established the reputation of Doctor Ricketts as a brilliant investigator. Rocky Mountain spotted fever was a disease of unknown etiology which occurs in certain regions of Montana and adjacent states and which was supposed to be communicated to man by the bite of a tick. Doctor Ricketts concluded that this disease is caused by a small bacillus which he was unable to cultivate on artificial media and which is transmitted from man to man by the bite of a tick, *Dermacentor occidentalis,* occurring in the region where this disease is endemic. He further proved that there is a hereditary transmission of the specific microörganism from tick to its offspring through the egg. These discoveries, if substantiated, are not only of importance as elucidating the etiology and epidemiology of the disease under consideration, but they disclosed new biological principles that promise to be of great significance to medicine. Hitherto it had been believed that only protozoan and spirochæte diseases were transmitted by ticks

and that only such diseases were capable of passing from the adult invertebrate host to offspring through infected eggs. Doctor Ricketts has shown that both of these processes can occur in bacterial diseases. How important these new biological facts may prove to be is indicated by Doctor Ricketts' subsequent investigations of typhus fever. The similarity of typhus fever, in some respects, to Rocky Mountain spotted fever led him to undertake the study of the former disease in Mexico. It was during this investigation that Doctor Ricketts fell a victim to the disease and died at Mexico City of typhus fever on May 3, 1910. It is a source of satisfaction to know that the sacrifice was not in vain. Before succumbing to the disease, he discovered, as in Rocky Mountain spotted fever, a small bacillus which could not be cultivated upon artificial media, which is probably that etiologic agent in typhus fever, and which appears to be transmitted from man to man by the bites of the body louse, *Pediculus vestimenti*.

E. L. W.

Manual of Practical Physiology. Designed for the Physiological Laboratory Course in the Curriculum of the American Association of Medical Colleges. By John C. Hemmeter, M. D., Ph. D., LL. D. With 55 illustrations. Philadelphia, P. Blakiston's Son & Co., 1012 Walnut Street. 1912. Pp. i–xxii+1–223. Price $2.50.

One is favorably impressed on first opening this book. The paper, type, and illustrations are good. The preface, but for a passage or two, might lead the reader to expect an improvement over the older manuals. Disappointment, however, begins with the first page of the book proper and increases as one reads further. The directions lack in definiteness, are wordy, and condescending. They contain irrelevant facts and irrelevant discussions, they dwell on nonessentials, new matter is introduced inopportunely, and inaccuracies abound. One or two quotations will give an impression of the inaccuracy of thought and of expression that pervades the book. On page seven, after the statement of the equation for the strength of the electric current, we read: "A simple example (presumably of the "electric current") is the flow of water through a nozzle of a syringe." And after speaking further about the syringe we find this: "Now if the nozzle of the syringe is longer (pressure same) less H_2O would flow, or if the hole in the nozzle is made smaller the same would happen, because in both cases resistance is increased. Applying this to the electrical circuit we learn that the longer

or thinner the conductor the greater the resistance and the less the flow of current." Thus endeth the discussion on "Electrical Measurements." This fault of inaccuracy, glaring as it is, is of minor importance, however, compared with another fault which mars the book. Instead of presenting the data obtained from the experiments in such a way as to lead the student to reason on the facts presented and so to develop the scientific attitude and habit of thought, the author presents to the student the conclusions ready made, and thus anticipates and forestalls all independent thought, making scientific training impossible.

A. O. SHAKLEE.

Veterinary Bacteriology. A Treatise on the Bacteria, Yeasts, Molds, and Protozoa Pathogenic for Domestic Animals. By Robert Earle Buchanan, Ph. D. With 214 illustrations. Philadelphia and London, W. B. Saunders Company. 1911.

In view of the scope of a work of this character it is quite impossible for a man of average training in the subject to pass a critical judgment upon the accuracy of all phases of the subject matter. In glancing through a book for this purpose one naturally pauses at the topics with which one feels especially familiar and subjects the statements of the author to scrutiny. Judged by such a method, the book is satisfactory and up to date with few exceptions.

The space devoted to Von Pirquet's cutaneous tuberculin reaction might better have been allotted to a discussion of the intradermal test for tuberculosis in cattle as described by Moussu and Mantoux. Their work was confirmed by Ward and Baker in a paper published in the Proceedings of the American Veterinary Medical Association for 1910 and in the American Veterinary Review for November, 1910, page 184. It is hoped that by the time the book is revised the intradermal test will have won more general recognition.

A review is not quite complete without a criticism of the use of at least one word. With all humility for my own shortcomings it is pointed out that the author uses the word epidemic instead of epizoötic on page 302. On the same line Dr. Brimhall's identity is masked by an unfortunate typographical error. Elsewhere the spelling of Johne is distorted by the addition of s.

In discussing antirinderpest serum the author accepts, as have many others, the statement of Kolle and Turner that "An injection of 50 to 100 cubic centimeters of the serum so secured will protect an animal against infection for a space of from 2 to 4

months usually." The accuracy of the experimental work upon which the foregoing statement is based seems not to have been challenged until the publication of Holmes' work in No. 1 of the Indian Civil Veterinary Department Memoirs, page 72. Holmes considers that serum alone will protect against the inoculated virus for about two weeks only. The present writer, on the basis of experiments, the results of which have not yet been published, is prepared to state that serum exerts no protection whatever against invasion by rinderpest virus.

The discussion of the nature of the virus of contagious pleuro-pneumonia would have been improved by reference to the work of Bordet, Borre, and others, appearing in the Annales de l'Institut Pasteur (1910), 25, No. 3.

A. R. WARD.

A Manual of Surgery for Students and Physicians. By Francis T. Stewart, M. D. Second edition with 553 illustrations. Philadelphia, P. Blakiston's Son & Co., 1012 Walnut Street. 1911. Pp. i–xi+1–682. Price $4.

This book contains the principles of surgery briefly and concisely stated. The manual has 31 chapters in which all the different diseases are considered separately. In the index, the most important references are placed first. It contains 553 illustrations, all of which are fairly demonstrative. In considering each disease, and particularly those sections dealing with diagnosis and treatment, the author has summarized as concisely as possible all of the various treatises on surgery for the student, physician, or general practitioner. This is very comprehensive and helpful, and it avoids loss of time for the reader. In a word, it is a useful book with clear style and logical and scientific arrangement.

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

THE SUBANUNS OF SINDANGAN BAY.

By EMERSON B. CHRISTIE.

121 pages, 1 map, 29 plates.

Order No. 410. Paper, $1.25 United States currency, postpaid.

Sindangan Bay is situated on the northern coast of Zamboanga Peninsula. The Subanuns of this region were studied by Mr. Christie during two periods of five and six weeks, respectively.

The following is an abstract from the contents of Mr. Christie's report on the Subanuns: Habitat and history; relations with the Moros; material culture; houses; industries; trade; agriculture; family life; social customs; administration of justice; religion; the medicine man; ceremonies; tales; word-lists; physical measurements.

The 29 plates illustrate the Subanuns at work and at play; their industries, houses, altars, and implements; and the people themselves.

THE HISTORY OF SULU.

By NAJEEB M. SALEEBY.

275 pages, 4 maps, 2 diagrams.

Order No. 406. Paper, $0.75 United States currency, postpaid.

In the preparation of his manuscript for The History of Sulu Doctor Saleeby spent much time and effort in gaining access to documents in the possession of the Sultan of Sulu. It is fortunate that these records have now been translated and preserved in permanent form. This book is a history of the Moros in the Philippines from the earliest times to the American occupation.

STUDIES IN MORO HISTORY, LAW, AND RELIGION.

By NAJEEB M. SALEEBY.

107 pages, 16 plates, 5 diagrams.

Order No. 405. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

This volume deals with the earliest written records of the Moros in Mindanao. Doctor Saleeb was fortunately able to obtain exact copies of carefully preserved early records written in the Magindanao dialect with Arabic characters. The author presents translations of these as well as 16 half-tone illustrations of certain pages from the originals. The names of the rulers of Magindanao are recorded in five folding diagrams.

NEGRITOS OF ZAMBALES.

By WILLIAM ALLAN REED.

83 pages, 62 plates.

Order No. 402. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

The introductory chapter deals with the general distribution of Negritos and with the distribution of the Philippine branch of the race. The succeeding chapters deal with the various industries, amusements, and social relations of these little men.

Plates from photographs, the greater part of which was taken for this publication, show ornaments, houses, men making fire with bamboo, bows and arrows, dances, and various types of the people themselves.

CONTENTS.

The "Philippine Journal of Science" is issued as follows:	U. S. currency.
Section A. Chemical and Geological Sciences and the Industries	$2.00
Section B. The Philippine Journal of Tropical Medicine	3.00
Section C. Botany	2.00
Section D. General Biology, Ethnology and Anthropology (Section D began with Volume V)	2.00
Entire Journal, Volume II, III, IV, or V	5.00
Entire Journal, beginning with Volume VI	7.00
Single numbers of Volume I	.75
Single numbers (except of Volume I)	.50
Volume I, 1906 (not divided into sections)	10.00
Supplement to Volume I (botany)	3.50
Volume I (without supplement)	6.50

Each section is separately paged and indexed.

Publications sent in exchange for the Philippine Journal of Science should be addressed: Library, Bureau of Science, Manila, P. I.

Subscriptions may be sent to the BUSINESS MANAGER, Philippine Journal of Science, Bureau of Science, Manila, P. I., or to any of the agents listed below:

AGENTS.

The Macmillan Company, 64–66 Fifth Avenue, New York City, U. S. A.
Wm. Wesley & Son, 28 Essex Street, Strand, London, W. C., England.
Martinus Nijhoff, Nobelstraat 18, The Hague, Holland.
Mayer & Müller, Prinz Louis Ferdinandstrasse 2, Berlin, N.W., Germany.
Kelley & Walsh, Limited, 32 Raffles Place, Singapore, Straits Settlements.
A. M. & J. Ferguson, 19 Baillie Street, Colombo, Ceylon.
Thacker, Spink & Co., P. O. Box 54, Calcutta, India.

Entered at the post-office at Manila, P. I., as second-class matter.

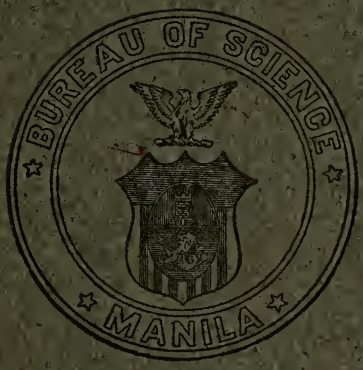
VOL. VII, SEC. B, NO. 6 DECEMBER, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

ALVIN J. COX, M. A., PH., D.
GENERAL EDITOR

SECTION B

THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE



MANILA
BUREAU OF PRINTING
1912

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

REPORT OF THE INTERNATIONAL PLAGUE CONFERENCE.

Held at Mukden, April, 1911, under the auspices of the Chinese Government.

Edited by ERICH MARTINI, G. F. PETRIE, ARTHUR STANLEY, AND RICHARD P. STRONG.

483 pages, 18 plates (2 colored, 4 half-tones, 12 charts and maps).

Order No. 416. Cloth, $3.50; paper, $2.50 United States currency, postpaid.

The proceedings of this International Conference and information gained therefrom, together with the results of certain bacteriological investigations, constitute the present report.

Nothing hitherto has been published which gives such a complete and comprehensive account of the entire subject of pneumonic plague.

Delegates from America (United States of), Austria-Hungary, France, Germany, Great Britain, Italy, Japan, Mexico, the Netherlands, Russia, and China attended the Conference.

The Bureau of Science of the Government of the Philippine Islands has been appointed sole agent for the distribution of the printed proceedings of the International Plague Conference.

THE SUGAR INDUSTRY IN THE ISLAND OF NEGROS.

By HERBERT S. WALKER.

145 pages, 10 plates, 1 map.

Order No. 412. Paper, $1.25 United States currency, postpaid.

Considered from the viewpoint of practical utility, Mr. Walker's Sugar Industry in the Island of Negros is one of the most important papers published by the Bureau of Science. This volume is a real contribution to the subject; it is not a mere compilation, for the author was in the field and understands the conditions of which he writes. The following is a brief synopsis of the contents:

Tables of soil analyses, both chemical and physical; analyses of the cane, juice and bagasse; estimates based on actual information as to the costs of production and of cultivation; and estimates of the cost and location of possible central factories. The island is considered by sugar-producing districts; the area of cultivation and the production per hectare are given, and the possibility for future expansion discussed.

The plates illustrate various phases of sugar industry from the cultivation of the field to the transportation of sugar in native sailboats.

A MANUAL OF PHILIPPINE SILK CULTURE.

By CHARLES S. BANKS.

53 pages, 20 plates.

Order No. 413. Paper, $0.75 United States currency, postpaid.

The silk industry is particularly adapted to be undertaken by persons with small capital, and like the making of hats in the Philippine Islands it should thrive with a little encouragement.

In A Manual of Philippine Silk Culture we have presented the results of several years' actual work with silk-producing larvæ together with a description of the new Philippine race. Half-tone plates illustrate in natural size silkworms in different stages of development, pupæ, adult moths, samples of cloth made from eri silk, hand reel, and silk house. Other plates illustrate the various appliances used in raising silkworms and in spinning silk; hand and power reels are illustrated; working drawings are given for a silk house and for a hand reel.

THE PHILIPPINE
JOURNAL OF SCIENCE
B. THE PHILIPPINE JOURNAL OF TROPICAL MEDICINE

VOL. VII DECEMBER, 1912 No. 6

THE RÔLE OF STOMOXYS CALCITRANS IN THE TRANSMISSION OF TRYPANOSOMA EVANSI.[1]

By MAURICE BRUIN MITZMAIN.

(*From the Veterinary Division,*[2] *Bureau of Agriculture, Manila, P. I.*)

This paper is one of a series of studies undertaken to incriminate, or to exclude from future practical consideration, the various species of bloodsucking insects that might be concerned in the transmission of surra. It is planned to duplicate these methods of experimentation, if practicable, with each species of ectoparasite of the draft animals of the Philippines. It was believed that this investigation could be made more valuable, and a more practical insight obtained into the problem of the epidemiology of surra, by such an intimate study of each species at close range, than by attempting a more or less hasty survey under field conditions of the several species of flies implicated in natural outbreaks of the disease.

Bagshawe, editor of the Sleeping Sickness Bureau Bulletin, has written in this connection as follows:

> It appears that an epidemic of surra may be started from an animal in which trypanosomes are very scarce. If it were known that one species of insect alone is capable of becoming infected from such an animal and that flies of this species transmit infection to other animals for a period of many weeks, such knowledge could not fail to lead to precision and hence economy in preventive methods.

In most of the literature concerning *Stomoxys* and the transmission of trypanosomiasis, the species of the insect carrier has not been determined. This can be pardoned when one realizes that the work has rarely been performed by entomologists, but

[1] To be published as Bulletin No. 24, Bureau of Agriculture of the Government of the Philippine Islands.

[2] Archibald R. Ward, chief.

mostly by medical men or veterinarians who are more vitally concerned in field operations. The species of fly under investigation and discussed in the present paper has been compared carefully with material brought from California and with the descriptions of the oriental species of *Stomoxys* recently compiled by Summers.(1)

From recent reports, the workers in the field, especially in tropical Africa, have been perplexed to account for the spread of trypanosomiasis in the absence of tsetse flies. Many investigations have followed in efforts to discover other insect carriers. Species of *Stomoxys* have been incriminated in many cases; in other instances the genus *Stomoxys* has been eliminated. Species of *Stomoxys* have been cited in the general literature as carriers of pathogenic trypanosomes by the following writers:

Bruce(2) found in Uganda that swarms of *Stomoxys* might bite infected and healthy animals freely without conveying the infection (nagana).

Bruce and others(3) in concluding a discussion on work done with *Trypanosoma pecorum,* the cause of cattle disease in Uganda, note that the carrier is probably not a *Stomoxys.*

Montgomery and Kinghorn(4) advance the view that the Rhodesian cattle trypanosome can be transmitted by *Stomoxys calcitrans.*

Dutton and Todd(5) failed to infect animals with *Tr. gambiense* or *Tr. dimorphon* by bites of *Stomoxys* which had been either freshly caught from an enzoötic focus or had been fed previously on an infected animal.

Theiler's(6) attempts to transmit m'bori, a nagana-like trypanosomiasis, with *Stomoxys* from horse to horse were negative.

Sander(7) mentions that he has demonstrated in East Africa that nagana of cattle is transmitted by *Stomoxys.*

Martin, Lebœuf, and Roubaud(8) advance the opinion that in experiments with flies "as simple carriers," the species of *Glossina* are of more importance than those of *Stomoxys;* yet the rôle of the latter can not be overlooked."

Novy(9) states that *Stomoxys* is apparently incapable of spreading the infection of sleeping sickness.

Austen(10) records a note by Captain Haslem of the finding, in 1898, of *Tr. brucei* in the abdomens of *Stomoxys* caught sucking the blood of sick mules.

Castellani and Chalmers(11) state that *Stomoxys* is suspected of spreading surra and that *Tr. evansi* appears to develop in the stomach of *Stomoxys.*

Sivori and Lecler(12) succeeded in infecting horses with *Tr. equinum* by subjecting them to bites of *Stomoxys* which had sucked the blood of sick animals.

Sieber and Gonder,(13) working with dourine in Hamburg, came to the conclusion that it was not unlikely that *Stomoxys calcitrans* was the responsible carrier in the infection produced.

Schat(14) concludes that *Stomoxys* is the chief agent in the propagation of surra among cattle and horses in Java.

Manders(15) states that in Mauritius *Stomoxys geniculatus* is almost

certainly the carrier of surra and that the mortality is greatest during the months when this fly is most prevalent.

Daruty[16] says that in Mauritius *Stomoxys nigra* plays the same part in the spread of surra as the tsetse fly does in Africa in the spread of nagana.

Diexonne[17] notes the fact that a surra epizoötic broke out in Mauritius simultaneously with the appearance of *Stomoxys*.

Laveran and Mesnil[18] mention *Stomoxys* as a probable transmitter of surra.

Mohler and Thompson[19] state that in the outbreak of surra among the imported cattle landed on an island near New York, *Stomoxys calcitrans* probably was not a factor in the spread of the infection. A species of *Tabanus* was incriminated.

Darling,[20] in discussing the mode of transmission of *Tr. hippicum*, the agent of murrina, believes that it is extremely unlikely that *Stomoxys calcitrans* conveys the infection in the Panama Canal Zone.

Sander,[7] in discussing surra in the Philippines, asserts that *Stomoxys calcitrans* is proved by Curry in 1902 to be the carrier, and that this was confirmed by Musgrave and Clegg.

Leese,[21] in discussing the comparative practical importance of *Stomoxys* as a surra transmitter, points out that, in an epizoötic, *Stomoxys* does not perform its work until the infection has already been introduced by a more capable carrier like *Tabanus* which usually transports the organisms from a distance. *Stomoxys* transmits under these conditions at close range, and usually among individuals in the same herd.

Curry[22] found the trypanosomes of surra still active in the proboscides and stomachs of *Stomoxys calcitrans* twenty-four hours after they had bitten an infected animal. He believes that *Stomoxys* is alone responsible for the propagation of surra in the Philippines. No experimental evidence is advanced.

Musgrave and Clegg[23] state in their report on surra in the Philippines, that they transferred the infection to the monkey, horse, rat, dog, and guinea pig by biting flies, in experiments so guarded as to make the results absolutely conclusive.

The inconclusiveness of the last reference is shown in the fact that the species of biting fly concerned is not given, nor are data of experiments involving procedure of method in obtaining results submitted. One is left to assume that the direct mechanical method was applied and the biting fly used was *Stomoxys calcitrans*. These omissions are noticeable in contrast to the general excellence in the carefully compiled literature and observations embodied in the remainder of the report.

Bagshawe,[24] in commenting on the consensus of opinion of authorities on surra, writes that it is *generally assumed* that flies act as mechanical transmitters or accidental carriers, but, as far as he is aware, no experiments are on record which prove or disprove it. This is before the appearance of Leese's paper in 1911.

MECHANICAL TRANSMISSION.

That the principal and probably the only method by which *Stomoxys* transmits the trypanosomes of surra and of other

trypanosomiases is purely mechanical has been taken for granted, and, in a few instances, proved by experiments. By the mechanical method it is assumed that there is involved a direct conveyance by the insect carrier of infection either immediately or in varying periods up to forty-eight hours after feeding on the infected host.

Novy, MacNeal, and Torrey,[25] referring to insects such as *Stomoxys*, affirm that the facts, such as they are, indicate that the flies merely transmit the surviving unaltered trypanosomes which have been taken up with the blood, and that such transmission can occur only during the few hours following the infective feed.

Evans[26] cites *Stomoxys* as the mechanical carrier of the trypanosomes of elephant surra. No experimental evidence is offered.

Jowett[27] obtained negative results in mechanical transmission experiments in cattle trypanosomiasis with *Stomoxys* fed on rats, sheep, and goats.

Fraser and Symonds,[28] working with surra and the mechanical transmission method with *Stomoxys*, were unsuccessful in five experiments. In two instances 8 and 11 flies, respectively, were used.

Gaiger[29] states that in some parts of India *Stomoxys* is found where there is an absence of Tabanidæ and the former is probably equally capable of transmitting surra mechanically.

In my experiments covering this point, an attempt has been made to view the problem exhaustively from every possible angle. First, the flies, transferred from their infected hosts, have been permitted to *complete* the initial feeding prior to biting the healthy animal. Second, the flies, feeding on the surra host, have been *interrupted* within a minute, after which they were transferred to a healthy animal to complete their meal. Third, this *interrupted* feeding was repeated during several hours of the day and through a period of several days. In these tests, guinea pigs, monkeys, and horses have been employed. It was found that the species of susceptible mammal used made no difference in the results of the experiments. The use of animals other than the natural hosts of *Stomoxys* has been criticized by several workers. A limited experience convinces me, so far as many negative results can convince, that the reaction to biting of infected flies is similar in all the hosts cited.

The experiments were carried on with animals in a large cage, or in a glass jar, or in the open with the host immobilized. In the first case the insects were placed in the cage or in the jar and permitted to bite at will. By the second method they were applied in a large bottle to the tail of the animal, and also individually in test tubes. Both wild flies and laboratory-bred flies were used, and in each case this condition is stated.

In all of the experiments reported upon in this paper the

failure to infect was concluded only after the following examinations. The temperatures of the horses and monkeys were registered twice daily. Microscopic examinations of the blood of horses, monkeys, and guinea pigs were made each day. In these examinations never less than 30 fields per blood film were scanned. In the experiments with horses and monkeys an additional control was provided by guinea-pig inoculations. From the horses 2 to 6 cubic centimeters of blood were drawn and inoculated, from the monkeys 2 to 3 cubic centimeters. One guinea pig was used for each animal tested.

The animals were held in quarantine, both before and after each experiment, in fly-screened sheds or cages; the horses in fly-screened enclosures provided with a suitable double-door vestibule, and the monkeys and guinea pigs in individual cages which were made fly proof with double screens of close-meshed gauze.

Unless otherwise stated, in every experiment included in this paper, an animal exposed to flies, whether through biting or subcutaneous inoculation, was examined daily for thirty days and afterward never less than twice weekly for ten days.

EXPERIMENTS WITH HORSES IN A SCREENED STABLE.

The experiments with the horses and *Stomoxys* were conducted in a specially constructed fly-proof stable made to simulate natural conditions as nearly as possible. The enclosure (Plate I) utilized in the present series was of the following description.

The walls and top were screened with brass wire of 16 to 18 meshes per inch. No roof was provided, and the animals were protected from the sun by canvas screens stretched overhead. A section was devoted to the growth of foliage provided by acacia trees and hedge plants. A constant flow of water was provided to aid in cooling the air within the enclosure. The manure was not removed from these quarters, but was permitted to accumulate in ant-proof wooden tubs at a little distance behind the horses. The animals were watered from removable iron containers within the mangers, filled by individual faucets. The screened enclosure was divided into two parts by means of a low partition formed of half-inch-mesh iron wire, ample for the ready interchange of flies, and high enough barely to prevent contact of the animals. A frame door closed the opening from one stall to another, and a capacious fly-proof double-doored vestibule served as a general entrance into the cage.

There were employed 26,666 flies collected from animals known to be surra-free, but the possibility of the migration of flies from infected sources is not ignored. These flies were placed, after they were etherized and examined, in the fly shed with horse 49, the blood of which contained many trypanosomes, every day during the six days of fly infestation.

Horse 49 which was used to supply infection contracted surra through subcutaneous inoculation March 8, 1912, of the blood of bull 3148, a carabao strain of infection. The blood inoculated from the bull into the horse contained an average of 8 trypanosomes to 30 fields. The incubation period of the disease in horse 49 was six days when, on March 14, 10 trypanosomes per field were seen in a drop of blood. The temperature rose from 37°.8 C. on the morning of March 14 to 40°.2 C. on the evening of that day. The following morning the temperature registered 39°.3 C., when blood was drawn to inoculate monkey A. This animal showed a positive reaction by a rise of temperature of 2 degrees above normal and the presence of trypanosomes in its blood upon the fourth day after injection of the blood of horse 49. The monkey died nine days later, showing marked emaciation and also numerous flagellates in its heart's blood.

During the six days of fly infestation, horse 49 did not show any marked symptoms of the disease, but two days later, March 22, there was a catarrhal discharge from the nose and a congestion of the conjunctivæ. Œdematous swellings manifested themselves beginning April 1, when the breast and forelegs were involved. This condition became more marked daily, until near the time of death when the œdema extended along the abdomen and involved the genitalia. The blood of horse 49 showed numerous trypanosomes daily from March 15 to March 20, after which time the animal was examined daily until April 12 and thrice weekly from that time to the time of death, which occurred May 7, 1912. The heart's blood was then swarming with trypanosomes, and the lesions found were characteristic of surra.

In the present experiment the flies were placed in the cage on the dates mentioned in the following numbers:

Date.	Number of flies.
March 15	3,000
March 16	5,000
March 17	6,874
March 18	3,000
March 19	6,804
March 20	1,988
Total	26,666

Careful note was taken at least five times daily of the approximate number of flies biting the diseased animal, horse 49. At no time during the six days were there fewer than 100 flies biting the horse. On the morning of March 20 there were estimated to be 350 flies either biting or resting on the horse. The horse was in the early stages of the infection from the seventh day to the thirteenth day, and capable of actively resisting the attacks of the flies. That the flies did draw blood from the infected host was demonstrated by microscopical examination of the emulsified abdominal contents of several of them at various times during the course of the experiment. Trypanosomes in moderate numbers were found in fresh preparations and in stained smears.

Horse H–4.—This healthy horse was the first used for exposure to the flies possibly contaminated with surra blood. The infected horse was first removed after a bath with cresol to drive off its parasites, and the stall was similarly sprayed thoroughly with the disinfectant. No. H–4 was not placed in the stall occupied by No. 49, but in the adjoining stall, where by this time the flies had been driven. No. H–4 was exposed for twenty-four hours, during which time it was observed at least five times to be infested by flies to the extent of 10 to 100 flies.

Horse 269.—Six hours after the removal of No. 49 it was replaced by the second contact, No. 269. The fly infestation had noticeably decreased both within the cage and on the horses. Before the end of twenty-four hours the number of flies had been reduced to a few thousands and the horses received the bites of relatively few, probably not more than 40 per cent, at the close of the period of experimentation.

Horse H–3.—The two horses in the foregoing experiments were withdrawn, after carefully ridding them of the flies they harbored, and were superseded by No. H–3 which served as host from the twenty-fourth to the forty-eighth hour. The fly infestation was marked by few bites, never more than 15 at any one time of the five daily observations.

The cause of the decrease in the number of flies was ascertained to be the depredations of four or five voracious lizards which were the survivors of hundreds killed by systematic spraying prior to the introduction of the flies. These lizards were observed to invade the ceiling and walls of the cage, and with characteristic darting movements destroy an astonishing

number of resting flies. One lizard consumed in three minutes 68 flies by actual count.

This condition, needless to say, rendered unfeasible any scheme of experiment except that involving direct mechanical transmission. Therefore, this course of experimentation was not pursued beyond a forty-eight-hour period.

Horses H–4, 269, and H–3 have showed no evidence of infection. The usual tests for the presence of trypanosomes were applied, such as registration of temperatures, blood examinations, and guinea-pig inoculations, and all with negative results. The blood of the horses was examined daily for thirty days. Their temperatures were taken during a course of forty-three days. No reaction was noted. Two cubic centimeters of blood from each of the 3 horses were inoculated into 2 guinea pigs on April 1, at which time no organisms were seen by microscopic examination. The 6 guinea pigs were examined for trypanosomes daily for a period of thirty-five days. They were negative upon every occasion. Horse 269 died June 13, 1912, from an unrecognized cause believed not to be surra. Horses H–4 and H–3 were alive and free from surra on August 15, 1912.

EXPERIMENTS WITH GUINEA PIGS IN A GLASS JAR.

In the following experiments closer observation was made possible by the use of the largest museum jars obtainable, which were screened with close-meshed surgical gauze. (Plate II.)

The method employed was to immobilize a closely cropped surra guinea pig on a wire frame, place it in the jar with a known number of laboratory-bred *Stomoxys*, and replace it at stated intervals, after the flies had fed voluntarily, by a healthy animal similarly prepared. The exchange was made by the aid of ether, the jar being lightly etherized so that flies near the opening would be driven back, and those feeding upon the animal stupefied. The new animal was prepared during the interim and substituted while the flies in the jar were still under the effects of the ether. In the substitution of one host for another the flies recovered from the anæsthetic within a few minutes, in each instance by the time the new animal was introduced and the jar screened. In the case of guinea pig 81, 6 flies commenced feeding on the new host in less than five minutes after the surra guinea pig was withdrawn from the jar.

The experiments were conducted during the daytime, beginning as early as practicable and ending before twilight. The

hosts and parasites were thus under ready observation and very accurate notes could be obtained. The number of flies biting was noted, and the guinea pigs were left in the cage until the flies were apparently satisfied.

On the fourth hour of the experiments the presence of the trypanosomes in the feeding flies was demonstrated in several flies taken from the jar. An emulsion of the stomach and intestinal contents showed abundant trypanosomes. These were present on an average of 15 parasites per field, nearly as many as found in the blood of the original host, guinea pig 35.

The surra guinea pig 35 received its infection through inoculation of an emulsion of a single specimen of *Stomoxys*. This fly had been fed five minutes on a surra guinea pig and six hours later was emulsified and examined microscopically. Numerous surra-like organisms were present prior to inoculation into guinea pig 35. This animal was first positive microscopically five days following injection, and died of surra on the forty-second day.

The experiment was begun on April 2 with 300 newly emerged *Stomoxys calcitrans* and heavily infected guinea pig 35. The following table represents the data compiled:

TABLE I.—*Flies fed on guinea pigs in jar.*

Guinea pig used.	Time after feeding on infected animal.	Number of flies counted on animal.	Length of time fed.
			Hours.
Surra infected: No. 35		225	3
Healthy animal:			
No. 81	5 minutes to 6 hours	155	6
No. 84	20 hours to 25 hours	90	5
No. 87	46 hours to 53 hours	70	7

The three healthy guinea pigs used in this experiment were held in quarantine for a period of forty-five days. They had been examined by the microscope twice to thrice weekly, but in no case were trypanosomes discovered. It was not thought necessary to waste animals in proving that the guinea pigs used were susceptible by blood inoculation. Subsequent experiments give sufficient evidence on this point.

Therefore, it is concluded that under the conditions stated *Stomoxys* did not convey surra by direct mechanical infection.

TRANSFERENCE OF FLIES TO IMMOBILIZED ANIMALS AFTER INFECTIVE FEEDING WAS COMPLETED.

In this section consideration is given only to experiments made in the attempt to transmit the infection mechanically. Other experiments made under similar conditions, but in which the primary aim was to demonstrate or eliminate a cyclical development, are for the present omitted.

By a "completed" feeding is meant a condition in which the parasite has, to all appearances, satiated its craving for blood. As will be shown later in the discussion of feeding habits of this insect, a fly of this species does not ordinarily feed more than once in six to eight hours. However, there are tabulated several instances in which feeding recurred within twenty minutes or less. The feeding is, therefore, considered as "complete" when the fly has not been experimentally disturbed or restricted.

The conditions of these experiments are highly artificial, let it be recalled, and this despite every conscientious effort to simulate natural environments. Under the conditions provided, full freedom of their biting was permitted, and their flight was restricted within the limits of the animal cage, a maximum range, in one series of experiments, of not less than 10 meters.

Reference is made to the results of completed feeding of this fly in experiments recorded by several workers:

Nabarro and Greig,[30] working with *Stomoxys* and trypanosomiasis in Uganda, failed to transmit cattle trypanosomes when the intervals between biting were as long as six to twenty-four hours.

Bouffard,[31] working with souma in French Sudan, succeeded in transmitting *Tr. cazalboui* by *Stomoxys*. The experimental transmission was direct in conveying the disease from an infected to a noninfected calf kept in the same stable for two days. Forty *Stomoxys* were used. Here interrupted feeding probably influenced the results.

Martini,[32] in trypanosome experiments and observations with dogs and horses in Berlin, records negative results. *S. calcitrans* was the fly used. Presumably no interrupted feeding was attempted.

Greig and Gray,[33] finding that they could not convey mule and cattle trypanosomes of Uganda by the bites of *Stomoxys* after intervals of eight to twenty-four hours, considered it proved that *Stomoxys* could not convey trypanosomes. Interrupted feeding was not attempted, although tsetse flies could transmit these trypanosomes by the direct method.

In the following table are outlined the data of the experiments under discussion. The four infected animals used in each instance contained trypanosomes in varying numbers at the

moment they were used to supply the infected blood. The number of trypanosomes per field is not given in the table.

Guinea pig 45, which had been infected by an inoculation of blood from carabao 3252, underwent an incubation period of five days, and died of surra twenty-six days after inoculation.

Monkey R was inoculated with blood from monkey A, drawn while the latter was dying of the disease.

The infection in monkey A was very light, trypanosomes in the blood being scanty. Monkey R reacted with the presence of surra organisms within four days, showing the usual febrile changes, followed in a few days by other characteristic symptoms. This monkey lived for twenty-two days after inoculation, showing a moderate number of trypanosomes in blood from its heart. The lesions showed characteristic changes of surra.

Monkey F was inoculated with a carabao strain of surra from bull 3148. Seven days after inoculation trypanosomes were recovered from the monkey's blood. It died fifteen days after inoculation, showing all the appearances of trypanosomiasis with characteristic lesions and a moderate number of flagellates in the heart's blood.

Monkey A, as has been previously noted, reacted to an injection of the blood of horse 49. In the present experiment it was used shortly before the death at a time when the blood showed only a moderate number of trypanosomes. The blood was used, while the animal was dying, to infect monkey R, which reacted with a heavy infection.

TABLE II.—*Mechanical transmission by Stomoxys on guinea pigs and monkeys, after completed feeding.*

No. of experiment.	Infected animal used.	Healthy animal used.	Number of flies fed on first host.	Length of time fed on infected host.	Interval between feedings.	Flies feeding at time of transfer.	Number of flies fed on second host.	Length of time fed on second host.
				Hrs. mins.	*Hrs. mins.*			*Minutes.*
1	Guinea pig 45	Guinea pig 18	2	0 11	0 20	None	2	12
2	do	Guinea pig 53	11	1 32	6 0	None	11	41
3	Monkey R	Monkey 3M	150	1 0	24 0	None	43	75
4	do	Monkey 2M	12	0 20	0 10	None	12	30
5	do	Monkey 2L	29	0 35	0 12	None	23	20
6	do	Monkey 3L	12	0 30	0 20	None	7	25
7	Monkey F	Monkey 2G	25	0 28	0 16	None	10	40
8	Monkey A	Monkey C	300	2 0	20 0	None	182	50

In each instance, after a lapse of six weeks to two months, the experiments yielded negative results. The healthy monkeys and guinea pigs used in these experiments have since been employed for other experiments.

AN ATTEMPT TO DEMONSTRATE WHETHER OR NOT A SMALL NUMBER OF FLIES ARE CAPABLE OF TRANSMITTING THE DISEASE.

Tables III and IV represent a single feeding of 1 to 3 flies in an effort to determine the minimum number of flies required to convey the organisms of surra. In the first series 17 experiments were made with wild flies. The flies were fed on surra guinea pig 20, and were not fed again until the time noted, a range of twenty minutes to three days.

Guinea pig 20 was used as the blood donor three days prior to its death, at which time the blood swarmed with trypanosomes. This animal reacted to an inoculation of the blood of a mule dying from trypanosomiasis. The blood was moderately supplied with trypanosomes, and at death the latter animal showed prominent lesions of the disease. Guinea pig 20 was not examined until death, on the fifty-first day after inoculation. The organs showed the general appearance of surra lesions, and the heart's blood fairly swarmed with trypanosomes.

In the second series of experiments a single laboratory-bred fly was permitted to feed once daily on a new guinea pig. The primary bite on the infected animal was of only three minutes' duration. The fly was applied to a guinea pig heavily infected with surra. This animal, guinea pig 35, was in the first stages of the disease, although trypanosomes were abundant in its blood. It was used previously in experiments with flies placed in a museum jar.

In this test thirty-one animals were used, each being bitten once by the fly which fed until apparently satisfied. The feeding with this one fly consumed thirty-one days, and the experimental animals were held for examination for a period of at least forty-two days prior to being declared negative. Blood examinations were made daily for thirty days, after which the examinations were discontinued until the day the animal was employed for a new experiment. Then the examinations were resumed.

TABLE III.—*Series of transfers of several Stomoxys.*

Interval after feeding on infected animal.	Number of flies used.	No. of healthy guinea pig used.	Length of time fed on new host.
Days. hrs. mins.			*Mins. secs.*
20	2	18	12 00
20	1	34	3 00
30	1	10	2 00
1 30	2	6	3 00
15 00	1	8	1 00
21 00	1	27	3 00
1 00 00	2	13	10 00
1 00 00	2	25	6 00
25 40	1	51	40
27 00	1	36	4 00
39 00	1	23	1 00
44 00	1	31	2 00
2 00 00	1	11	4 00
2 00 00	2	15	18 00
64 00	1	7	4 00
64 00	1	38	40 00
3 00 00	3	17	14 00

TABLE IV.—*Series of transfers of a single Stomoxys.*

Interval after feeding on infected animal.	No. of healthy guinea pig used.	Length of time fed on new host.	Interval after feeding on infected animal.	No. of healthy guinea pig used.	Length of time fed on infected animal.
Days. hrs.		*Mins. secs.*	*Days.*		*Minutes.*
21	39	2 00	21	68	6
2 00	22	30	22	71	4
3 00	32	1 00	23	73	4
4 00	37	3 00	24	75	6
6 00	12	6 00	25	77	5
8 00	42	6 00	26	79	3
9 00	16	5 00	27	81	4
10 00	28	3 00	28	83	4
11 00	1	5 00	29	85	4
12 00	52	5 00	30	87	5
13 00	54	2 00	31	90	6
14 00	57	9 00	----------	----------	----------
15 00	59	6 00	----------	----------	----------
16 00	61	6 00	----------	----------	----------
17 00	63	4 00	----------	----------	----------
18 00	40	5 00	----------	----------	----------
19 00	65	4 00	----------	----------	----------
20 00	66	3 00	----------	----------	----------

The experiments of both series were concluded with negative results.

MECHANICAL TRANSMISSION BY INTERRUPTED FEEDING.

In this series of experiments I offer no apology for the unusual number of repetitions made to arrive at a conclusion. Scrupulous care has been taken for the details of experimental procedure. Numerous assertions are made by writers that positive results are infallible when a few flies are transferred while feeding on a surra host to an experimental animal. The careful observers are more cautious, and present more accurate and specific data:

Dutton, Todd, and Hanington[34] state: "The experiments of all observers show that it is frequently necessary to feed hundreds, almost thousands, of flies on a susceptible animal before it becomes infected. In this regard fewer flies are, of course, needed when there is practically no interval between the feeds."

Austen[35] summarizes that from the evidence compiled *Stomoxys* can convey trypanosomes directly from an infected to a healthy animal when the bites follow one another immediately, and, when the interval between the bites is longer, although active trypanosomes may be present in the intestine of the fly, its bite is innocuous.

Schuberg and Kuhn[36] transmitted *Tr. brucei* and *Tr. gambiense* in interrupted feeding by the bite of *Stomoxys calcitrans*. Eight and 13 flies were used in two experiments with *Tr. brucei*, and 9 and 8 flies in two experiments with *Tr. gambiense*. One positive result was obtained with feeding after a ten-minute interval.

Schuberg and Kuhn[37] give an account of various attempts in Hamburg to transmit by means of *Stomoxys* the diseases of nagana, dourine, sleeping sickness, and rat trypanosomiasis. Rats and mice were used in interrupted feedings. Positive results were obtained in all cases except in the attempt to convey the rat trypanosomes.

Sergent, Ed. and Ét.,[38] investigating the method of transmission of *Tr. soudanense*, the cause of debab, a camel disease, obtained one positive result with *Stomoxys* in 14 feeding experiments by the interrupted method.

Minchin, Gray, and Tulloch[39] obtained 1 positive result in 4 experiments with the "Jinja" cattle disease of Uganda by using *Stomoxys*, while by using *Gl. palpalis* 4 out of 5 results were positive. These were experiments in direct transmission with no interval between bites of the flies.

Martin, Lebœuf, and Roubaud[8] show that *Tr. brucei* can be conveyed mechanically by *Stomoxys*. In the positive experiment 3 flies were used to convey infected blood to a healthy kitten after intervals of thirty seconds to one and one-half minutes. In a similar experiment a negative result was obtained with 3 flies on a healthy guinea pig at intervals of ten and fifteen minutes.

In Table V the data show the feeding of flies on monkeys. Here are tabulated 14 experiments with 10 animals, 4 of these being used a second time at the expiration of three to four weeks.

Flies bred in the laboratory were used in this series, and they were discarded after each experiment. The interval of time between feeding on an infected animal and a healthy animal is stated in the table as the approximate average per fly. The flies were not fed individually, but from a common bottle into which the monkey's tail was introduced. (Plate III.)

TABLE V.—*Mechanical transmission by interrupted feeding of Stomoxys on monkeys.*

No. of experiment.	Infected monkey used.	Number of trypanosomes found.	Healthy monkey used.	Number of flies used on infected monkey.	Length of time flies were applied on infected monkey.	Interval between feedings, approximate average per fly.	Flies feeding at time of transfer.	Number of flies fed on healthy monkey.	Length of time fed on healthy monkey.
					Minutes.	*Minutes.*			*Minutes.*
1	F	Scanty	D	9	18	2	4	9	20
2	R	Moderate	C	15	4	1	15	15	15
3	R	Numerous	S	22	15	3	11	22	20
4	F	Moderate	M	5	2	2	4	15	13
5	F	Numerous	P	19	53	2½	7	19	60
6	F	do	B	5	5	2	5	5	20
7	F	Moderate	L	9	20	3	2	9	24
8	F	Numerous	H	12	6	2	6	4	18
9	F	Swarming	J	12	20	2	5	12	30
10	F	Numerous	N	2	3	2	2	2	7
11	F	do	2C	9	18	2	4	9	20
12	F	Swarming	2O	9	12	2½	7	9	60
13	F	do	2S	18	35	3	15	18	60
14	F	do	2M	1	2	3	1	1	3

The negative results of this series are checked in one experiment by the inoculation of surra blood from an infected bullock into the tail of monkey B. The animal reacted first on June 10, 1912, and died on June 22, 1912.

The relatively long interval between feedings is accounted for by the fact that much time was consumed in manipulating the tails of the respective monkeys, in forcibly interrupting the biting of the flies, and the renewed processes on the second host.

In Table VI, 11 experiments with an equal number of guinea pigs are represented. Here the flies were more easily controlled in the element of time, and, for purposes of close observation, each fly was fed from an individual test tube. The time was accurately noted with respect to three considerations; namely, feeding on the surra host, the interval interrupting the feeding during the transfer, and the completion of the meal on the healthy

animal. The time elements of these are averaged per fly in each experiment.

The surra guinea pig 127 used to supply the infection in these experiments was infected through subcutaneous inoculation of an emulsion of house flies which showed a great number of trypanosomes as the result of feeding on the abraded tail of a surra monkey. This monkey died showing marked lesions of the disease at necropsy. Guinea pig 127 was used when its blood was positive for trypanosomes, for a great number of experiments outlined in this paper. The animal died on the sixty-fifth day of the disease, at which time blood from the heart showed an exceedingly rich infection.

TABLE VI.—*Mechanical transmission with interrupted feeding of Stomoxys on guinea pigs.*

No. of experiment.	Surra guinea pig used.	Condition of blood of donor relative to trypanosomes.	No. of healthy guinea pig used.	Number of flies applied.	Length of time fed on surra host (average per fly).	Interval between feedings (average per fly).	Time required to complete meal on healthy host (average per fly).	
					Seconds.	*Seconds.*	*Mins.*	*secs.*
1	127	Numerous	68	30	20	40	3	3
2	127	Swarming	87	20	45	120	2	30
3	127	Moderate	118	15	15	52	3	30
4	127	do	115	12	15	45	3	20
5	127	Numerous	130	12	18	45	4	00
6	127	do	126	15	20	25	2	45
7	127	Moderate	111	21	20	30	3	00
8	127	Numerous	116	26	30	120	1	00
9	127	Moderate	81	8	20	40	1	30
10	127	do	95	8	15	20	1	45
11	127	do	106	6	15	45	1	35

Negative results were obtained in all of these experiments.

Fifteen to thirty seconds are consumed by the fly in inserting the proboscis to the depth of the bulb of the labium and to the stage of aspiring the blood. Much depends on the strength and rigidity of the labium in this regard, for, in a hungry fly newly emerged, as much as two minutes is sometimes required before the proboscis is sufficiently embedded to start the blood flow either by capillarity or suction.

Ordinarily, under conditions of an experiment, if the interruption takes place after two minutes, renewed feeding on the second host does not take place for twenty minutes or more; on the other hand, some flies may become engorged in twenty

to thirty seconds. The flies used in this series were laboratory bred, applied on a single occasion only, with the exception of those in experiments 10 and 11, wherein the flies had been used previously in experiment 9. (Table VI.)

Two attempts at mechanical transmission by interrupted feeding were made with horses as the second hosts. The method pursued was the same as before, but the flies employed were not laboratory bred. It was aimed in this series to exaggerate the normal conditions as much as possible by using as virulent a strain of surra as could be obtained and by transferring the infected flies to the weakest animals available. Unfortunately the number of flies employed was not adequate, due mainly to the great length of time required to feed them and the desire to save needless suffering of the horses strapped to the operating table. Four to five hours were required to complete each experiment.

The experiments were performed in the screened operating room of the laboratory where the horse was strapped to the operating table and bitten as rapidly as the flies could be transferred from the infected guinea pig on the adjoining table. As many as 4 flies could be fed simultaneously on the horse in this manner. Individual tubes were used to hold each parasite. On July 1, 1912, horse 275 was bitten by 25 flies which were applied at intervals of from ten seconds to two minutes after contaminating their labiums with blood of guinea pig C. The time required to complete the meal varied with the individual flies from forty seconds to five and one-half minutes.

On the following day, July 2, horse 279 was similarly treated with 38 flies. These were fed for from twenty to thirty seconds on surra guinea pig A, which had a maximum infection at this time. The flies required from thirty seconds to six minutes to become completely engorged on the second host.

Details of the work appear in the following table:

TABLE VII.—*Experiments and interrupted feeding of Stomoxys on horses.*

Infected guinea pig used.	Average number of trypanosomes present in blood per field.	No. of horse employed.	Number of flies applied.	Length of time fed on surra host (average per fly).	Interval between feedings (average per fly).	Time required to complete meal on the horse (average per fly).	Duration of experiment.
				Seconds.	*Seconds.*	*Minutes.*	*Hrs.* *mins.*
C	50-60	275	25	20	30	3.5	4 20
A	65	279	38	25	25	4.0	5 00

Guinea pigs C and A used in Table VII received their infections from subcutaneous inoculations of the peritoneal fluid of guinea pig 128 which was a mate to guinea pig 127, receiving the disease from an emulsion of infected house flies. Death of 128 occurred on the fifty-second day after the injection. Guinea pig C died forty days after inoculation. Numerous trypanosomes were seen in a drop of its heart's blood. Guinea pig A was also positive at death fifty-four days after injection. Blood taken from the spleen was found swarming with trypanosomes.

After the experiments the horses were replaced in the fly-screened stable where they were held for thirty days for examination. During this period no symptoms of surra developed, after which blood was drawn from each, and inoculated into guinea pigs. The horses were further tested as to susceptibility to the disease by the inoculation of infected blood from a sick guinea pig. Trypanosomes were recovered from horse 275 on August 17, 1912, and from horse 279 on the same day. The characteristic febrile changes occurred in both horses beginning on the evening of August 17, 1912.

MECHANICAL TRANSMISSION BY SUCCESSIVE INTERRUPTED FEEDINGS.

In this series of experiments 3 guinea pigs were subjected to interrupted bites of infected flies for from six to eight days. Guinea pig 177 was bitten from June 20 to June 27 by 40 flies, guinea pig 187 was bitten from June 28 to July 5 by 28 flies, and guinea pig 129 received the bites of 206 flies from June 30 to July 5. Laboratory-bred flies were not used in the first two experiments as the breeding jars were not productive at this time. In the third experiment laboratory-bred flies were used daily during the course of the experiment.

In the experiment with guinea pig 129 as the host, the flies were applied in the six days during thirty-two hours, which represents a fairly constant infestation by infected flies. The precaution was taken in this instance, as in the other experiments, to distribute the feeding area over various parts of the body in order to abrade the skin as little as possible each day.

The usual animal stock was employed as well as the method of feeding individual flies from test tubes. A fresh collection of flies was used daily.

TABLE VIII.—*Representing successive interrupted feeding from infected to healthy guinea pigs.*

Date.	Infected animal used.	Condition of blood of donor relative to trypanosomes.	No. of healthy guinea pig used.	Number of flies applied.	Length of time fed on surra host (average per fly).	Interval between feedings (average per fly).	Time required to complete meal on healthy host (average per fly).	Duration of experiment.
					Seconds.	*Seconds.*	*Mi. secs.*	*Hr. mins.*
June 20	127	Swarming	177	6	35	35	3 30	1 00
June 21	127	Numerous	177	5	30	60	4 00	1 00
June 22	127	Swarming	177	5	20	60	2 00	30
June 23	127	do	177	5	20	10	3 00	36
June 24	127	do	177	5	25	30	3 30	20
June 25	127	Numerous	177	4	25	5	2 30	40
June 26	127	Swarming	177	5	25	15	2 00	30
June 27	127	do	177	5	20	30	3 00	25
June 28	C	Numerous	187	4	20	10	2 30	20
June 29	C	Scanty	187	4	20	50	2 00	25
June 30	C	Moderate	187	4	20	40	2 00	15
July 1	C	do	187	4	20	20	2 00	20
July 2	C	Numerous	187	3	25	25	2 00	25
July 3	C	Swarming	187	3	20	20	2 00	15
July 4	C	do	187	3	25	30	3 00	15
July 5	C	Numerous	187	3	20	35	3 00	10
June 30	A	Scanty	129	31	15	50	3 00	6 00
July 1	A	Moderate	129	28	15	25	3 00	6 00
July 2	A	Numerous	129	25	20	35	1 30	3 00
July 3	A	Scanty	129	20	20	30	2 00	1 00
July 4	A	Moderate	129	42	20	25	3 00	8 00
July 5	A	do	129	60	20	30	1 30	8 00

The guinea pigs employed in the first two experiments were negative up to August 1, 1912, when they were inoculated with blood of a guinea pig positive for surra. Both reacted in the usual manner, showing numerous trypanosomes on the fifth and sixth days, respectively. Both were alive and positive for surra up to August 26, 1912.

A positive result was obtained in the third experiment with guinea pig 129 which showed scanty trypanosomes on July 11, six days after the last lot of flies was applied to it. On the following day trypanosomes were present in moderate numbers, and two guinea pigs were inoculated with its blood. These showed trypanosomes on the seventh and eighth days after inoculation. Guinea pig 129 was examined daily until August 11, 1912, during which time trypanosomes were seen in numbers from

moderate to numerous. The animal died August 12, 1912, when its heart's blood was used to test the disease susceptibilities of the 2 horses, 275 and 279, used in a previous experiment. Trypanosomes in moderate numbers were recovered from these animals August 17, 1912.

DURATION OF THE INFECTION IN THE PROBOSCIS OF STOMOXYS.

Dutton, Todd, and Hanington(34) found that red cells and *Tr. gambiense* were almost always present in the labium of *Gl. palpalis* up to ten minutes after feeding. The longest period in which trypanosomes were found in the labium was one and three-fourth hours, and red cells seven and one-half hours.

As far as can be determined no authentic records exist in which *Stomoxys* has been investigated in this connection.

An effort was made to determine how long the proboscis of *Stomoxys* can retain trypanosomes. Six experiments were performed with 2 animal inoculations in each. The method employed was to feed laboratory-bred flies on an infected guinea pig and after certain intervals stupefy the insects and immediately sever the head from the body. With another set of instruments the proboscis was dissected and at once emulsified with normal saline solution and injected on a cotton pledget into a subcutaneous pocket of the abdomen of a guinea pig previously etherized. This was followed by a similar mode of inoculation, using disinfected instruments, with the macerated abdomens. The thorax was invariably discarded. The interval of time between the withdrawal of the insect's labium from the infected animal and the dissection of the mouth parts was carefully noted.

In two experiments the flies were purposely interrupted in the biting process, and in the other trial the flies were allowed to complete the meal unmolested. In the cases of interrupted feeding one-half to three minutes were allowed for each fly to insert the proboscis to the depth of the bulb of the labium, the feeding being interrupted at a stage when there ensued a barely perceptible inflation of the abdomen.

When permitted to feed uninterruptedly it has been noticed that this insect sucks its food cleanly, no residue adhering to the labellum of the mouth or to the labium externally. In one instance (experiment 5) it was observed that in 2 flies chloroformed prior to dissection droplets of fresh blood oozed from the proboscis. The abdomens of these flies were fairly engorged with blood. It is suggested that the phenomenon observed was a regurgitation of blood from the pharynx into the labium, resulting either from the engorgement of the stomach or from the

effects of the chloroform on a full stomach. The latter is regarded as the more plausible explanation.

Dutton, Todd, and Hanington[34] write: "It was also found that flies (*Gl. palpalis*) caught after they had fed on an infected animal, frequently regurgitated a drop of blood as large as a pin's head, which was full of parasites, many of them identical in form with those ingested. This was observed up to twenty-eight hours after infection." The significance of regurgitation as a means of transmission is noted.

Koch[44] also found that, by pressure of the proboscis, trypanosomes could be obtained from the labium of an infected *Glossina*.

Table XV contains data of experiments concerning the point under discussion.

TABLE XV.—*Infectivity of dissected flies.*

No. of experiment.	Time of completed or interrupted feeding.	Number of flies used.	Interval prior to dissection of flies.	Guinea pig receiving proboscides.	Guinea pig receiving abdomens.	Results of inoculation and fate of guinea pigs.
			Minutes.			
1	Interrupted ½ to 3 minutes.	3	1.5	R	U	R negative. U positive tenth day.
2	Complete, 5 minutes	1	0.5	T	S	T positive twelfth day, dead thirtieth day. S positive twelfth day, dead thirty-second day.
3	Complete, 40 seconds to 1½ minutes.	5	0.5	103	102	103 positive ninth day. 102 negative.
4	Interrupted 30 seconds	5	5.0	121	117	121 negative, dead twenty-fifth day. 117 negative, reacted positive to inoculation of subsequent experiment.
5	Complete, 1 to 7 minutes.	5	0.5	113	105	113 positive tenth day. 105 negative.
6	Complete, 1 to 2½ minutes.	5	5.0	101	28	101 negative. 28 positive ninth day, dead twenty-fourth day.

Attempting to draw a deduction from the above data, it is found that the surra organism remains in the proboscis for thirty seconds, but disappears in one minute and thirty seconds after the infective meal. The guinea pigs inoculated with the abdominal contents of the flies serve as a control of the experiments. The table demonstrates also that the proboscis of a fly interrupted in its feeding, under the conditions stated, does not appear to be infective. These experiments are by no means conclusive.

It was thought desirable to make an effort to ascertain whether or not infection by direct transmission is due to any external contamination. In other words, in what manner other than

through feeding can infection be transported by the fly. This would involve the introduction from without of infective materials into the punctured skin of the host. Such external factors might include excretory contamination, contamination from the insect's pulvillus, and more remotely that from hairs of the insect's body or that from the wings.

A series of experiments was performed to decide whether or not the wound caused by the fly's proboscis was suitable for the entrance of infective material. In these trials a varying number of bred *Stomoxys* flies were induced to bite healthy guinea pigs whose skin was thoroughly shaved but not abraded. A generous platinum loopful of blood freshly drawn from the ear of a surra guinea pig was rubbed into the fresh bite immediately after each fly was withdrawn. In this series of experiments the infected blood used was taken from guinea pig T, which reacted to inoculation of a single proboscis of a fly fed on a surra animal. Guinea pig T, which is accounted for in Table XV, was used here when its blood swarmed with surra trypanosomes. In every instance, after a lot of flies were fed, the area of the skin covered by the inverted test tube was vaccinated with a saline solution containing heavily infected surra blood. The following table contains information as to the work done on this subject:

TABLE XIV.—*Results of rubbing infected blood into wounds caused by proboscides of flies.*

Number of bites.	Guinea pig used.	Results.
8	121	Negative.
20	105	Do.
7	102	Do.
13	103	Do.[a]

[a] Reacted six weeks later to inoculation of surra blood.

To what extent the fæces from infected flies are contaminated has not been systematically determined. One experiment to determine the range of this infection was tried up to eighteen hours with fæces of infected flies. According to the results, although degenerative forms were detected microscopically, the injected material was devoid of infective trypanosomes. The experiments were concluded in each case with a negative result. For the present, therefore, with the evidence at hand, the possibility of infection by fly dejecta rubbed into the bitten skin is considered as nil.

The possibility of infection being carried by the fly's pulvillus was tested by using flies (*Musca domestica*), not bloodsuckers, whose pulvilli were as large as, or larger than, those of *Stomoxys*. Both monkeys and guinea pigs were used in these tests. The tests were made more conclusive by using large numbers of flies in bottles applied to the monkeys and a smaller number in large glass tubes on guinea pigs.

In the first of the monkey experiments, 30 laboratory-bred *Stomoxys* were applied to the tail of the healthy animal immediately followed by 50 flies (*Musca*) from a separate bottle, which previously had been applied to the abraded tail of a surra monkey. Twenty minutes were allowed the *Musca* to carry the infected contents of feet and mouth parts into wounds left by the clean *Stomoxys*. In the other experiment with the monkey, 200 *Stomoxys* and 250 *Musca* were employed. The 3 guinea-pig experiments were performed in a similar way with fewer flies.

All 5 experiments resulted negatively, the animals being used later for other purposes. One of the guinea pigs subsequently reacted to an inoculation of infected blood.

THE RELATION OF NONBITING FLIES TO STOMOXYS IN CONTAMINATIVE INFECTIONS.

In considering the relations existing among flies of the family Muscidæ and their parasitism, a peculiar phase is brought to light. I was curious to learn why such an abnormal percentage of nonbiting flies was generally found in collecting insects from domestic animals. In an examination of extensive collections made with a net swung over the backs of the animals, the majority of the nonbiting flies were found to contain blood-engorged abdomens. These when dissected and examined microscopically showed mammalian blood to be the principal food constituent.

A quiet bullock was selected for closer observation. Some 150 to 200 flies, mostly muscids, were seen to collect on him. Many hundreds of dung flies, including house flies, were scattered about on the floor of the stall, and an occasional one of these was seen to join the others on the host's body.

In a short while my attention was attracted to the peculiar grouping of the ectoparasites; groups of 2 to 4 and 5 prevailed. On closer inspection the group was found invariably to consist of more than one species, a *Stomoxys* usually providing the central figure. Where this species was lacking it was found that the group fed from a common area with the heads of the individuals in close contact. The food of the latter was found to be a

droplet of freshly exuding blood, and among these often not an individual belonged to a species with a piercing mouth; they consisted principally of house flies. Other groups of flies surrounding the *Stomoxys* attracted attention by the fact that while it fed the rest waited. The latter gave evidence of great impatience and eagerness in the movements of nudging one another and colliding with the *Stomoxys*, apparently making efforts to dislodge it. The *Stomoxys* having been satisfied, the other flies pounced upon the feeding spot where a well-rounded blood-drop trickled, and lapped the blood as it oozed from the wound. In a moment the group disbanded with abdomens more or less reddened and distended, the individual either flying off the host to rest or joining another biting *Stomoxys*. In many instances the *Stomoxys* was accompanied by a single fly which hovered about it in a highly provoking fashion. Several minutes elapse, however, before the *Stomoxys* is fully engorged and the blood is left to the disposal of the secondary passive parasite.

It has been noticed that even other bloodsucking flies found on cattle often take advantage of the action of the more powerful proboscis of the *Stomoxys*. *Lyperosia* was found to await its turn with other nonbiting flies for the free-for-all blood feast. This was noted in two instances on the pachydermic skin of the carabao where the relatively feeble mouth of this diminutive muscid was a decided handicap. In this instance, especially among grazing carabaos, *Lyperosia* will hover in a swarm above a lone bloodsucking *Stomoxys*. To be sure the *Lyperosia* will probe for blood on its own initiative, as will smaller flies like some of the Chironomidæ, but apparently when so much energy is required on a thick-skinned animal like the carabao, blood in the readily available form provided by the *Stomoxys* will be imbibed readily. *Lyperosia* was never observed to provide blood for other hawking dung flies, although this probably occurs. Another haustellate muscid, a *Philoematomyia*, was observed to feed independently of other flies. Although its mouth is not strictly a piercing organ, the epidermis is penetrated, blood being drawn to the surface of the skin and sucked cleanly.

In order to secure additional evidence of the blood-feeding habits of the nonbiting flies, experiments were conducted to determine the relationship of the common house fly, *Musca domestica*, to *Stomoxys* as a harborer and carrier of trypanosomes. In these experiments it was aimed first to prove that *M. domestica* can harbor within its body infective trypanosomes. The normal protozoan fauna of these flies was not taken into consideration,

as no great stress was laid on microscopical findings. Emulsions from dissected flies fed on surra blood did, however, show organisms resembling *Trypanosoma evansi.* In the following experiments house flies were employed which had emerged April 23 and 24, 1912, from laboratory cultures. A large number of these were applied to the abraded tail of a surra-infected monkey, and three hours later an emulsion from 3 flies was found swarming with trypanosomes. At this time 20 flies of the lot were inoculated into 2 guinea pigs, the abdominal contents only being used. Stained smears of the solution that was inoculated revealed the presence in moderate numbers of organisms indistinguishable from *Tr. evansi.*

The two inoculated guinea pigs, 127 and 128, were found to be infected on the seventh and eighth days respectively. Both showed trypanosomes on numerous occasions and also at death, which occurred on the sixty-fifth day after inoculation in the case of No. 127, and on the fifty-second day in the case of No. 128.

Two hundred fifty flies of this lot were utilized in carrying through the following experiment. Prior to infection of the house flies, 200 *Stomoxys* were placed on a surra monkey's tail (which had not been previously abraded). After thirty minutes the majority of the flies had fed, and then a fresh bottle, containing the 250 *Musca,* was substituted. The house flies fed ravenously on the blood brought to the surface by the probes of the first flies. When a large number of the *Musca* showed partly blood-engorged abdomens, which occurred in fifteen minutes, they were withdrawn and applied to a healthy monkey after 200 hungry, newly emerged *Stomoxys* were turned loose in the same bottle, both species being then applied to the tail of the fresh monkey. Here the attempts to simulate natural conditions were successful; the *Musca* fed after the *Stomoxys,* lapping the fluid from punctures made by the latter. The flies were not disturbed until all were apparently satisfied, which was a matter of forty minutes.

In a second experiment 30 laboratory-bred flies were applied to a healthy monkey and 25 bites were recorded. Immediately 50 *Musca* which had fed from a fresh wound on a surra animal were substituted for the *Stomoxys.* In twenty minutes 30 to 40 of the *Musca* had lapped blood from the healthy monkey's tail. Full opportunity was given them to carry infected material on labella and pulvillus into the wounds presented. Three other experiments were conducted with guinea pigs as hosts. In one, 40 *Musca* accompanied 20 *Stomoxys;* in another, 14 *Stomoxys* and 80 *Musca* were used; and in the last, 20 *Stomoxys* were

followed by 60 *Musca*. The flies were used in much the same manner as in the preceding experiments, the *Musca* feeding, after contamination, from the wound made previously by healthy *Stomoxys* on guinea pigs free from disease.

All of these experiments were followed by negative results.

There is demonstrated at least, that a wound caused by the mouth prick of *Stomoxys* is not suitable for the entrance of surra-infected material transported by the mouths and feet of many house flies. A logical sequel to this series would be to transfer the muscids, after they were supplied with infected blood from *Stomoxys*-probed wounds, to open sores and scratches found on work animals. This work is under way at the present time.

The probability of success by this method is indicated by the experiments of the following writers:

Musgrave and Clegg[23] transmitted surra to healthy animals through the agency of house flies.

Darling,[56] in the Panama Canal Zone, recently conveyed *Tr. hippicum* to the mule by means of 18 house flies.

THE CYCLICAL DEVELOPMENT OF TRYPANOSOMA EVANSI IN STOMOXYS CALCITRANS.

The literature is abundantly supplied with theories and conjectures in regard to the development of trypanosomes within the body of the intermediate insect host. Aside from the monumental work of Kleine, Bruce, and his collaborators, on the development of trypanosomes in tsetse flies, we possess little definite knowledge. In regard to *Stomoxys* as a definitive host, the experiments that have been performed are far from satisfactory, the most serious obstacle encountered being the inability of various workers to keep this species of fly alive long enough for complete investigation. The views of various investigators are cited as follows:

Austen[35] finds from the evidence submitted, no indication that trypanosomes ingested by *S. calcitrans* pass through a developmental cycle and they apparently disappear within forty-eight hours.

Manson[40] notes that *Stomoxys* probably acts as the definitive host for *Tr. evansi* and *Tr. equinum.*

Schat[14] is apparently convinced that *Stomoxys* serves as the definitive host of *Tr. evansi* and that surra parasites propagate in the body of this fly.

Ziemann[41] thinks that *Tr. vivax* is transmitted by *Stomoxys* which acts as a definitive host, the trypanosomes multiplying in its body. No experimental evidence is cited.

Leese[42] discusses cases of camel surra in India. He considers the mechanical theory of transmission perfectly adequate, and that a life cycle of the development of the trypanosomes in the biting flies, *Stomoxys* and others, is not tenable except by analogy.

Gaiger[29] in speaking of *Stomoxys* and other flies mentions that no

experiments have yet been carried out in India, on the lines of those of Kleine and Bruce in Africa, to show that, in an odd fly or two, trypanosomes may survive as in a culture medium and that possibly a sexual cycle may occur.

Baldrey[43] believes with Schat that there is evidence of a cyclical development in flies infected with surra. He attempts to show that the development of *Tr. evansi* in the fly is probably completed through a mammal. He finds the trypanosomes in the fly quickly dying, and sees a spore stage which is incapable of reproducing the disease. This suggests to him that direct transmission by the fly is not the usual method since it is rare to find trypanosomes in the proboscis of the fly immediately after feeding. The longest time *Stomoxys* is kept alive for his experiments is ten days. All feeding experiments were negative. Injections of flies were found positive within twenty-four hours after infection.

Leese[21] fed wild *Stomoxys*, caught on surra animals, on a white rat after five to twenty-one days of capture from infected hosts. The result was negative for evidence of a cycle of development. Three experiments were conducted with *S. calcitrans* in interrupted feedings of one-half- to three-minute intervals. Fifteen flies transferred from a white rat to a healthy guinea pig gave a negative result. Ten flies fed from surra animals in the field transferred to a white rat proved negative. Ten flies from an infected white rat to a healthy white rat produced a positive result when fed—1 on the first day, 2 on the second day, and 7 on the third day. The flies were applied from tubes inverted over the animals.

Koch[44] in a measure anticipated Kleine and Bruce in their classical studies on cyclical development in insects. Koch's investigations in sleeping sickness with *Glossina* "led him to conclude that the flies did not transmit the disease by carrying the blood directly from an animal to another as is usually supposed, but that the trypanosomes pass through a developmental stage in the fly."

Kleine[45] with the use of laboratory-bred *Glossina* was able to show convincingly a distinct cycle of development of *Tr. gambiense* in the flies.

Bruce and others,[46] working with *Tr. gambiense* and *G. palpalis*, found that from a lot of 60 flies 1 survived on the seventy-fifth day after infection and after previously infecting a monkey reproduced the disease by subcutaneous inoculation. A tiny drop of the emulsion was sufficient. Salivary glands, besides other organs, were infective in this fly.

Bagshawe,[47] criticizing Baldrey's paper, says: "Such transmission experiments as these should be continued with a large number of flies and, if possible, for longer periods. In the case of the rat-flea and the tsetse-fly, only a small percentage get a permanent infection with trypanosomes; hence the odds against experiments with single flies succeeding are considerable. No reliable evidence of a cycle of a pathogenic trypanosome in *Tabanus* or *Stomoxys* will be obtained from a study of the parasites found therein after infected feeds till the flies have been bred."

Speaking of the carriers of surra in this connection, the author last quoted remarks: "As it has been pointed out before, the first essential is to breed and keep in captivity the flies which are under suspicion, and until this has been done we shall remain in uncertainty whether there is or is not a special development of the surra organism in the invertebrate host. Our knowledge of the life history of the African species of trypanosomes makes it very probable that there is."

EXPERIMENTS ON CYCLICAL DEVELOPMENT.

The first of this series of experiments was conducted with a small number of wild flies at a time when bred flies were not available. The experiment was followed out to completion mainly to acquire a technique for keeping flies alive under laboratory conditions. In this respect the tests were successful. The flies were kept individually in glass tubes and fed daily until the last fly of the original lot died. Fourteen flies were used on the first day after infection by one bite per fly on a heavily infected guinea pig (45). The duration of the experiment was sixty-seven days from the initial infective feeding. The sole survivor was too enfeebled to feed on the sixty-eighth day, when it was inoculated in a subcutaneous pocket of a healthy guinea pig. Fifty days elapsed without any infection resulting; therefore, it was assumed that the feeding experiments were negative.

Two other experiments were tried with laboratory-bred flies with the object of using as many flies as possible at once. Large bottles were utilized into which the monkey's tail was introduced to be fed to the flies. The stock of flies rapidly diminish until the twenty-eighth and thirtieth days.

Prior to the beginning of the first experiment (Table X), the flies were applied for two days on monkey A, which upon both occasions had only a very few trypanosomes in each field of blood examined. Trypanosomes were seen in emulsions of 3 flies of this series on the second day of biting the infected monkey.

The flies used in the second of these experiments (Table XI) were fed twice on the blood of surra monkey R. At each feeding a moderate number of trypanosomes were present in its blood. A single fly which was injured after feeding on monkey R showed a large number of surra-like flagellates in an emulsion of its intestinal tract.

In one instance the survivors of the experiment were inoculated into guinea pigs to test the presence of infective organisms. These animals did not react. The other experiment ended on the thirty-first day with the death of the last 2 flies of the original 75 flies which had been applied to guinea pigs at the beginning of the experiment.

None of the guinea pigs and monkeys employed in the series was used for other purposes until forty-four days after the completion of feeding by the flies. During this time the animals were examined at convenient intervals, but no indications of the infection were encountered.

A final experiment to complete the series was made one month later with laboratory-bred *Stomoxys*, kept individually in suit-

able tubes. This test was begun with 90 flies which for three days were applied to a guinea pig having a high degree of infection. On the fourth day the first of a series of monkeys was employed with 87 flies. The monkey host was changed daily as long as any flies remained. Beginning with the twenty-sixth day of the experiment, monkeys were used for 3 successive feedings. The experiment ran its course in forty-two days when the last 2 flies died. No infection resulted up to a period of thirty-eight days, the length of time the experimental animals had been under observation.

The results are embodied in Tables IX, X, XI, and XII.

TABLE IX.—*Successive feeding of Stomoxys from infected to healthy animals.*

Interval after feeding on infected animal.	No. of healthy guinea pig used.	Number of flies used.	Interval after feeding on infected animal.	No. of healthy guinea pig used.	Number of flies used.
Days.			*Days.*		
¼	53	11	35	105	6
1	55	14	36	106	6
2	56	13	37	107	6
3	58	12	38	108	6
4	60	11	39	109	6
5	62	12	40	110	6
6	19	19	41	111	6
7	64	9	42	112	6
8	67	9	43	113	6
9	69	9	44	114	6
10	70	9	45	115	6
11	72	9	46	116	5
12	74	9	47	117	5
13	76	8	48	118	5
14	78	8	49	119	5
15	80	7	50	120	5
16	82	7			
17	84	6			
18	86	6	51	121	5
19	88	6	52	122	5
20	89	6	53	123	5
21	91	6	54	124	5
22	92	6	55	125	5
23	93	6	56	126	4
24	94	6	57	127	4
25	95	6	58	128	4
26	96	6	59	129	3
27	97	6	60	130	3
28	98	6	61	131	3
29	99	6	62	131	3
30	100	6	63	131	2
31	101	6	64	131	2
32	102	6	65	131	2
33	103	6	66	131	1
34	104	6	67	131	1

TABLE X.—*Successive feeding of Stomoxys from infected to healthy animals.*

Length of time after the last infective meal.	Healthy host employed, monkey—	Number of flies applied to healthy animal.	Number of flies biting healthy animal.	Length of time after the last infective meal.	Healthy host employed, monkey—	Number of flies applied to healthy animal.	Number of flies biting healthy animal.
Days.				*Days.*			
1	C	190	182	16	C	23	22
2	D	134	115	17	D	22	19
3	E	123	114	18	F	22	21
4	F	113	100	19	B	20	20
5	G	98	93	20	K	18	16
6	H	70	68	21	L	14	13
7	I	65	60	22	N	14	12
8	J	56	53	23	O	14	12
9	K	52	49	24	P	14	10
10	N	49	45	25	T	14	14
11	O	46	35	26	U	12	11
12	P	43	28	27	X	10	7
13	Q	32	24	28	G	6	5
14	S	24	21				
15	T	24	22				

TABLE XI.—*Successive feeding of Stomoxys from infected to healthy animals.*

Length of time after the last infective meal.	Healthy host employed, monkey—	Number of flies applied to healthy animal.	Number of flies biting healthy animal.	Length of time after the last infective meal.	Healthy host employed.	Number of flies applied to healthy animal.	Number of flies biting healthy animal.
Days.				*Days.*			
1	M	60	43	16	Monkey B	8	6
2	N	60	48	17	Monkey C	5	4
3	O	54	56	18	Monkey S	4	4
4	P	44	28	19	Guinea pig 89	4	4
5	D	36	36	20	Guinea pig 84	4	4
6	H	34	20	21	Guinea pig 111	2	2
7	J	29	23	22	Guinea pig 92	2	2
8	K	26	25	23	Guinea pig 99	2	2
9	L	23	23	24	Guinea pig 50	2	2
10	2N	18	13	25	Guinea pig 110	2	2
11	2O	18	16	26	Guinea pig 131	2	2
12	2P	14	12	27	Guinea pig 88	2	2
13	G	12	9	28	Guinea pig 88	2	2
14	2H	12	11	29	Guinea pig 88	2	2
15	2J	9	7	30	Guinea pig 88	2	2

TABLE XII.—*Successive feeding of Stomoxys from infected to healthy animals.*[a]

Interval after feeding on infected animal.	Healthy animal used, monkey—	Number of flies applied.	Interval after feeding on infected animal.	Healthy animal used.	Number of flies applied.	Interval after feeding on infected animal.	Healthy animal used.	Number of flies used.
Days.			*Days.*			*Days.*		
1	C	87	19	J	53	37	8	14
2	D	79	20	M	49	38	9	13
3	G	90	21	N	47	39	9	12
4	L	85	22	O	45	40	9	9
5	M	83	23	P	43	41	11	4
6	N	81	24	S	42	42	11	2
7	P	80	25	1	40			
8	S	77	26	2	40			
9	1	73	27	2	38			
10	2	72	28	2	37			
11	3	70	29	3	37			
12	4	67	30	3	35			
13	8	66	31	3	33			
14	9	65	32	4	31			
15	10	61	33	4	30			
16	11	58	34	4	30			
17	C	58	35	8	28			
18	G	55	36	8	20			

[a] Guinea pig A was used to feed the 90 flies of this series for three days prior to their application upon the first healthy monkey. During the three days the blood of guinea pig A was richly infected with trypanosomes. In emulsions made, 3 out of 4 flies examined showed tremendous numbers of trypanosomes indistinguishable from those seen in the host's blood.

INOCULATION OF FLIES FED ON INFECTED ANIMALS.

To complete the discussion of the cyclical development of the trypanosomes within the fly, it is necessary to refer to the length of time flies remain infected after imbibing infective material. Although, because of the uniformly negative results obtained in many transmission experiments, this information remains of no immediate practical value, it is included because the literature on this subject is regarded as tending to mislead by magnifying its importance.

The length of time the infection is held in the insect certainly is of prime significance where the infection is produced normally through crushing of the intermediate host or through fæcal contamination. In both instances the transmission is consummated by injection of the contaminative material into an abrasion produced by the insect's mouth parts.

The presence of surra trypanosomes in the fly has been demonstrated up to forty-eight hours by several authors. The organism in all cases has been found in the intestinal tract and never within the salivary glands and rarely in the proboscis. In some instances the contents of the intestines of an infected fly have given rise to the disease through inoculation into animals, while in others the writer appears contented with the microscopical findings. From a survey of the literature at hand it appears that the infection was never reproduced by the former method beyond twenty-four hours.

Bruce[48] states: "a *Glossina* fly, a few hours after feeding on an infected animal, crammed with blood showing active haematozoa under the microscope, if minced up and injected under the skin of a susceptible animal, fails to give rise to the disease (nagana)."

Bruce and others[49] note, in an attempt to ascertain the number of tsetse flies infected with *Tr. gambiense*, that in one case in which no trypanosomes were found in 12 flies examined, when their combined contents were injected into a healthy monkey, sleeping sickness resulted.

Bruce and others[50] injected monkeys with a single fly (*Glossina palpalis*) one day; 2, 3, and 4 flies two days after an infected feed. These caused sleeping sickness. Between the second and twenty-fourth days after infection 249 flies were inoculated, in all with negative results, although 15 of these flies proved microscopically to be swarming with living trypanosomes at the time of inoculation.

Martini[32] found trypanosoma in *Stomoxys calcitrans* twenty-three hours after an infected meal. The organisms were not observed on the day following, and they were apparently digested.

Nabarro[18] cites a case where trypanosomes from a mule in East Africa were found in the stomach of *Stomoxys* as long as thirty hours after a meal of infective blood.

Dutton, Todd, and Hanington[34] found trypanosomes (*Tr. gambiense*) unchanged in the gut of *Stomoxys* up to twenty hours after feeding on a sick horse. Also on two occasions they found fusion forms of the trypanosome in a fly fed eighteen hours previously.

Nabarro[18] states that the organisms of sutoko, a trypanosome disease of the nagana group, were found active in the stomach contents of *Stomoxys* up to twenty-four hours after infection.

Bruce[51] found in Uganda scanty trypanosomes in the proboscis of *Glossina morsitans* fed forty-six or fewer hours previously on a nagana-infected animal.

Nabarro,[18] referring to fly trypanosomiases of Uganda, recalls that organisms remain active for a longer time in the stomach of *Stomoxys* than in that of *Gl. palpalis*. Feeding experiments with eight- and twenty-four-hour intervals from infected to healthy animals were negative in *Stomoxys*. *Stomoxys* was positive in direct transmission in interrupted feeding with dogs.

Nabarro[18] writes that trypanosomes taken from an infected monkey (Abyssinian strain of trypanosomiasis) by *Stomoxys* remained active in the stomach for twelve hours, in that of *Gl. palpalis* five and one-half hours.

The following table shows the length of time during which *Stomoxys* was found to harbor the surra organisms. The few laboratory-bred flies that could be spared for the purpose were fed on a virulent strain of guinea-pig surra and injected into healthy guinea pigs at stated intervals. When the fly was to be kept beyond twenty-four hours, it was fed a few minutes each day on an animal not included in this experiment. In every case the entire fly was inoculated.

TABLE XIII.—*Results of inoculating flies fed on an infected host.*

Length of time of infective meal.	Time elapsing after feeding on infected host.	Number of flies injected.	Trypanosomes present or absent at the time of injection.	No. of the test guinea pig used.	Results of inoculation.
Minutes.	*Days. hrs.*				
3	(a)	1	Present	37	Positive on eighth day. Positive on thirty-eighth day at death.
5	6	1	do	35	Positive on sixth day. Positive on forty-second day at death.
4	18	1	Few alive	50	Animal negative.
5	18	1	Few active	168	Do.
4	24	1	Absent	91	Do.
6	24	3	do	32	Do.
6	30	3	do	93	Do.
7	48	2	do	130	Do.
9	54	3	do	126	Do.
8	29 00	6	do	73, 74	Do.
10	68 00	1	do	34	Do.[b]

[a] Used immediately.

[b] A wild fly used for successive feedings on guinea pigs.

A check on the experiment in the use of this species of fly is offered in a former experiment by an inoculation of a forty-two-hour infected mosquito, *Stegomyia fasciata*. Here a positive result was obtained.

THE QUESTION OF HEREDITARY TRANSMISSION.

The experiments next described were performed with the purpose of eliminating all possible avenues through which infection might possibly be transmitted by means of the fly.

Sergent, Ed. & Ét.(38) recount experiments with Algerian trypanosomiasis in which feeding tests, with young ticks hatched from eggs laid by adults removed from heavily infected animals, were negative.

Dutton, Todd, and Hanington(34) write: "It is possible that the progeny

of infected tsetse flies are capable, or are alone capable, of transmitting the trypanosomes." (*Tr. gambiense.*)

Fraser and Duke(53) give detailed results in feeding hundreds of laboratory-bred *Glossina* thirty days upon healthy monkeys to determine if a hereditary transmission of *Tr. gambiense* existed. Only negative results were obtained.

Kleine and Taute(54) used thousands of tsetse flies bred from pupæ without encountering a single instance of hereditary transmission of the sleeping-sickness trypanosome. They view with skepticism the finding of trypanosomes in the eggs of infected flies.

Kleine(55) found that none of the experiments with *Gl. morsitans* and *Tr. gambiense* supported the theory of hereditary transmission of the trypanosome. Hundreds of flies were used.

Bruce and others,(49) in experiments with laboratory-bred *Glossina* and sleeping sickness, obtained no evidence of hereditary transmission in the use of several hundreds of flies.

Baldrey(43) expresses a belief in the theory of transmission by heredity. His observations relate to *Stomoxys*, Tabanidæ, and surra.

Minchin writes that, so far as it is permissible to draw general conclusions from experiments which yield negative results, it appears that trypanosomes are not transmitted from parent to offspring in insect carriers. The experiments referred to were carried on in 1911 with fleas and *Trypanosoma lewisi*, by Minchin and Thomson. These authors sum up their experience thus: Experiments on a large scale had been done to see if transmission can take place hereditarily in the flea, that is to say, whether the offspring of the infected flea themselves may be infected. These were continued for some months, but have always been negative.

Aside from the biological significance of hereditary transmission, there is involved a practical problem for the laboratory worker. If pathogenic trypanosomes were inherited, the same objection for employing wild flies would hold for laboratory-bred flies whose parents were wild. Under these circumstances the newly emerged laboratory-bred flies would need to be proved surra-free prior to their experimental use.

In the present series of experiments the aim was, first, to test the possibility of the transmission of surra from fly to fly through the egg to the new generation, and, second, to simulate the possibility of conveyance of the trypanosomes through the imago of flies, the larvæ of which were fed on infected material.

In the first of these experiments the flies used were the progeny of flies fed, previous to egg laying, on surra-infected guinea pigs for periods of from three to five days. The eggs were laid from February 27 to March 15, 1912; within a day after emerging the new flies were fed on a healthy guinea pig. Daily additions to the number of flies fed were made as fast as they emerged. The feedings were conducted during nine days, at first with 7 flies and later with 25 flies. Data on the subject appear in the following table:

TABLE XVI.—*Feeding the progeny of infected flies.*

Date.	Number of flies applied.	Total length of time flies were fed.	No. of animal used.
		Hours. mins.	
Mar. 21, 1912	7	36	Guinea pig 68.
Mar. 22, 1912	8	41	Do.
Mar. 23, 1912	7	36	Do.
Mar. 24, 1912	15	1 1	Do.
Mar. 25, 1912	19	1 29	Do.
Mar. 26, 1912	22	1 37	Do.
Mar. 27, 1912	23	1 49	Do.
Mar. 28, 1912	25	1 55	Do.
Mar. 29, 1912	25	2 3	Do.

The result of this experiment with guinea pig 68 was negative. This animal has been used since for surra inoculation to which it reacted positively August 4, 1912.

A second experiment of this type was carried out with the progeny of flies fed on a surra horse. The horse was kept in a fly-screened stall for six days during which time flies were permitted to feed undisturbed. Several hundreds of the flies were removed from the stall and placed in a jar with horse manure. Seventeen days later new flies emerged, 75 of which were selected for feeding on a guinea pig. The flies were fed daily for eight days when the animal was kept under observation for forty-five days, after which time the experiment was judged to be negative.

Surra organisms have never been encountered microscopically in numerous lots of eggs laid by infected flies nor in emulsions of larvæ developing from eggs deposited by surra-fed adults.

On May 9, 1912, this was tested in a more convincing way by inoculating material of this sort. With laboratory-bred flies as the parents, 30 larvæ, the progeny of 13 flies which had been fed several days on a surra monkey, were emulsified in salt solution and then inoculated into 2 guinea pigs, 97 and 98. This also gave a negative result.

The experiments of the next series, in which attempts were made to transmit the surra trypanosomes through the larvæ, are obviously grossly mechanical, although the principle involved in hereditary transmission as set forth by Calkins(58) is readily recognized as also mechanical in the sense of inheritance by contact.

In this experiment the eggs produced by several hundreds of wild flies were placed, April 27, 1912, in a jar containing a medium of horse manure with fresh blood from a surra horse. The blood was lightly infected on this day. On May 2, the larvæ were changed to a clean jar with fresh, boiled manure, cooled and sprinkled generously with heavily infected blood of a monkey recently dead from surra. On May 4, pupæ had formed, emergence taking place five days later when 11 flies appeared. Forty-eight flies were fed daily as they emerged from May 9 to 13, inclusive, on monkey 2M. On May 14, 12 flies remained, and of these 7 fed on the monkey. After feeding, the flies were emulsified and inoculated into guinea pigs 93 and 94, which after the usual tests did not react.

Within two to three days after the blood was added to the fly-breeding medium, the presence of the blood diet could be detected by the terra-cotta color of the alimentary tract of the larvæ. The surra-blood-fed larvæ were not injected to demonstrate the presence of the specific organism; however, it is thought that the disease could be reproduced by animal inoculation with fresh material. Trypanosomes were found on microscopical examination in larvæ four hours after the introduction of the infected blood. These had been passed through four changes of salt solution prior to macerating for examination.

The data embodied in Table XVII represent a summary of all of the foregoing experiments in the attempts to convey the infection of surra by the agency of *Stomoxys calcitrans*.

TABLE XVII.—*Summarized data of feeding experiments with Stomoxys.*

Time after feeding on infected animals that the flies were applied.	Number of experiments.	Total number of flies used.	Number and kind of animals exposed to infected flies.	Nature of experiment, or method of applying flies.	Results.
Immediate to 48 hours.	1	26,666	3 horses	Direct completed feeding.	Negative.
5 minutes to 53 hours.	3	225	3 guinea pigs	do	Do.
10 minutes to 3 days.	25	565	6 monkeys and 19 guinea pigs.	do	Do.
21 hours to 31 days.	1	1	31 guinea pigs	do	Do.
20 seconds to 2 minutes.	11	173	11 guinea pigs	Direct interrupted feeding.	Do.
1 to 3 minutes	14	139	14 monkeys	do	Do.
25 to 30 seconds	2	63	2 horses	do	Do.
5 seconds to 1 minute.	3	274	3 guinea pigs	Successive interrupted feeding.	1 positive, guinea pig received 206 bites during 6 days.

TABLE XVII.—*Summarized data of feeding experiments with Stomoxys*—Continued.

Time after feeding on infected animals that the flies were applied.	Number of experiments.	Total number of flies used.	Number and kind of animals exposed to infected flies.	Nature of experiment, or method of applying flies.	Results.
6 hours to 67 days	1	14	61 guinea pigs	Successive daily feeding.	Negative.
1 day to 28 days	1	190	18 monkeys	Attempts to transmit through a cyclical development.	Do.
1 day to 30 days	1	60	8 guinea pigs and 18 monkeys.	do	Do.
1 day to 42 days	1	90	18 monkeys	do	Do.
Immediate to 68 days.	11	23	12 guinea pigs	Inoculations of infected flies.	2 positive, 1 to 6 hours, 1 immediate injection.
30 seconds to 5 minutes.	6	24	6 guinea pigs	Inoculations of soiled proboscides.	3 positive, all in 30-second intervals.
Immediate	4	48	4 guinea pigs	Rubbing infected blood into fly-bitten skin.	Negative.
30 days to 38 days	1	25	1 guinea pig	Hereditary transmission, progeny of infected flies.	Do.
About 25 days	1	75	1 guinea pig	do	Do.

METHODS EMPLOYED IN FEEDING AND KEEPING FLIES FOR LABORATORY PURPOSES.

The technique employed in maintaining the normal longevity of *Stomoxys* applies equally to bloodsucking flies of other genera, for example, species of *Lyperosia* and of Hippoboscidæ. The greatest difficulty was encountered in attempting to keep flies, in either small or great numbers, in a common enclosure.

Screened stable.—In a screened stable, aside from the artificial obstacle of confinement, the difficulties presented are summed up in the presence of natural enemies, and, do what one may, it is well-nigh impossible to wholly eradicate these. Particular reference is made to the common insectivorous lizard and the ubiquitous spider. Spraying with pure cresol was effective against the individuals present, but the disinfectant did not prevent the entrance of other lizards and spiders.

Glass vessels.—Large bottles and museum jars of 3 liters' capacity were used when it was desired to confine and to feed at one time large numbers of flies. Thirty days was the longest time flies were kept alive in these containers. In this instance,

it was found necessary for the prolongation of life during the last ten days to transfer the flies to individual test tubes after each feeding. In this method with the use of glass vessels untimely death resulted from mite infestation, cannibalism, and excess of moisture.

Mite infestation.—An unknown mite, not restricted to these flies, was found both in the hypopial stage and in the adult form. The first of these stages did not prove a menace unless present in great numbers either on the body, thus precluding proper functioning of the spiracles, or on the proboscis, which prevented insertion of the beak in feeding. When the mite was present as a true parasite in the adult form, an occasional one or two did not affect the host, but when present in larger numbers they were sufficient to enfeeble the fly on account, no doubt, of lowered resistance brought about by the artificial environment.

Cannibalism.—Newstead (57) calls attention to a case of cannibalism in *Stomoxys calcitrans*. I have found it prevalent to an unusual degree. Often the disability of an individual fly attracted the attention of another more active member which promptly attempted, and usually succeeded, in puncturing the helpless fly's abdomen. This disability resulted from engorgement, infirmities resulting from broken labium, or from the wings adhering to the glass, due to an excess of moisture. Numerous cases of flies have been found actually fracturing the labium in attempting to penetrate the host's epidermis. This may result also from the fly pricking at the glass in attempting to sip moisture from the container. Such a condition, of course, makes feeding impossible, as the proboscis is not rigid enough to puncture the skin; and, as a result, the fly dies.

Excess of moisture.—Where a large number of flies are quartered together, it is difficult to prevent an excess of moisture, even though a bibulous filter paper is provided. The condition is the result of, first, excretion; and, second, probably, condensation of the moisture of the air in the bottle, when at the temperature of 20° to 26° C.

The use of individual glass tubes.—By the use of individual glass tubes the difficult problem of keeping the flies alive in captivity was most successfully solved; for the flies can be observed at all times and longevity is increased to approach the normal. Ninety-four days was found to be the maximum life of adult *Stomoxys* kept individually under laboratory conditions in glass tubes.

A test tube of 24-millimeter bore, plugged with cotton, was

found the most convenient. A piece of white filter paper conforming to the size of the tube was found ideal to regulate the moisture requirements, and this was changed at least every two or three days. It was found advantageous to change the tube not oftener than twice each week. In feeding it was not found necessary to screen the mouth of the tube. The base of the tube was directed toward the window light and the filter paper removed; the tube was then inverted immediately over the animal's body. The fly after feeding was induced to release its hold on the skin of its host by gently tapping the tube, and gradually inclining it toward the light, after which the filter paper was restored and the tube closed with a cotton plug.

The flies when not feeding were kept in the dark at a temperature between 20° to 26° C.

Martini[32] kept experimental flies, *Stomoxys calcitrans*, at a temperature of 23° C. The longevity is not stated.

METHODS OF APPLYING THE FLIES TO THE HOST.

Monkeys.—In applying large numbers of flies in a bottle, the following method was pursued. First the monkey was strapped, abdomen down, to an improvised stock by means of surgical gauze or twine, securing the wrists and ankles which were bandaged previously to prevent chafing. Then the tail was closely cropped, bound to a stout wire with straps of gauze, and thrust into a narrow-necked bottle which harbored the flies to be fed. The other end of the wire was kept at a convenient distance from the mouth of the bottle to facilitate manipulation. Wiring the tail was resorted to on account of the animal switching the appendage against the glass and crushing numerous flies.

Another method was employed with flies fed individually from tubes inverted over the thigh or other convenient portions of the monkey, held in a similar position on the stock. At least two flies could be fed at once in this manner. (Plate IV.)

Guinea pigs.—When a guinea pig was subjected to fly bites in a large museum jar it was found to be of advantage to immobilize it by strapping to a frame of brass wire. (Plate II.) This was done in order that movements of the animal would not interfere with taking the fly census during feeding, and to prevent the guinea pigs from eating the flies. Cropping the hair of this host was found to assist the parasites in feeding.

In the use of a museum jar it was necessary to hold it horizontally with the bottom toward the light. Here the majority of

flies assemble when not feeding, and the light reactions of the fly are taken advantage of in withdrawing and introducing them. If desired, ether can be used to advantage in the transfer of animals. It should be applied at the screened end of the jar, lightly enough to prevent flight, but not sufficient to stupefy the insects.

Tubes containing single flies were also applied to guinea pigs strapped to a stock. The fly was usually placed on some convenient part of the body, preferably on the side of the abdomen. (Plate V.)

Horses in sheds.—Horses for experimentation were kept in a shed screened from flies, a method commonly employed by investigators. Here it is not possible to make close and accurate examinations. Despite the fact that many thousands of flies could be applied at once, they did not, in my experience, live longer than eight days, usually dying in five days even when food was constantly available.

Dutton, Todd, and Hanington[34] made attempts to keep tsetse flies alive longer by more nearly reproducing their natural habitat in their cages. In a cubical gauze cage, 18 inches along the side, containing water and growing grass, guinea pigs and rats were used. Flies were found to feed much better when animals were immobilized in cages. Smaller cages than the above were found more advantageous for purposes of closer observations.

Horses on operating table.—In this method, the obvious advantage is in obtaining accurate data in feeding operations, and timing can be done when desirable. This method supplanted the cruder one of throwing the horse to the ground and feeding flies from inverted bottles. The violent struggling of the unwilling host is not favorable for obtaining accurate results.

In all of the methods attempted with the various animals, the hair was closely cropped with scissors. To avoid abrasions a razor was never employed. If the skin were broken in this manner and a positive result obtained, obviously it might invalidate the conclusions to be drawn from the experiment. Contamination might be produced under these conditions by the pulvilli of the feet, and possibly, though remotely, by the body hairs and wings of the insects. It was found advantageous to slightly dampen the skin of the host to make the animal odor more attractive to the fly and arousing its blood-drawing instincts.

In conclusion, it must constantly be borne in mind that all of these artificial accessories in methods may possibly jeopardize valid results by increasing the opportunities for contaminative infections.

GENERAL SUMMARY.

1. Only negative results were obtained in the attempts at direct mechanical transmission of surra with flies which were induced to bite healthy animals at intervals ranging from five minutes to three days after being permitted to complete the feeding upon infected animals. Thousands of *Stomoxys calcitrans* were employed in 29 experiments involving the use of 3 horses, 6 monkeys, and 22 guinea pigs.

2. Twenty-seven experiments were performed in attempts to transmit surra by the interruped method of feeding. All attempts proved negative *where a single application of a varying number of flies was used*, as many as 38 on a horse, and a maximum of 40 on a small guinea pig. The intervals between feeding on infected and healthy animals averaged twenty-five to forty seconds in the two instances cited.

3. In 3 trials, interrupted feeding was employed in successive daily applications. In attempting to determine the minimum number of bites necessary to infect an animal, as high as 40 were followed by negative results. The only positive result obtained was produced from a succession of 206 interrupted bites in which the flies were transferred immediately from the infected to the clean animal. The flies were applied thirty-two hours during a period of six days.

4. The results of these experiments indicate that *Trypanosoma evansi* does not develop in the body of *Stomoxys calcitrans*. Ninety-four days was the longest period in which laboratory-bred flies were tested for a cyclical development, and sixty-seven days the maximum for wild flies.

5. Organisms of surra were not found in *Stomoxys calcitrans* beyond eighteen hours after feeding on an infected animal, and the limit for infection by inoculation was ascertained in these experiments to be six hours.

6. Pathogenic trypanosomes were found in the proboscis of the fly thirty seconds after feeding on infected blood. Within one minute and thirty seconds the organisms were not present in the mouth parts in a form capable of infecting by inoculation into guinea pigs.

7. The wounds made by the labium of *Stomoxys* were not found to be a suitable channel for infection. Consequently it is not likely that surra in domestic animals is produced through this avenue by external contamination; namely, fæces, mouth parts, and pulvilli of infected flies.

8. The intimate relation in the feeding habits of *Stomoxys* and of house flies has been pointed out. *Stomoxys* has been demonstrated to provide through its bites the infection of *Musca domestica* and other dung flies. These flies have been demonstrated to act as carriers, harboring the surra organisms for several hours.

9. No evidence was obtained to indicate that *Tr. evansi* is hereditarily transmitted to the offspring of *S. calcitrans.* The larva of this fly fed on surra blood does not continue to harbor the trypanosome and the fly is "clean" upon reaching maturity.

10. It is demonstrated that the individual glass-tube method is the most suitable for applying flies in feeding on experimental animals and for keeping flies for long periods under laboratory conditions.

REFERENCES.

(1) Summers. Revision of the Oriental Species of *Stomoxys*. *Ann. & Mag. Nat. Hist.* (1911), VIII, 8, 235.
(2) Bruce. Sleeping Sickness Investigations in Uganda. *Bull. Sleeping Sick. Bur.* (1910), 2, 251.
(3) Bruce, Hamerton, Bateman, and Mackie. Trypanosoma pecorum in Uganda. *Proc. Roy. Soc. London* (1911), B, 82, 468–479.
(4) Montgomery and Kinghorn. A Report on Trypanosomiasis of Domestic Stock in Northwestern Rhodesia. *Ann. Trop. Med. & Parasit.* (1908), 2, 129.
(5) Dutton and Todd. First Report of the Trypanosomiasis Expedition to Senegambia. *Mem. Liverpool School Trop. Med.* (1903), No. 2, 40.
(6) Theiler. Quoted by Laveran and Mesnil (18), p. 202.
(7) Sander. Tropische und Subtropische Viehseuchen. In Mense's Handbuch der Tropenkrankheiten. Barth, Leipzig (1906), 3, 695–713.
(8) Martin, Lebœuf, and Roubaud. *Bull. Soc. path. exotique* (1908), 1, 356. Quoted in (35), pp. 150–151.
(9) Novy. The Rôle of Protozoa in Pathology. *Proc. Path. Soc. Phila.* (1907), 10.
(10) Austen. A Monograph of the Tsetse Flies. The British Museum of Natural History, London (1903), 304.
(11) Castellani and Chalmers. Manual of Tropical Medicine. Baillière, Tindall, and Cox, London (1910), 258.
(12) Sivori and Lecler. Quoted by Laveran and Mesnil (18), p. 307.
(13) Sieber and Gonder. A Case of Dourine under Conditions in which the Usual Method of Infection is Excluded. Abstracted in *Bull. Sleeping Sick. Bur.* (1911), 3, 164.
(14) Schat. Verdere Mededeelingen over Surra. Mededeel Proefstation Oost-Java (1903), III, No. 44. Copied from (35), p. 149.
(15) Manders. Surra as it occurs in Mauritius. *Journ. Roy. Army Med. Corps* (1905), 5, 623–626.
(16) Daruty. Quoted in (18), p. 279.
(17) Diexonne. Quoted in (18), p. 280.

(18) LAVERAN and MESNIL. Trypanosomes and Trypanosomiases. Nabarro edition. Baillière, Tindall, and Cox, London (1907), 186, 206, 208, 209, 210.

(19) MOHLER and THOMPSON. A Study of Surra Found in an Importation of Cattle Followed by Prompt Eradication. *Twenty-sixth Ann. Rep. Bur. Animal Ind.* (1909), 81–98.

(20) DARLING. The probable Mode of Infection and the Methods used in Controlling an Outbreak of Equine Trypanosomiasis (Murrina) in the Panama Canal Zone. *Parasitology* (1911), 4, 83–86.

(21) LEESE. Experiments Regarding the Natural Transmission of Surra Carried out at Mohand in 1908. *Journ. Trop. Vet. Sci.* (1909), 4, 107–132.

(22) CURRY. A Report on Surra with Studies on the Mode of Transmission. *Am. Med.* (1902), 4, 95–99.

(23) MUSGRAVE and CLEGG. Trypanosoma and Trypanosomiasis with Special Reference to Surra in the Philippine Islands. *Publ. Bur. Gov. Labs.* (1903), No. 5, 85–87.

(24) BAGSHAWE. Editorial. *Bull. Sleeping Sick. Bur.* (1911), 3, 262.

(25) NOVY, MACNEAL, and TORREY. The Trypanosomes of Mosquitoes and other Insects. *Journ. Infect. Dis.* (1907), 4, 264.

(26) EVANS. Elephant Surra. *Journ. Trop. Vet. Sci.* (1910), 5, 237.

(27) JOWETT. Further Note on a Cattle Trypanosomiasis of Portuguese East Africa. *Journ. Comp. Path. & Therap.* (1911), 24, 31–35.

(28) FRASER and SYMONDS. Surra in the Federated Malay States. Studies from the Institute for Medical Research. Federated Malay States (1908), No. 9, 24.

(29) GAIGER. Further Observations on Trypanosomiases, 1909–10. *Journ. Trop. Vet. Sci.* (1911), 6, 21–43.

(30) NABARRO and GREIG. Rep. Sleeping Sick. Comm. Roy. Soc. London (1905), No. 5, 40.

(31) BOUFFARD. Sur l'Etiologie de la Souma, Trypanosomiase du Soudan Français. *Compt. rend. Soc. biol.* (1907), 62, 71. Referred to in (35), pp. 149–150.

(32) MARTINI. Ueber die Entwickelung der Tsetseparasiten in Säugethieren. *Zeitschr. f. Hyg.* (1903), 5, 341–350. Quoted in (23), p. 85.

(33) GREIG and GRAY. Rep. Sleeping Sick. Comm. Roy. Soc. London (1905), 6, 203–208.

(34) DUTTON, TODD, and HANINGTON. Trypanosome Transmission Experiments. *Ann. Trop. Med. & Parasit.* (1907), 1, 201–229.

(35) AUSTEN. African Blood-sucking Flies. British Museum of Natural History, London (1909), 153.

(36) SCHUBERG and KUHN. Quoted in *Bull. Sleeping Sick. Bur.* (1911), 3, 370.

(37) SCHUBERG and KUHN. Über die Übertragung von Krankheiten durch einheimische stechende Insekten. *Arb. a. d. kais. Gesundheitsamte* (1909–11), 31, 377–393. Abstracted from *Bull. Sleeping Sick. Bur.* (1911), 3, 162–164.

(38) SERGENT, ED. and ÉT. El-Debab, trypanosomiase des dromadaires de l'Afrique du Nord. *Ann. Inst. Pasteur* (1905), 19, 31. Quoted by Nabarro in (18), p. 219.

(39) MINCHIN, GRAY, and TULLOCH. Rep. Sleeping Sick. Comm. Roy. Soc. London (1907), No. 8, 124.
(40) MANSON. Tropical Diseases. Cassell and Company, London (1909), 844.
(41) ZIEMANN. Trypanosomiases of Cameroon. Quoted by Nabarro in (18), p. 200.
(42) LEESE. Biting Flies and Surra. *Journ. Trop. Vet. Sci.* (1912), 7, 17–32.
(43) BALDREY. The Evolution of Trypanosoma evansi through the Fly: *Tabanus* and *Stomoxys*. *Ibid.* (1911), 6, 271–282.
(44) KOCH. Vorläufige Mitteilungen über die Ergebnisse einer Forschungsreise nach Ostafrika. Referred to by Novy in (59), p. 397.
(45) KLEINE. Weitere Beobachtungen über Tsetsefliegen und Trypanosomen. Reviewed in *Bull. Sleeping Sick. Bur.* (1909), 1, 321–323.
(46) BRUCE, HAMERTON, BATEMAN, and MACKIE. The Development of *Trypanosoma gambiense* in *Glossina palpalis*. *Journ. Roy. Army Med. Corps* (1909), 16, 115–125.
(47) BAGSHAWE. Editorial. *Bull. Sleeping Sick. Bur.* (1911), 3, 372-373.
(48) BRUCE. Appendix to Further Report on the Tsetse Fly Disease or Nagana. Harrison and Sons, London (1903), 6.
(49) BRUCE, HAMERTON, BATEMAN, and MACKIE. Trypanosomes and Tsetse Flies. The Development of Trypanosomes in Tsetse Flies. *Proc. Roy. Soc. London* (1910), B, 82, 368-388.
(50) IDEM. The Transmission of Trypanosomes. *Ibid.* (1910), B, 83, 345-348.
(51) BRUCE. Further Report on Nagana. Harrison and Sons, London (1896), 10.
(52) GONDER. Untersuchungen über Arzneifeste Mikroorganismen. Transmission of *Trypanosoma lewisi*. Reviewed in *Bull. Sleeping Sick. Bur.* (1912), 4, 16.
(53) FRASER and DUKE. Antelope Infected with *Trypanosoma gambiense*. *Proc. Roy. Soc. London* (1911), B, 84, 485.
(54) KLEINE und TAUTE. Ergänzungen zu unseren Trypanosomenstudien. Sleeping Sickness Investigations in *Bull. Sleeping Sick. Bur.* (1911), 3, 165-174.
(55) KLEINE. Weitere Beobachtungen über Tsetsefliegen und Trypanosomen. Reviewed in The Development of Trypanosomes in Tsetse Flies and other Insects. *Bull. Sleeping Sick. Bur.* (1909), 1, 321-323.
(56) DARLING. Experimental Infection of the Mule with *Trypanosoma hippicum* by means of *Musca domestica*. *Journ. Exp. Med.* (1912), 15, 365-366.
(57) NEWSTEAD. On the Life History of *Stomoxys calcitrans* Linn. *Journ. Econ. Biol.* (1906), 1, 157-166. Reprinted in *Ann. Trop. Med. & Parasit.* (1907), 1, 76-85.
(58) CALKINS. Protozoölogy. Lea and Febiger, New York and Philadelphia (1909), 196.
(59) NOVY. The Trypanosomes of Tsetse Flies. *Journ. Infect. Dis.* (1906), 3, 397.

ILLUSTRATIONS.

(Photographs by W. H. Boynton.)

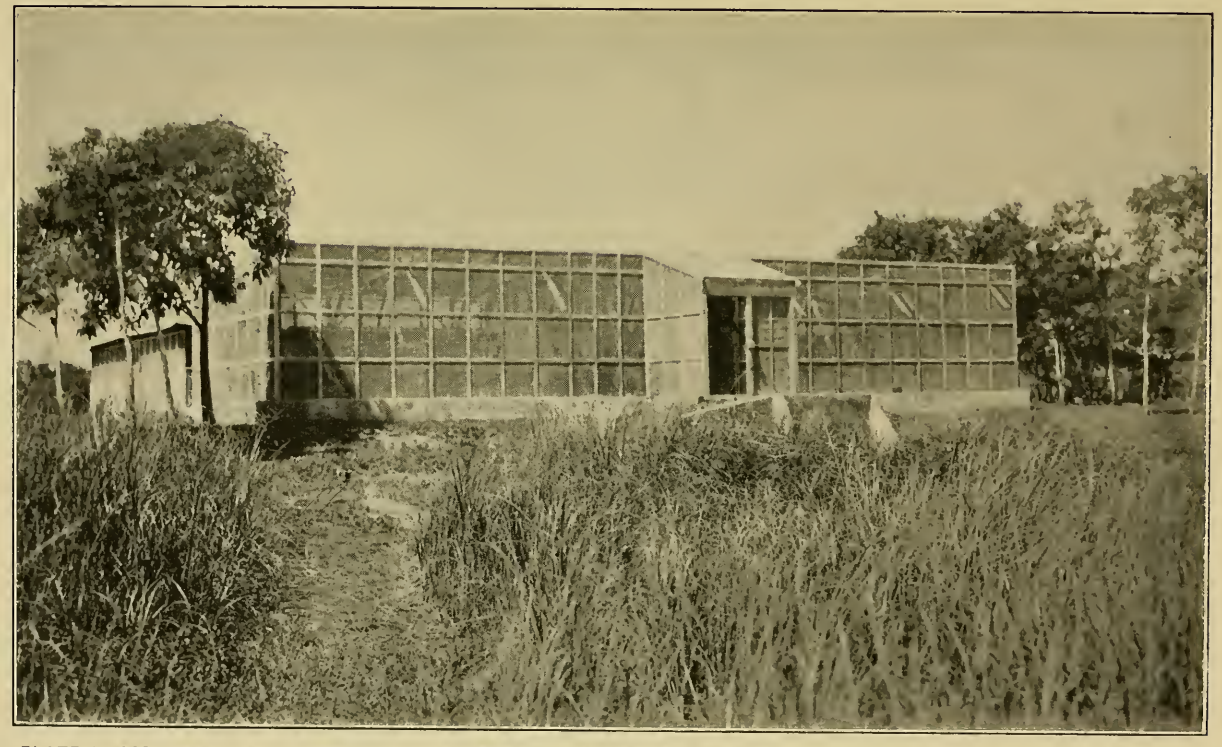


PLATE I. SCREENED STABLE FOR FLY EXPERIMENTS WITH HORSES—THE OUTER DOOR IS OPEN TO SHOW THE INTERIOR OF THE FLY-TRAP VESTIBULE.

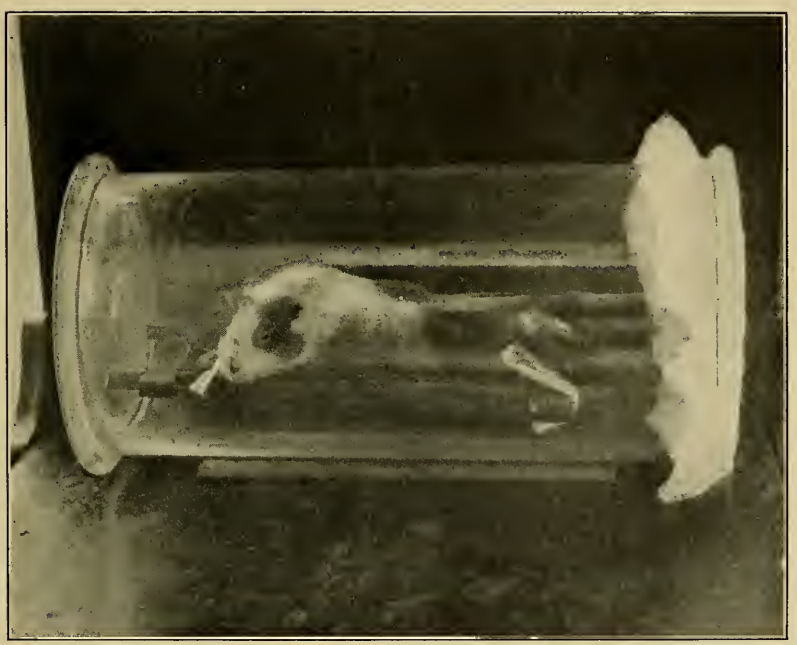


PLATE II. IMMOBILIZED GUINEA PIG IN A LARGE MUSEUM JAR FOR EXPERIMENTS WITH GREAT NUMBERS OF FLIES.

PLATE III. ILLUSTRATING METHOD OF APPLYING AN UNLIMITED NUMBER OF STOMOXYS FLIES TO THE MONKEY'S TAIL INCLOSED IN A LARGE BOTTLE.

PLATE IV. ILLUSTRATING THE FEEDING OF STOMOXYS FLIES IN INVERTED TUBES ON IMMOBILE MONKEY.

PLATE V. SHOWING SINGLE TUBE APPLICATION OF STOMOXYS ON A GUINEA PIG.

THE SUSCEPTIBILITY OF COCKROACHES TO PLAGUE BACILLI INOCULATED INTO THE BODY CAVITY.

By M. A. Barber.

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

The methods and results of these experiments may be illustrated by a detailed description of two or three series.

In one series 26 cockroaches, 11 *Periplaneta americana* Linn. and 15 *Rhyparobia maderæ* Fabr.,[1] all adults except 2 well-grown nymphs, were inoculated with a virulent strain of plague from a 24-hour culture. Inoculations were made under a magnifying lens with a very fine pipette of hard glass, the outer diameter of the point of which was 0.08 millimeter. The dose, approximately 0.3 cubic millimeter of a thick suspension in salt solution, was estimated in two ways. The cubic contents of the pipette below the dose mark measured with the eyepiece micrometer gave 0.4 cubic millimeter. The dose was delivered on the counting chamber of a Thoma Zeiss counter, the cover adjusted, and the cylindrical drop measured, giving 0.3 cubic millimeter. This quantity, corresponding approximately to the cubic capacity of the pipette, may be taken as approximately the dose delivered. The number of bacilli, estimated by counting dilutions, was approximately two and one-half millions, a quantity far in excess of the fatal dose for guinea pigs,[2] and enormous for insects of an average weight of about 1.2 grams.

Inoculations were made in the leg, in most instances in the basal sclerite of the dorsal surface of the coxa where the chitin is thin enough to permit the easy passage of the pipette. In order to prevent contamination with other bacteria, the surface inoculated was rubbed with a small pledget of cotton moistened with alcohol just before inoculation, and after inoculation again rubbed with the alcohol and the minute wound covered with sterile vaseline. Each insect was put after inoculation into a separate receptacle and left at a room temperature of 25° to 31°.

[1] Identifications by Charles S. Banks, Bureau of Science.

[2] *This Journal, Sec. B* (1912), 7, 251–254.

Of the 26 inoculated in this manner, 6 were dead the next day. A femur of each of them was washed with alcohol, cut off with hot scissors, and the contents pressed out at the cut surface without allowing them to touch anything not sterile. From these contents, hanging drops, smears, and cultures were made. The hanging drops were examined at once and again after seven to twenty-four hours' growth. Of the 6, two showed apparently a pure culture of plague in hanging drops examined immediately and in the smear, but all cultures showed in addition to plague-like bacilli numerous small, actively motile bacilli.

On the second day 5 more were dead. Four of these showed apparently a pure culture of plague in hanging drops and smears, and the hanging drops after growth showed apparently typical plague chains. The fifth showed a mixture of plague-like bacilli with the small motile bacilli mentioned above.

On the third day 2 more were dead. One in culture showed the small motile bacillus, the other *Bacillus prodigiosus*, both apparently in pure culture. One died on the eighth day with no indications of plague at necropsy, and 2 died on the thirteenth and fourteenth days respectively. Therefore, 12 of the 26 survived twelve days or longer—all of them *Rhyparobia maderæ*—and 10 survived two weeks or longer.

Agar-cultures were made from the four dying on the second day which showed a pure culture of apparently typical plague, and guinea pigs were inoculated subcutaneously with about one-fifth of a 24-hour agar slant. As a control, a guinea pig was inoculated with a much smaller dose of the original plague culture with which the cockroaches had been inoculated. The control died in nine days with typical lesions of plague; while of the four others only one showed signs of infection. This one died in four days with lesions in all respects typical of bubonic plague.

The nonmotile plague-like bacillus which failed to infect the guinea pigs in the three cases has not been identified. It is very improbable that it could be attenuated plague, since very large doses failed to infect guinea pigs, and since cultures on agar and in vaseline-covered broth were not typical of plague.

Of the entire 26, then, only one died of unmixed plague infection. In the case of the 10 others which died on or before the second day, plague may have contributed to their death, but in no case did plague bacilli occur in pure culture at necropsy.

In all series the commonest contaminating organism found alone or mixed with plague in insects after death was a small actively motile bacillus, very closely resembling plague in stained

preparations. Culturally its characteristics resemble those of the *Bacillus enteriditis* group. It has occasionally appeared in mammals inoculated with plague in this laboratory, and may persist with plague through several animal passages. It is pathogenic for cockroaches; for in one series of 12, inoculated with material from the lung of a monkey containing this organism probably mixed with plague, all 12 died in one day. Material from one of these insects carried to a new series gave a small proportion of fatal infections in very small doses, and a larger proportion with massive doses. A series of 5 inoculated with a pure culture of this organism isolated from a cockroach gave 3 fatal infections.

In the disappearance of plague from noninfected insects, phagocytosis must play some part. In one insect of another series, body fluid both from the leg inoculated and from a leg on the opposite side of the body was removed two hours after inoculation. Plague bacilli were found in both samples in phagocytes (in one phagocyte 18 bacilli) and outside of them.

In the series of the 26th mentioned above, the plague culture was of highly virulent strain, but was the third remove from an infected guinea pig and had been kept some days at refrigerator temperature after the first transfer from the pig. In another series, 5 large cockroaches were inoculated with material from the second transfer on agar from an infected guinea pig. Two days after inoculation 2 were found dead with numerous, apparently plague, bacilli in the body fluid. Material taken from the leg of one of the survivors showed no bacteria microscopically or culturally. All of the 3 survivors were alive and apparently well after eleven days, and 2 of them after eighteen days.

Bacilli taken from one of the infected insects of this series were grown in serum broth and this culture inoculated into 4 cockroaches. Of these four, 1 was sacrificed after two days, but showed no infection. Of the three, 2 were alive and well fourteen days after inoculation and 1 twenty-six days.

In another series, 7 were inoculated with an emulsion of the spleen of an infected guinea pig. One died in two days with apparently a pure culture of plague in the body fluid. Of the remaining six, 4 were alive after fourteen days, and 2 after twenty-seven days.

In all, 61 cockroaches were inoculated with virulent plague. Of this number, only 9 showed at necropsy a pure culture of bacilli morphologically resembling plague. Four of these cultures were inoculated into guinea pigs and only one brought about a plague infection. So of the entire 61, only 6 at most could have died

of unmixed plague infection, and in only one of these was the culture identified by guinea-pig infections.

Of the noninfected insects, at least one-half were living from twelve to twenty-seven days after inoculation. Since all which died of plague, either alone or mixed with some other bacteria, died within two days after inoculation, it seems probable that those surviving six days were not infected. At least 28 survived two weeks or more after inoculation.

In summary, it has been clearly shown that cockroaches may be infected by large doses of virulent plague bacilli; but from the fact that massive doses failed to infect a large proportion of cases, it may be concluded that these insects, especially *Rhyparobia maderæ*, are little susceptible to plague inoculated into the body cavity.

NOTES ON THE MUSCULAR CHANGES BROUGHT ABOUT BY INTERMUSCULAR INJECTION OF CALVES WITH THE VIRUS OF CONTAGIOUS PLEUROPNEUMONIA.[1]

By William Hutchins Boynton.

(From the Veterinary Division,[2] Bureau of Agriculture, Manila, P. I.)

In looking up the literature concerning the muscular changes in pleuropneumonia, there has come to notice but one article on the subject by Meyer,(1) who gives a very good description of the changes. The writer agrees with him in practically every respect, but will try to bring out some points of comparison between the muscle and lung lesions which were not included within the scope of his studies.

The animals used in the experiment were young native calves, apparently in vigorous health before they were inoculated, which had the best of care during the entire experiment.

The muscle tissues used for histological purposes were taken from three calves, which died as a result of intermuscular injection of lymph secured from the thoracic cavity of animals dead of contagious pleuropneumonia.

The muscle tissue was fixed in formalin and, in some cases, in Zenker's fluid. Both paraffin and frozen sections were made, and stained with hæmotoxylin-eosin, Giemsa, Wright's stain, Jenner's stain, and Weigert's special method for fibrin.

Upon microscopic examination of the subcutaneous connective tissue, the most striking change which one notices is its marked distention, the tissue being infiltrated with a coagulated fibrinous exudate. The connective-tissue fibers are either pushed to one side or have undergone necrosis as a result of the coagulation of exudate around them.

Scattered through the distended connective-tissue spaces will be noticed isolated or confluent dark-staining areas, which vary

[1] Reprinted from Bull. No. 20, Bureau of Agriculture of the Government of the Philippine Islands.—The Bureau of Agriculture is indebted to the biological laboratory, Bureau of Science, for the use of the laboratory facilities utilized in carrying out this work.

[2] Archibald R. Ward, chief.

approximately from 50 to 160 microns in diameter. Located in or near the center of these areas are either single or ramified blood vessels distended with blood. In some instances these contain a considerable number of leucocytes, which are as a rule situated near the vessel wall, showing that the blood stream had been retarded in its flow. It is a known fact that "a greater or less number of leucocytes pass over into the peripheral plasma zone, when the slowing of the circulation has reached a certain degree."(2)

In some instances the vessel walls apparently have not deviated from normal to any great extent, while in others migration of leucocytes and diapedesis of red cells may be observed.

The dark-staining areas situated around the blood vessels take on different appearances at different stages of development, of which four can be easily recognized.

First. The congested blood vessel is surrounded by a zone of leucocytes, being composed of both round cells and polynuclears. These areas average from 50 to 70 microns in diameter.

Secondly. The congested blood vessels are surrounded by a zone of round cells and polynuclear leucocytes. Around this is a zone of broken down leucocytes and cell detritus intermixed with the fibrinous exudate. These areas average from 80 to 120 microns in diameter.

Thirdly. The congested blood vessels are surrounded by a light-staining zone of new-forming connective-tissue cells, intermixed with a few leucocytes, and in some instances new-forming blood vessels which are congested. Around this zone of new-forming connective tissue is a deeper staining zone composed of leucocytes, and situated around this area is a zone of broken down leucocytes and cell detritus extending into the fibrinous exudate. These areas average from 100 to 160 microns in diameter. (Plate IV.) Hence it will be noticed that as the irritant persists, a chronic inflammation is produced, which leads to the production of new-forming connective tissue and of blood vessels.

Fourthly. In a few instances blood vessels are completely occluded by thrombus formations. In these cases the vessel walls are degenerated to a considerable extent and leucocytes situated around them are undergoing karyorrhexis.

Where the blood vessels are situated close together, the inflammatory zones around them coalesce, forming oblong dark-staining areas or bands, with the congested vessels in the center, and the deeper staining areas of leucocytes along the periphery.

Summarizing the changes which take place in the older lesions,

there will be noticed proceeding from the inside outward: First, the congested blood vessels; secondly, a zone of new-forming connective tissue, in some instances containing new-forming blood vessels; thirdly, a zone of leucocytes; fourthly, a zone of broken down leucocytes and cells detritus; fifthly, the coagulated fibrinous exudate. All of these changes are shown more or less distinctly in Plate IV.

The vascular changes in the subcutaneous connective tissue are very similar to those occurring in lung tissue affected with contagious pleuropneumonia. The writer has noticed new formation of connective tissue around the blood vessels in the lung, especially in the vicinity of sequestra where the area involved is being walled in by a fibrous capsule. The earlier vascular changes of the subcutaneous tissue also simulate the changes seen around the arteries and veins in affected lung tissue, also the thrombi agree with those found in the veins of affected lung tissue.

The changes in the epimysium are very similar to those observed in the subcutaneous connective tissue. The bands of connective tissue surrounding the muscle bundles are markedly distended with a fibrinous exudate, causing degeneration of the connective-tissue fibers or pushing them to one side. The vascular changes, also, correspond to those already described in the subcutaneous tissue.

One very striking lesion is the accumulation of leucocytes, in various stages of degeneration, into foci and lines along the margin of the epimysium. These take a deep stain and can thus be traced with the unaided eye, forming very distinct lines which mark off the borders of the epimysium as it extends through the muscle tissue. This border of cells extends along the edges nearest the muscle tissue, and even extends around the individual muscle fibers, causing them to degenerate. The changes in question are brought out distinctly in Plates I (*a*) and II (*b*). These borders of cells correspond exactly with those found along the edges of the interstitial tissue in lungs affected with contagious pleuropneumonia, and are regarded by Smith(3) to be one of the characteristic lesions of that disease.

From the inner surface of the epimysium, septa are sent in which divide the muscle into a number of large secondary bundles. These septa are markedly distended with a fibrinous exudate which may contain leucocytes scattered throughout. As a rule, the leucocytes are thickest along the edges of the septa nearest the muscle, simulating the line formation described above.

One of the striking lesions in these septa is the enormous distention of the blood vessels, as shown in Plate I (*e* and *f*). In some instances, these vessels contain large numbers of leucocytes situated around the periphery; in others, they are scattered uniformly throughout the blood stream, indicating that there has been a slowing or even complete stasis of the flow. This is undoubtedly caused by thrombus formation, as both parietal and obturating thrombi are present, Plate I (*b* and *e*). The presence of a parietal thrombus partly occluding the vessel is shown in Plate I (*e*). This particular thrombus is of the gray type, being composed of fibrin and leucocytes, while the rest of the vessel is filled with blood. The vessel wall is undergoing degeneration. A few mixed and two organizing thrombi have been noticed, but as a rule they are of the gray variety.

The accumulations of leucocytes around the blood vessels in the septa are not so marked as those seen in the epimysium and subcutaneous tissue.

Extending from the septa are connective-tissue bands designated as the perimysium which divide the muscle into primary bundles or fasciculi. This perimysium is also distended with a fibrinous exudate intermixed with leucocytes. In places in the perimysium thus affected, the vessels are distended with blood, both parietal and obturating thrombi being present. Plate I (*b*) shows an obturating thrombus becoming organized. In many instances the vessel walls are undergoing degeneration, emigrating leucocytes are seen passing through them, and also diapedesis of red cells occurring.

The perimysium is not all affected alike. For instance, in Plate I (*h*) it is not so distended, contains a few leucocytes, some fibrin, and also new-forming connective-tissue cells, thus taking on more of the chronic type of inflammation. This may be accounted for by the fact that the pleuropneumonia virus seems to attack primarily the connective tissue, and as the process extends downward into the areas where there is less connective tissue there would naturally be fewer changes as there is less material for the virus to work upon. Where the virus is not sufficiently abundant to bring about marked changes, its continuous irritating action may be the cause of the chronic inflammatory process. In those areas where new-forming connective tissue is present, new-forming blood vessels are occasionally seen, slightly congested, but no thrombus formations have been noticed in these particular parts.

The perimysium sends off connective-tissue fibers which pass between the individual muscle fibers. These constitute the endomysium. Plates II (*d*) and III (*d*) show the endomysium around the individual muscle fibers. In places the endomysium is infiltrated with a slight fibrinous exudate intermingled with leucocytes, while in other places it has become hyperplastic by the new formation of connective tissue. Now and then new-forming blood vessels are found in this hyperplastic endomysium, Plate III (*b*), showing the presence of a productive inflammation.

It will be noticed that the muscle tissue situated closest to the epimysium has undergone the most marked pathological changes, Plates II (*e* and *f*) and III (*c* and *e*). This seems plausible as the predominant changes are situated in the epimysium, the exudate of which by continuity extends among the muscle fibers. In these areas the endomysium is distended with a fibrinous exudate which is composed of large numbers of leucocytes, especially in the vicinity of the bands of cells mentioned above. Under the influence of this exudate, the muscle fibers become in some instances filled with vacuoles, lose their striations, take on a granular appearance, and lose their nuclei. Thus they present a typical picture of granular degeneration which may be brought about by the coagulation of the exudate around them, shutting off their nutrition, or the toxin from the pleuropneumonia virus may have a vital influence.

Another characteristic lesion is the degeneration atrophy of the muscle fibers. In many cases the fibers have completely disappeared, leaving the endomysium surrounding the spaces which were once occupied by them.

Upon examination of sections of tissue thus affected, muscle fibers are found in all stages of degeneration, and as the degeneration advances the fibers become more shrunken and finally disappear entirely.

CONCLUSIONS.

1. From all appearances, the contagious pleuropneumonia virus seems to have a specific action upon muscle and connective tissue, affecting chiefly the connective-tissue elements.

2. The appearances suggest that the virus multiplies in the lymph spaces of the connective tissue and blood vessels, gradually working its way through the walls of the blood vessels, causing an inflammation of the intima and thus giving rise to thrombus formations.

3. The virus having invaded the tissue gives rise to a serofibrinous exudate, intermingled with groups of leucocytes, leading to thrombosis of both lymph and blood vessels.

4. The muscle lesions correspond with the lung lesions of contagious pleuropneumonia in the following respect:

(*a*) Thrombus formation occurs in the veins in both tissues.

(*b*) The inflammatory areas around the blood vessels are similar.

(*c*) The connective tissue is chiefly affected in both tissues.

(*d*) The abundant serofibrinous exudate is present in both.

(*e*) The deep-staining line of leucocytes along the edge of the connective tissue is characteristic in both tissues.

(*f*) The tendency toward a chronic productive inflammation is present in both.

5. Thus in summing up all the lesions, the lung and muscle lesions are found to correspond in practically every respect.

REFERENCES.

(1) MEYER, K. F. Notes on the pathological anatomy of pleuro-pneumonia, contagiosa bovum. The Veterinary Bacteriological Laboratories of the Transvaal, issued in commemoration of the Opening of the new Laboratories at Onderstepoort, Pretoria, October, 1908. Pretoria (1909), 135.

(2) ZIEGLER, ERNST. General Pathology. Eleventh Edition. Wm. Wood & Co., New York (1908), 321.

(3) SMITH, THEOBALD. *Annual Rep. Bur. Animal Ind.*, U. S. Dept. Agr., (1895–96), 143.

ILLUSTRATIONS.

(From photomicrographs in the collection of the Bureau of Science, Manila, P. I.)

Plate I.

a Markedly distended epimysium, showing the wall of infiltrating leucocytes along its border.
a' The fibrinous exudate containing very few cells in the central part of the distended epimysium.
b An obturating white thrombus occluding a vein in the perimysium.
c New-forming connective tissue causing a hyperplasia of the perimysium.
d A partly occluded artery in the septa.
e A mixed parietal thrombus in an enormously engorged vein of the septum.
f An enormously congested vein of the septum, showing the numerous leucocytes in the blood; also their migration through the degenerated wall of the vessel.
g The atrophied and degenerating muscle fibers throughout the specimen.
h Hyperplastic perimysium containing a few leucocytes but mostly new-forming connective tissue.

Plate II.

a Fibrinous exudate containing very few cells, located in the central part of the markedly distended epimysium.
b The well of infiltrating leucocytes along the edge of the markedly distended epimysium.
c Vein containing blood with numerous leucocytes. In the walls of the vessel are migrating leucocytes.
c' New-forming connective-tissue cells with some migrating leucocytes.
d Hyperplastic endomysium composed mostly of new-forming connective tissue, with a few migrating leucocytes.
e Vacuoles left where the muscle fibers have completely disappeared.
f Atrophied muscle fiber, showing space it should occupy, and the hyperplastic endomysium around it.

Plate III.

a Wall of leucocytes along the edge of the epimysium.
b New-forming blood vessel in the hyperplastic endomysium.
c One of the many vacuoles where the muscle fibers have entirely disappeared.
d New-forming connective tissue with a few migrating leucocytes forming the hyperplastic endomysium.
e Two of the numerous atrophied and degenerating muscle fibers.

Plate IV.

a Congested blood vessel in the subcutaneous tissue, showing numerous leucocytes in the blood.
b Zone of new-forming connective tissue around the blood vessel.
c New-forming blood vessels distended with blood in the connective-tissue zone.
d Zone of leucocytes, principally polynuclears with a few round cells.
e Zone of broken down leucocytes and cell detritus.
f Fibrin from the inflammatory exudate.

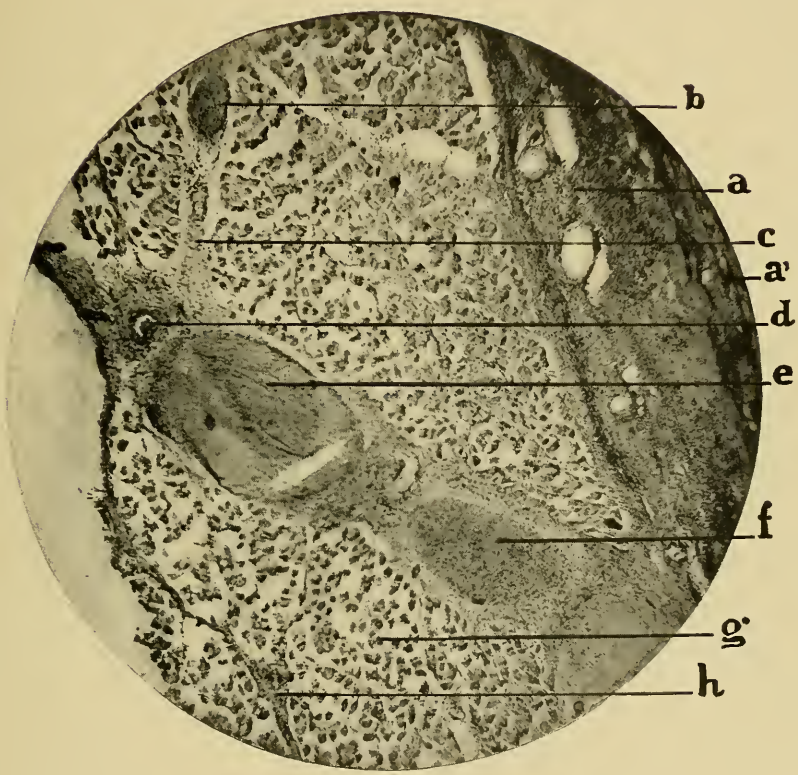


PLATE I.

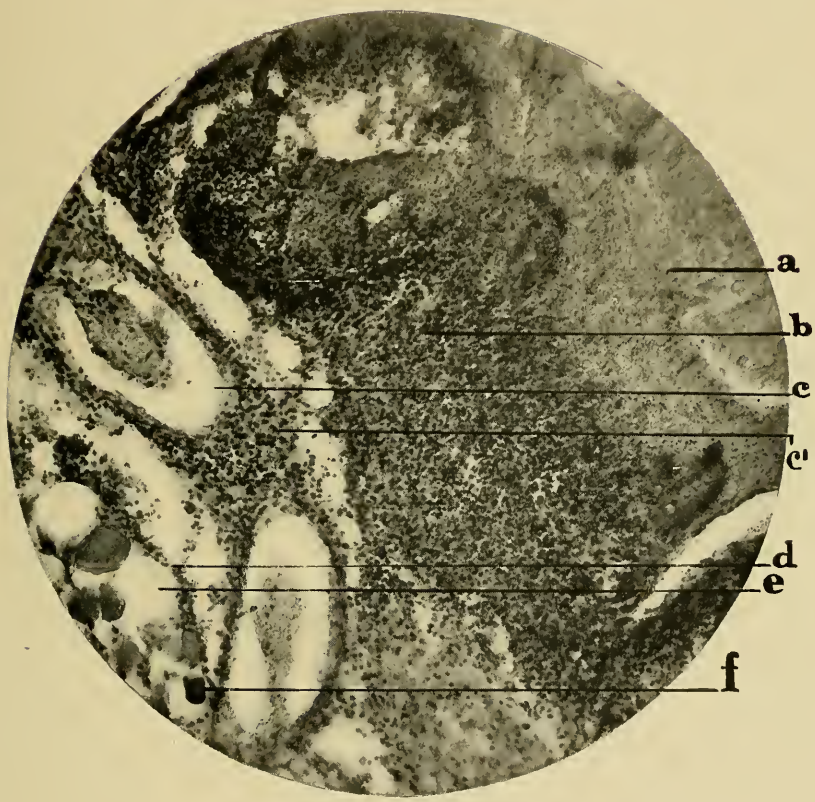


PLATE II.

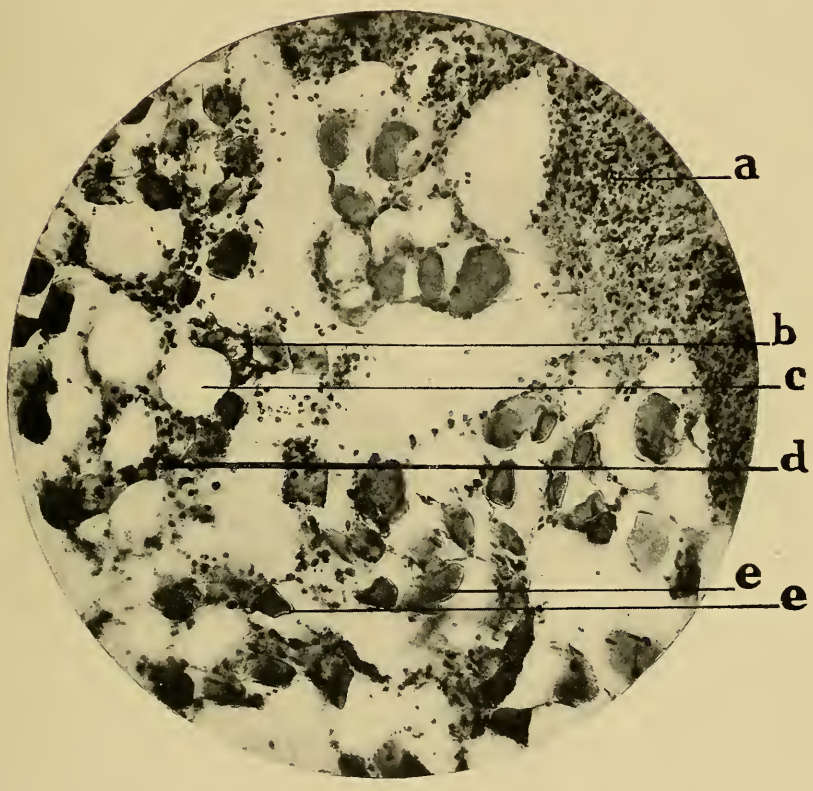


PLATE III.

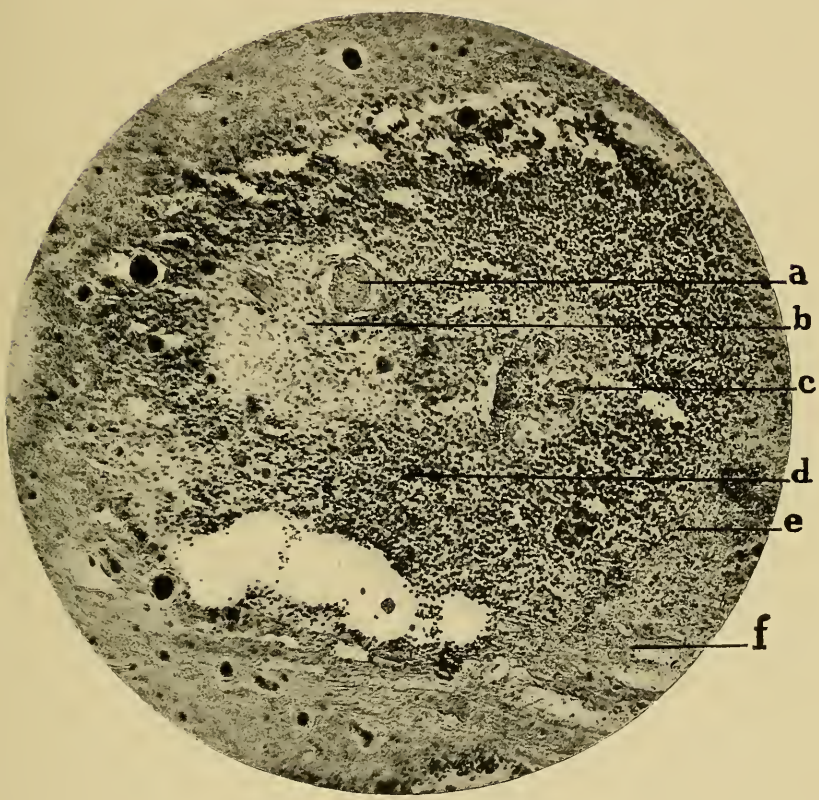


PLATE IV.

INDEX.

PUBLICATIONS FOR SALE BY THE BUREAU OF SCIENCE, MANILA, PHILIPPINE ISLANDS

THE SUBANUNS OF SINDANGAN BAY.

By Emerson B. Christie.

121 pages, 1 map, 29 plates.

Order No. 410. Paper, $1.25 United States currency, postpaid.

Sindangan Bay is situated on the northern coast of Zamboanga Peninsula. The Subanuns of this region were studied by Mr. Christie during two periods of five and six weeks, respectively.

The following is an abstract from the contents of Mr. Christie's report on the Subanuns: Habitat and history; relations with the Moros; material culture; houses; industries; trade; agriculture; family life; social customs; administration of justice; religion; the medicine man; ceremonies; tales; word-lists; physical measurements.

The 29 plates illustrate the Subanuns at work and at play; their industries, houses, altars, and implements; and the people themselves.

THE HISTORY OF SULU.

By Najeeb M. Saleeby.

275 pages, 4 maps, 2 diagrams.

Order No. 406. Paper, $0.75 United States currency, postpaid.

In the preparation of his manuscript for The History of Sulu Doctor Saleeby spent much time and effort in gaining access to documents in the possession of the Sultan of Sulu. It is fortunate that these records have now been translated and preserved in permanent form. This book is a history of the Moros in the Philippines from the earliest times to the American occupation.

STUDIES IN MORO HISTORY, LAW, AND RELIGION.

By Najeeb M. Saleeby.

107 pages, 16 plates, 5 diagrams.

Order No. 405. Paper, $0.25; half morocco, $0.75 United States currency, postpaid.

This volume deals with the earliest written records of the Moros in Mindanao. Doctor Saleeby has fortunately able to obtain exact copies of carefully preserved early [illegible] written in the Maguindanao dialect with Arabic characters. The author presents translations as well as the half-tone illustrations of certain pages from the originals. The names [illegible] of Maguindanao are recorded in five folding diagrams.

NEGRITOS OF ZAMBALES.

By [illegible] Artemio Tee.

[illegible] pages, 62 plates.

[illegible] $0.25; half morocco, $0.75 United States currency, postpaid.

The introductory [illegible] the general distribution of Negritos and with the distribution of the Philippine branch of [illegible] race. The succeeding chapters deal with the various industries, amusements, and social relations of these little men.

Plates from photographs, the greater part of which was taken for this publication, show ornaments, houses, men making fire with bamboo, bows and arrows, dances, and various types of the people themselves.

CONTENTS.

The "Philippine Journal of Science" is issued as follows:	U. S. currency
Section A. Chemical and Geological Sciences and the Industries	$2.00
Section B. The Philippine Journal of Tropical Medicine	3.00
Section C. Botany	2.00
Section D. General Biology, Ethnology and Anthropology (Section D began with Volume V)	2.00
Entire Journal, Volume II, III, IV, or V	5.00
Entire Journal, beginning with Volume VI	7.00
Single numbers	.50
Volume I, 1906 (not divided into sections)	10.00
Supplement to Volume I (botany)	3.50
Volume I (without supplement)	6.50

Each section is separately paged and indexed.

Publications sent in exchange for the Philippine Journal of Science should be addressed: Library, Bureau of Science, Manila, P. I.

Subscriptions may be sent to the BUSINESS MANAGER, Philippine Journal of Science, Bureau of Science, Manila, P. I., or to any of the agents listed below:

AGENTS.

The Macmillan Company, 64–66 Fifth Avenue, New York City, U. S. A.
Wm. Wesley & Son, 28 Essex Street, Strand, London, W. C., England.
Martinus Nijhoff, Nobelstraat 18, The Hague, Holland.
Mayer & Müller, Prinz Louis Ferdinandstrasse 2, Berlin, N.W., Germany.
Kelley & Walsh, Limited, 32 Raffles Place, Singapore, Straits Settlements.
A. M. & J. Ferguson, 19 Baillie Street, Colombo, Ceylon.
Thacker, Spink & Co., P. O. Box 54, Calcutta, India.

Entered at the post-office at Manila, P. I., as second-class matter.

VOL. VII MEMORIAL NUMBER JULY, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

In Memoriam

PAUL CASPAR FREER

MANILA
BUREAU OF PRINTING
1912

Paul C. Freer.

OBITUARY

Paul Caspar Freer

DIRECTOR OF THE BUREAU OF SCIENCE OF THE GOVERNMENT OF THE PHILIPPINE ISLANDS
DEAN OF THE COLLEGE OF MEDICINE AND SURGERY AND PROFESSOR OF
CHEMISTRY OF THE UNIVERSITY OF THE PHILIPPINES, AND
FOUNDER AND EDITOR-IN-CHIEF OF THIS JOURNAL

We are deeply grieved to announce the death of Doctor Freer at Baguio, Philippine Islands, on April the seventeenth, in his fifty-first year, from arterio-sclerosis and acute nephritis.

In an effort formally to express our sorrow and to honor his memory a memorial meeting of the members of the Staff of the Bureau of Science, the Council of the University of the Philippines, and the members of the Philippine Islands Medical Association was held on July 1, 1912. The addresses delivered at this memorial meeting are published in this number.

At a meeting of the members of the Staff of the Bureau of Science, held on the eighteenth day of April, the following resolutions were adopted:

Whereas it has pleased Almighty God in His Wise and Inscrutable Providence to remove from our midst Paul Caspar Freer, M. D., Ph. D., Director of the Bureau of Science of the Government of the Philippine Islands, since the time of its organization as the Bureau of Government Laboratories in the year 1901, Dean of the College of Medicine and Surgery, and Professor of Chemistry, University of the Philippines, and Founder and Editor-in-Chief of the "Philippine Journal of Science," who, for many years, has been our Leader, Counselor, and Friend; and

Whereas at best we can do little to indicate at this time our real appreciation of him as a man and as a worker for the general good: Therefore be it

Resolved, That we, the Members of the Staff of the Bureau of Science in Manila, Philippine Islands, do hereby express our deepest sorrow and keen feeling of personal loss in the death of Doctor Freer; and be it further

Resolved, That he holds a place of highest respect, admiration and appreciation both officially and personally in the hearts of all of us, and especially of those who were most intimately associated with him in scientific work; and be it further

Resolved, That it is the sense of the Members of this Institution that the Bureau of Science has suffered a very great loss and that the cause of Science in these Islands has been deprived of one of its most zealous and conscientious advocates; and be it further

Resolved, That we extend our sincere sympathy and condolence to his Widow in her overwhelming grief, to his Sister, Brother and other Relatives; and be it further

Resolved, That copies of these resolutions be engrossed and sent to the bereaved Widow and Brother of Doctor Freer, and that they be filed in the Archives of the Bureau of Science, transmitted to the Bureau of Civil Service, published in the forthcoming Number of each Section of the "Philippine Journal of Science," in the newspapers of Manila, in a paper in the City of Chicago, Doctor Freer's birth-place, and in "Science," the Official Organ of the American Association for the Advancement of Science, of which Doctor Freer was a Fellow.

For the Staff of the Bureau of Science:

[L. S.]

RICHARD P. STRONG,
CHARLES S. BANKS,
E. D. MERRILL,
ALVIN J. COX,
OSCAR TEAGUE,
A. E. SOUTHARD,
Committee.

At Manila, Philippine Islands, this eighteenth day of April, in the year of our Lord one thousand nine hundred and twelve.

VOL. VII MEMORIAL NUMBER JULY, 1912

THE PHILIPPINE JOURNAL OF SCIENCE

In Memoriam

PAUL CASPAR FREER

MANILA
BUREAU OF PRINTING
1912

112297

CONTENTS.

THE LIFE AND CAREER OF DOCTOR FREER.

By Martin Egan,
Editor of the Manila Times.

When Doctor Musgrave asked me to come to this memorial gathering and sketch in brief the life and career of Paul Freer, my first thought was to ask him to excuse me from a task so painful. I knew that if I did so I must bare my heart in sorrow for my friend who has gone and then I realized that we would all be here to-day with our hearts bared in sorrow, that no man need hide his heart in such a communion of friendship in grief, and so I come to take my place among those chosen to pay tribute to the memory of the good man whom we have lost from our councils, the friend passed from the narrowing circle. Paul Freer descended of a line worthy of him, its product, he worthy of his lineage. His father was a man of scientific attainments, who gave his life in that noblest aim of science, the saving of human life; his mother, a scholar, a linguist, of high culture, of rare mind, and compelling maternal love for the well-being of her children. The elder Freer, born in New York of an old family of Dutch extraction, settled in Chicago, then a scattering town of 7,000, and entered upon the practice of medicine. He quickly advanced to leadership in the growing city, and became president of Rush Medical College which he had helped to found. Overwork in a severe epidemic of typhoid fever that swept the city led to his breakdown and death, and the care and education of his children, including him whom we honor and mourn to-day, passed to the widow and mother. Mrs. Freer, his mother, was born in Württemberg and as a girl went to New Orleans to make her home with her uncle. Herself an advanced student, she devoted herself assiduously to the education of her children. It is related of the family that it was a rule to conduct table

conversation in Latin, French, or German and that good books were the first of its household gods. It was in this wholesome and stimulating atmosphere that Paul Freer received the first inspiration for study and investigation that was the compelling influence of his whole career. He was taken to Germany as a child for his rudimentary training, and he was destined to go there again to complete his education and receive from the Germanic school his chief methods and ideals in science, in education, and in general thought. Returning to Chicago, he entered the high school and when his class was graduated he stood at its head, the first student of the school. He had already determined to follow in the footsteps of his father, and from high school he entered Rush Medical College and began the study of medicine and surgery. It was at Rush that chemistry with its wonders and unsolved mysteries made its great appeal to his opening mind. He learned its rudiments at the feet of Professor Haines, well remembered as a sound scholar and instructor, and there resolved to specialize in it. He continued his medical work and graduated with the class of 1882, still a year under the age of 21. Germany was then leading the world in science and it appealed to the young student with all the forces of enthusiasm and instinct for he had the blood of the Fatherland in his veins. He determined to go to Munich and join the classes under the great von Baeyer, then the leading chemist of Europe. The choice proved a happy one for there grew a great and lasting friendship between the master and student that was deep in its influence upon the career and work of the younger man. I have recently seen a letter from Doctor Schieffelin, himself an eminent American physician, who went to Munich the year Paul Freer graduated and took his high honors, and in it he wrote:

> When I went to Munich in 1887 to study chemistry, I found that Professor von Baeyer, probably the most eminent chemist living, and the laboratory chiefs were all full of the praises of Paul Freer who had just taken the degree of doctor of philosophy, *summa cum laude*, which I believe was the first time a foreigner had achieved this distinction. And for twenty-five years I have watched with interest and pride his service to science and the government. He was an American gentleman of the highest type and of a charming personality.

Our departed friend has talked to me many times of those golden days at Munich, and I have always believed that they gave him the perfection of his ideals and logic and the soundness of his methods and thought and work. He left Munich fully equipped for work, and for a brief period labored and studied in England, first in the private laboratory of Sir William Perkin, where he devoted himself to analin dyes, and later at Owens College, Manchester, where he was an assistant instructor. But his desire was to return home, and when Tuft's College offered him a place he gladly accepted. But he was not to remain there. The faculty of the University of Michigan had heard of his ability and rising fame and offered him a larger field and scope of work. He went to Ann Arbor as lecturer in 1889 and a year later was honored with the professorship of inorganic chemistry, with a chair in the Medical School as well as in the School of Arts. It has been testified by many that Paul Freer brought to Michigan a wonderful stimulus for original work. He had the high ideals of the German university, less known and understood then in our American universities, he had the enthusiasm of youth, and he had ability as his commanding talent. He was impatient of mediocrity, and gave the best of himself to the earnest worker, the advancing student who came to him for instruction and guidance. His seriousness amounted at times to austerity, but it produced results and was in keeping with the high standard of scholarship of the members of the faculties at Michigan. In 1895 the University of Chicago sought his services, offering him a professorship of chemistry, but he declined the flattering offer, electing to stay where he was accomplishing so much good work. There he remained until 1901, when the United States Government gave him a chance for service in this field, so rich in opportunity for practical scientific work. He accepted the task, and here are written the last and greatest chapters of his life. You know them perhaps better than I. I was his personal friend and could share but little in the multiplicity of his official and professional activities, many of you were of them with him. I do know that we meet to-day in one institution and are surrounded by

others that are to a large extent monuments to his ability and service. In whole or in part they were born in his mind, shaped by his thought and plans, projected upon his knowledge, constructed with his advice, and administered by his direction and counsel. You who have shared with him in this work may well be proud for here humanity suffering is hourly served.

I have known no man better equipped for his place and part in life than Paul Freer. He was born for his profession and crowned natural equipment with the best education and training that the world can give. He was an advanced investigator. He sought the truth and he entered the house of truth with open mind, without prejudice or fear. His industry bore constant fruit. He had the rare quality of detachment. He could drop the cares and burdens of administration for the laboratory or the literature of science, in both of which he gained distinction. His talents were of wide range, his industry boundless, his service faithful. He was a true friend.

To his widow, his kinsmen, his friends there is left a rare consolation. He did a man's work, and that is the best record that any of us may hope to carry to the Master of sciences.

PAUL CASPAR FREER, HIS INFLUENCE UPON OTHER MEN.

By Charles H. Brent,
Bishop of the Philippine Islands.

There are two distinct, though not mutually exclusive, types of influence exerted by men upon their fellows: that which is let loose by conscious volition, and that which is automatically given off by inherent virility, just as perfume is exhaled by the flower. The former focuses certain powers to achieve a given end and then relaxes, like the fitful spouting of a geyser; the latter is a milder though more consistent flow, like the bubbling of a perennial spring: the former aims at, and succeeds in making, an impression; the latter naturally and simply creates an atmosphere.

Both types of influence are necessary and valuable, but of the two the most potent and constant is that unconscious pressure of the whole personality which was characteristic of Paul Caspar Freer. If, on occasions, he could effectively impress a companion in accord with definite determination, it was because he possessed the consistent background of cultured manhood.

It is chiefly men with an imperfect education who find it necessary to be vociferous and theatrical in their efforts to influence others. They fret and scheme, and are never wholly themselves. But the man who is highly educated, that is to say, who, like Doctor Freer, has established many points of contact with nature, animate and inanimate, enjoys a repose which in itself is power. His composure was, doubtless, sometimes disturbed, else he would have been less than a man, but ordinarily he left you with the feeling that life was too good to allow of haste, too safe to justify panic, too sacred to tolerate scheming.

His versatility was such as to make a pleasant companion, full of surprises. Now it was some detail of scientific knowledge which slipped out of his well-stored mind, not as instruction pedantically imparted, but as the unpremeditated expression of his thought; now a reminiscence of the Tyrol, or an anecdote of Chopin, called up by some strain of classical music to which he was devoted.

Almost the last glimpse I had of him was on the golf course. His lank form was striding over the links with that abandon and freedom which denote complete absorption in a pursuit. It was indicative of his entire life. He traveled hopefully, joyously, whether in the quiet retreat of the laboratory, or through the mountainous home of Igorot and Calinga, or in the valley of the shadow of death.

Strong personalities never seem more alive than in that gloaming which succeeds life's sunset. They refuse to die. Their littlenesses drop out of sight, and the full force of their true character influences us. That Paul Caspar Freer lives yonder with God in the conscious enjoyment of manhood not quenched but vivified through the discipline of death, who dare doubt? But he also lives as an influence rather than a memory among us men whose hands are still busied for a short while with the affairs of here and now. Personality can not die even if it would.

DOCTOR FREER AND HIS GENERAL INFLUENCE UPON SCIENTIFIC WORK IN THE PHILIPPINE ISLANDS.

By Richard P. Strong,
Chief of the Biological Laboratory, Bureau of Science.

We are here to honor the memory of a faithful and able worker, an earnest teacher, a loyal son of this Government, and a good and kindly friend. Paul C. Freer has left behind him a record of work well performed and, to those of us who knew him, the memory of a well-spent life. Although the real achievement of every great man of science lies particularly in his original contributions to science, and Doctor Freer's publications will be told of by others who are here to-day, for those who have formed their image of him largely through his writings I shall try to relate a few of the details of his scientific career and of how he moved among his fellow workers in his daily life; for, since he came to these Islands, I have, perhaps, been more closely associated with him in his work than any one else.

To him belongs the great merit of having been the pioneer in the general scientific work of the Government of these Islands. For more than ten years he has encouraged in every way at his command the cultivation of these scientific branches, and, since the establishment of the Bureau of Science and of the College of Medicine and Surgery, has unselfishly devoted his time to the best interests of these institutions. Indeed, there has been practically no scientific movement of value in these Islands since his arrival in which he has not been interested or has not taken an active part. Though, when he first began his work among us, chemistry was the branch of knowledge to which his mind most distinctly inclined and the one in which he took

the greatest interest, nevertheless, on assuming the directorship of the Bureau of Science, he threw himself into the work of its organization and development with an energy, industry, and ability that could not fail to bring success to his efforts. In this Bureau, with its various divisions, biology (including medicine, general biology, botany, and entomology), chemistry, mining, ethnology, ornithology, and fisheries, there was not one division in the work and development of which he did not take a deep interest, and, more than this, he knew what work was being carried on in each division and much of its value. Moreover, he planned and followed with great interest and attention, born of a clear insight and knowledge of chemical problems, practically all of the investigations carried on in the chemical laboratory. In this remarkable breadth of interest and in the comprehensiveness of his knowledge he will always hold a unique position in the history of scientific work. It is not too much to say that no bureau chief in these Islands ever had the welfare of his bureau more at heart than Paul C. Freer and none have fought harder and with a greater persistence than he did to secure the annual appropriation from the Government, necessary to carry on the scientific work here. With all this, and apart from his natural ability, he brought to the Bureau and maintained there an exalted professional standard. Nevertheless, his directorship in this institution has been arduous and complex and has required the exercise of the very highest qualities of the mind.

One of his early aims was the establishment of a scientific journal to be published by the Bureau of Science, and this was accomplished as soon as the necessary legislation was enacted by the Government. In this journal (The Philippine Journal of Science), of which he was the editor, he took a remarkable pride and interest. He was an editor in every sense of the word, and but few realize the number of hours he spent at this work, preparing manuscript for the printer. Often have I found him at home on his holidays with a large pile of articles by his side, and sometimes he would spend many hours of the day correcting and rewriting poorly prepared manuscript with a

patience and good nature that was truly remarkable. However, the ripeness of his critical judgment and the facility of his literary taste made most of this work easy for him, and not infrequently he earned the gratitude of some young author by having caught the spirit of his clumsily and illy-expressed ideas and transcribed them for him into terse and lucid language. His work of this nature was ever done with the conscientious desire to benefit the writer to the greatest degree. By the majority of the scientific staff of his Bureau he was particularly admired not only for the things which he had done in science, and not only for his intellect and for the wide grasp of his mind, but also for his fairness of judgment in all scientific matters and for his love and appreciation of scientific truth. In all the little disputes in his laboratory, he evidently endeavored never to let himself be led away by his personal feelings, but to give his decision in an impartial manner. His attitude finally inspired, among many of his colleagues, a confidence that he would judge their differences calmly and impartially, and there existed an intellectual bond between him and many of his laboratory workers. In the latter years of his life, his personal judgment of men and things was extensively sought after and his advice cheerfully and unselfishly given. I never knew him so busy with his own work that he would not willingly be interrupted by a colleague who wished to discuss with him some scientific problem or who sought his aid or advice. At such times it ever seemed to be his earnest desire to give the most efficient assistance to those who so came to him.

If we attempt to analyze his success, if we ask ourselves what were the qualities of his mind and character (for the two can not be separated in an investigator) by which he stood above many of his colleagues, we shall find as conspicuous traits, his comprehensive knowledge of scientific problems in general, his diligence and accuracy in the details of daily life, and his wholly upright and open character in all scientific matters. These traits were certainly powerful factors in contributing to his successful career.

However, my effort to-day is not only to pay a deserved

tribute to the memory of one in whom energy and industry were prominent traits of character and who was always so loyal a friend to his colleagues in their scientific work, but also to point out the importance of his labors in an educational way and to emphasize the importance of his establishment of a scientific institution in which the criteria of the true spirit of inquiry were always insisted upon.

Finally, his life must ever serve as a beacon to those of us who strive to emulate faithful devotion to duty.

DOCTOR FREER AND THE BUREAU OF SCIENCE.

By Dean C. Worcester,
Secretary of the Interior of the Government of the Philippine Islands.

At the time civil government was established in the Philippine Islands, there fell to my lot the drafting of legislation which had for its object the establishment of scientific work upon a firm and lasting foundation.

As a member of the zoölogical staff of the University of Michigan, I had had abundant opportunity to learn by practical observation how such work should *not* be carried on. This institution supported a zoölogical department and a medical college. In the zoölogical department we taught among other things the zoölogical half of a beginner's course in general biology, the anatomy of the cat, comparative anatomy, the embryology of the chick, and comparative embryology. In connection with these courses we operated the necessary laboratories, and for purposes of reference we had a very incomplete library.

In the medical college there were a histological laboratory, a pathological laboratory, a so-called hygienic laboratory which was in reality a bacteriological laboratory, and an anatomical laboratory.

The pathologist maintained that it was necessary for him to teach his students normal histology because the histologist did not know his business and students could not appreciate pathological conditions of tissues until thoroughly familiar with such tissues in their normal state. Similarly the histologist felt called upon to teach his students pathology because of the supposed incompetence of the pathologist. Each had trouble with bacteriologists over questions as to where histology and pathology left off and bacteriology began. At the outset only

human anatomy was taught in the anatomical laboratory, but later the anatomist in charge felt called upon to inaugurate other work in mammalian anatomy and in comparative anatomy as well. The histologist ultimately branched off into the embryology of the chick and began to talk about giving courses in comparative embryology.

Here then, within the limits of a single institution, I had observed no less than five different laboratories, each with its staff of instructors, its library, its expensive instruments, apparatus, and reagents; each more or less undermanned and inadequately equipped; each duplicating or striving to duplicate work carried on in one or more of the others. The result was needless expense, lack of readily obtainable efficiency, and constant bickering.

Furthermore, there had come to my attention rather startling instances of the duplication of scientific work in the departments at Washington.

While the complete lack of adequate facilities for carrying on imperatively necessary biological and chemical work which confronted us when civil government was organized in the Philippine Islands was appalling, I was nevertheless inclined to derive comfort from the old saying "Blessed be nothing," for we had at least the opportunity to *start* right, unhampered by costly but antiquated equipment, by worthy but incompetent investigators, or by quarrels as to who should do what needed to be done.

The materials with which to concoct a muddle worse than any of those with which I was already familiar lay ready to hand. At one time or another the Bureau of Customs has wished to establish a chemical laboratory and a so-called "microscopic laboratory." The Bureau of Forestry has thought that it needed laboratories for chemical, botanical, and entomological work. The Bureau of Agriculture has urged precisely similar needs and has desired to take up bacteriological and pathological work as well. The original Board of Health and its successor, the Bureau of Health, have been disposed to demand laboratories in which to conduct both routine work and original investiga-

tions in chemistry and biology. And so on to the end of the chapter.

I early decided to make a determined effort to centralize the laboratory work of the Insular Government under the control of one man, to the end that unnecessary and wasteful duplication of staff and equipment might be avoided and that maximum efficiency might be attained at minimum cost. With these ends in view, I drafted, and on July 1, 1901, secured the passage of "An Act providing for the establishment of Government Laboratories for the Philippine Islands." The passage of this Act laid a reasonably broad foundation, but did nothing more. It was necessary to plan and construct a modern laboratory building which should afford adequate facilities to meet the then existing, and probably future, needs of the Government; to list, buy, house, and properly catalogue a fairly complete scientific library; to purchase and install costly and complicated scientific apparatus; to provide seasonably a formidable array of expendable reagents and supplies; and most important of all, to secure the services of a large staff of well-trained scientists, capable not only of performing necessary routine examinations with unfailing accuracy, but also of grappling with some of the many scientific problems whose early solution was then imperatively needed. To the end that the best possible results should be obtained, it was necessary that the work of the members of the staff should be coördinated and directed by a master mind.

It was obvious that the man who could undertake such a task with hope of success must combine an unusually broad knowledge of the different branches of laboratory work with a wide acquaintance among scientific investigators, familiarity with cost and sources of supply of books, apparatus, and reagents, sound business judgment, good administrative ability, and hard common sense.

I chose for this important and difficult position Dr. Paul Caspar Freer, then professor of inorganic chemistry in the University of Michigan, and never was man more fortunate in his choice.

Doctor Freer's preliminary scientific training, begun in the United States and completed in Europe, had been exceptionally thorough and broad. He had displayed very distinguished ability as an original investigator and had always been most successful in directing the investigations of others. He had placed his own laboratory at the University of Michigan on a sound basis and had made numerous helpful suggestions calculated to promote efficiency and economy in the work of others of the university laboratories. Incidentally he was the youngest man ever appointed to a full professorship in the University of Michigan. I, myself, had been a student there at the time of his appointment.

Later, when both of us were members of the University faculty, we had repeatedly discussed the possible reorganization and centralization of the laboratory work of the university and had agreed that greatly increased economy and efficiency might readily be secured were some one competent person put in charge with power to act.

When the opportunity came to make a clean start in the Philippines, I felt that Doctor Freer was just the man whom I needed, and having first secured due authority, I offered to him the newly created position of Superintendent of Government Laboratories, at the same time outlining my plans for the future. The opportunity for creative work appealed to Doctor Freer, and to my very great satisfaction he accepted the position. We have profited by his mature knowledge, amazing in its breadth and accuracy.

At the outset he had no thought of permanently abandoning his university career, but requested and obtained a year's leave of absence in order to help us get started. At the end of that year his work was only begun. Mr. Taft, then Civil Governor, secured an extension of his leave for another year, and at the end of this second period successfully urged upon the university regents the almost unprecedented act of granting to a member of the faculty a third consecutive year's leave.

Meanwhile things had been happening here. At the outset Doctor Freer had found himself in the embarrassing situation of

being compelled to plan the future buildings, equipment, and personnel of the Bureau of Government Laboratories, and at the same time immediately to provide for the carrying on of urgently necessary routine examinations and original researches.

The new bureau had had small beginnings in a little building, which might without serious inaccuracy be called a shack, situated to the rear of the private residence in which the Civil Hospital had been established. In the cramped, inadequate, and unbearably hot quarters which it afforded, there were inaugurated and carried out scientific investigations of far-reaching practical importance in connection with amœbic dysentery, Asiatic cholera, and bubonic plague. More than one comparatively unknown worker here laid the foundation of an international reputation.

The preparation of plans and estimates for the permanent laboratory building, the completion of lists of necessary scientific books, apparatus, and supplies, and the figuring out of an adequate laboratory staff occupied much of Doctor Freer's time during a period of two years. I speak whereof I know when I say that plans and estimates so complete and accurate as those which he ultimately furnished were never before nor since presented to the legislative body of these Islands.

The aggregate sum of money involved was so large as to make its appropriation at one time inexpedient if not impracticable. Furthermore, it would have been worse than useless to have books and apparatus arriving without a proper place in which to house them, or to employ scientific workers prior to the provision of adequate laboratory accommodations for them. Doctor Freer was, therefore, compelled to give most careful consideration to a scheme for spreading the necessary expenditures over a period of years.

His elaborate plans and estimates proved adequate and final. They were never departed from in any essential particular, so far at least as concerns the work then under contemplation. The only changes which have proved necessary were incident to providing for a large amount of additional scientific work when the scope of the original Bureau of Government Laboratories

was added to and its designation was changed to "The Bureau of Science."

After all plans and estimates had been perfected, it was necessary to persuade a legislative body, including in its membership only one lone scientist, to provide the necessary funds. Doctor Freer was naturally required to state why he wanted what he wanted, with the result that he got it.

The work speedily outgrew the little one-story building in which it started. The biological laboratory was transferred to a much larger building on a distant street, and administration was thus complicated.

There was endless delay in the completion of the new building. Grossly exaggerated rumors as to its cost led to the charge that its erection had involved needless and wasteful expenditure. Salaries were necessarily small.

The underpaid members of the Bureau staff were publicly attacked, collectively and in some cases individually, as impracticable and visionary beings, who were devoting their energies to wasting the funds of a poverty-striken government in useless abstract investigations.

One member of the Philippine Commission who had conceived the idea that scientific books were intended only for filing in imposing ranks on the wall, as is done with formidable looking tomes by lawyers of a certain class, for years bitterly assailed every appropriation requested for the Bureau. Through good report and ill Doctor Freer held on his course with clear foresight and unwavering tenacity of purpose, convinced that he should win in the end because he was right. He lived to see this belief abundantly justified!

As the end of his third year of leave approached, he received an ultimatum from the Michigan University authorities to the effect that he must again take up his university work or sever his connection with that institution. An immediate reply by cable was necessary. I asked him to state to me the conditions under which he would be willing to remain in the Insular service, and he did so. No quorum of the Commission was present on that day and, as immediate action was imperative, I stated the

facts to four of my colleagues, with a view to obtaining their prior approval. Doctor Freer's proposition was perfectly clear to me and I thought that I made it clear to them. They agreed to accept his offer as they understood it. With a majority of the Commission thus pledged to its acceptance, I informed him that it would *be* accepted, and he then immediately severed his connection with the University of Michigan by cable. A few days later when I requested definite official action by the Commission, I found to my consternation that two of the members with whom I had consulted had failed clearly to understand the terms on which Doctor Freer was willing to remain. When the matter came to a vote my action was not confirmed. I was, therefore, compelled to inform him that he would not be given the salary for which he had stipulated and that the fault of this unfortunate blunder lay entirely with me for the reason that I had failed to submit his proposition to my colleagues in writing and to secure on the face of the document their written approval.

He immediately cabled to ascertain whether he could withdraw his resignation from the faculty of the University of Michigan, but before his message was received his place had been filled.

It is a significant commentary on his character that, although he felt, rightly, that a grave injustice had been done him, he remained loyal both to the man who was primarily responsible for it and to the Government which he served.

With the lapse of time the work conducted under his wise guidance rapidly and steadily developed. The Bureau of Government Laboratories absorbed the Bureau of Mines, took up botany, ornithology, entomology, fisheries, cement testing, and other new lines of investigation, and thus became the Bureau of Science. It furnished its own light, power, steam, and gas so economically that it was required to perform these functions for the College of Medicine and Surgery and for the Philippine General Hospital. These changes meant larger working quarters and a material addition to the power plant, which were provided under Doctor Freer's always competent and efficient direction.

As the volume of research work grew and the necessity for the prompt publication of its results became urgent, the Bureau entered upon the risky venture of beginning the publication of a scientific journal, which must depend for its subject matter upon the results of the work of a limited number of investigators, much of whose time was necessarily occupied by routine examinations. To-day the Philippine Journal of Science is one of the world's standard scientific publications. In it have been published the results of scientific investigations of far-reaching importance. In my opinion, it has done more than any other one thing to spread throughout the world knowledge of work being done in the Philippines for the uplifting of a people and to spread that knowledge among men whose opinion really counts.

The business affairs of the Bureau of Science have been exceptionally involved. It has often been necessary to order apparatus a year or more in advance in order to be sure of having it ready when required. Important book orders have sometimes remained unfilled for years and have had to be repeatedly canceled and re-placed. The Bureau has been dependent in part upon its receipts for money with which to operate and the annual total of such receipts could not be accurately foreseen. It was known to Doctor Freer that deficits would not be approved by the Secretary of the Interior. There have been none.

Scientists of established reputation have strenuously objected to taking civil service examinations and have had to be reasoned with. After arrival at Manila some of them have even more strenuously objected to accounting for their time and have in many ways displayed a desire to be considered in a class by themselves. It has been necessary for Doctor Freer to teach them that they were very much like other people, and would be so considered.

New men have not infrequently desired to reserve for themselves certain fields of investigation which they were not ready immediately to enter and have needed to be inspired with a broader and more truly scientific spirit. Doctor Freer has been peculiarly fortunate in dealing with this too common foible of

research men, and the unseemly brawls which so often occur over questions as to who shall do what, and as to priority of results, have been conspicuously absent.

For a long time the Bureau served as a training school for other and wealthier institutions which could afford to buy our employees away from us and did not hesitate to do so. The fight for more adequate salaries was a long and tedious one, but it has achieved important results.

In another particular he has deserved well of the Government. My original plan contemplated a close and helpful relationship between the Bureau of Government Laboratories, a medical college, and a great general hospital. I was told that my scheme was chimerical because three such institutions would never work together harmoniously. This prophecy has proved false. Doctor Freer thoroughly understood the meaning of the word *coöperation,* and on more than one occasion taught it to others, both by precept and example. Under his direction the Bureau of Government Laboratories and its successor, the Bureau of Science, have maintained a helpful relationship with the Bureau of Health and the University of the Philippines.

Doctor Freer may most truly be said to have lived for his work. While he sometimes shortened his afternoon hours sufficiently to make possible the taking of sorely needed exercise, he habitually labored far into the night and on holidays as well. During his last year he had repeated and prolonged attacks of acute suffering. In each such instance he resumed his work before he could rise from his bed. In the course of the last day of his life his thoughts turned again and again to the work and the needs of the Bureau of Science. His relationship to that Bureau may be very briefly summarized. *I* dreamed a dream. *He* made that dream come true. It is not too much to say that he created the Bureau. It will be a lasting monument to his unquestioned scientific and business ability, his clear foresight, his sane judgment, and his unwavering perseverance.

There have not been lacking prophets of evil who have felt that the success of the work of the Bureau of Science was so

intimately associated with the peculiar abilities of its director that the Bureau would go to pieces now that his guiding hand has been palsied by death.

It is not to be expected that anyone else could, at the outset, run so complicated a machine with the capable and peculiarly sympathetic touch of the man who built it, but ability to produce a machine which *can* be operated successfully by others determines the value of the builder's work. As the years go by, it will be realized that the constructive work of Doctor Freer for the Bureau of Science has successfully met this, the final test.

PROFESSOR FREER AND THE UNIVERSITY OF THE PHILIPPINES.

By William Everett Musgrave,
Chief of Clinics, Philippine General Hospital.

History records no more complete and unselfish devotion to science than is exemplified in the life of Paul Freer.

He was essentially an investigator and teacher, combining these virtues in such a manner as to make every man who became closely associated with him his pupil. In personality, in the character of his researches, in versatility of mind, in the utilitarian aim of all his work, in his generous attitude of help to all who applied for assistance and advice, and in many other points Professor Freer very closely resembled the illustrious Pasteur.

Pasteur was the father of bacteriology and lived to guide this great science from uncertainty to the road to success. Paul Freer was the father of modern science in the Philippine Islands and he lived to see and guide the developments of his creation to success.

Starting with nothing but a fertile soil and a legislature whose friendly interest was secured and maintained by the untiring activities of the Honorable Dean C. Worcester, he built up a great research institution that to-day is classed with the best in other countries.

During the early years of our residence in this country, he watched the development of elementary education with much interest, and his counsel during these years was a potent influence upon the policy of the Government in educational development.

Educational progress was so satisfactory that in 1905, at its annual meeting, the Philippine Islands Medical Association rec-

ommended the establishment of a Medical School. Doctor Freer was chairman of the committee which, with the active co-operation of Mr. Worcester, succeeded in securing satisfactory legislation. "The Philippine Medical School" opened its courses of instruction in 1907, and was merged with the University of the Philippines as the College of Medicine and Surgery in 1909. Doctor Freer was dean and, also, professor of chemistry from the organization of the school until his death, which occurred just five years after the opening of the school and shortly after graduation of the first class of physicians who had taken their entire course of instruction in this institution.

He always stood for high standards in educational work, and it was due largely to his efforts that the College of Medicine and Surgery was able to establish and maintain rigid entrance requirements, a five years' course of instruction, and to secure a faculty of research workers who are paid for teaching. This was no easy task. The public demand for more physicians, the small number of thoroughly prepared students, the limited resources of the Government, and the political exigencies were such that the pressure brought to bear for lower requirements for admission with larger classes, shorter courses of instruction, and less expensive teachers and methods was very strong. Doctor Freer very correctly considered that the stand taken by the Philippine Medical School would determine, for a long time to come, the policy of higher educational methods, and in winning this fight for high standards he not only gained world-wide recognition for our school from the first, but a precedent was established that made a similar policy practicable for other colleges and prepared the way for a University before one was created.

During the first years of our work, while searching the world for suitable teachers for the Medical School, Doctor Freer crippled the efficiency of his own Bureau by furnishing a large proportion of the faculty from the members of the staff of the Bureau of Science. Not only this, but he gave freely of his own time and even diverted funds, as far as practicable within the law, in order to insure the success of the school.

The methods of successful men are always interesting and instructive. Professor Freer's methods were very simple. In dealing with his superiors he usually made a direct request and reënforced this request by a presentation of all the facts bearing upon the subject. If the first effort failed, he would repeat the request until he secured what was wanted or was ordered to desist. In dealing with his colleagues and assistants, his watchword was *efficiency* and all men were judged upon this basis, a very satisfactory method for a man of his broad learning and experience, but a hazardous one for a less experienced leader.

Something of Doctor Freer's conception of the function of a medical school is shown in his Commencement Address to the graduating class in 1910 in which he said:

> The exact training which the graduate of a modern medical school obtains from his work in the various laboratories; the development of his powers of observation by a study of physics, chemistry, bacteriology, pathology; by his contact with the methods of diagnosis and clinical reasoning in the hospital and by the broad phases of hospital discipline which surround him during the final years of his course of study, will have been without meaning if they have not shown him one fundamental fact, that all of this hard work will have been valueless, if he has not had introduced within his being the divine spark of independent thought * * *. If he has not this ambition, his future will be first one of stagnation, then of retrogression. It has been one of the chief missions of the Faculty to cultivate this spirit among the students, and the members of the latter body themselves must be constantly extending their view-points and developing the various special branches to which they are devoting their attention. What is true of the individual members holds good of any institution of learning, a condition of dependence on what is already known and a tendency to look backward into the past is in reality retrogression; and intellectually such an institution must die, no matter how magnificent its buildings, how extensive its equipment, or how generous its means. The teaching force must itself not only be capable of advancing new thought and of developing new methods, but it must utilize these capabilities to the best advantage, continually and restlessly pressing forward to higher ground. Otherwise, the teacher is not capable of inspiring his pupils, he becomes a mere repeater or reciter of text-books, a monitor or supervisor of method which of itself is cast into fixed molds and is already passing toward its end.

Continuing in this same address, our dearly beloved friend and teacher has left us the following advice for the future policy and guidance of the school:

> We must therefore, in the future as in the past, strive to obtain and retain men in the school of the best capability for advancing their own technical specialties. Mere teaching will not do, it lacks that peculiar force which renders the pupils in after life capable of independent development. Mere study on the part of the expectant graduate will also not do. He must continue his scientific growth by observation, thought, study and reasoning from the facts as he finds them to those lying in the higher realms of advance beyond. Faculty and students form the institution as a whole, and it is for them to see that, through the many years of its existence, it continues to play its part in the great advance of human thought as a vigorous entity in the community of schools of learning.

In this last quotation we are given a duty that is made sacred by the martyrdom of him who gave it. The duty is a hard one; no one realized more fully than did Doctor Freer that our greatest difficulty would be to inculcate the spirit of independent thought in our students. Five years of experience has shown that there are local causes, intrinsic and acquired, that make this the greatest problem of our institutions of advanced learning, and the ultimate success of our work depends upon our being able to surmount these difficulties which only may be done by constant effort and the revolutionizing of the customs and practices of centuries.

This is the one phase of our educational development that had not been satisfactory to Doctor Freer, and I bespeak the coöperation of the members of the Faculty to make the appeal contained in his last public utterance to us our watchword for success; and may our efforts not cease until the Paul Caspar Freer Professorship of Chemistry in the University of the Philippines is freely recognized as one of the positions of honor in the scientific world.

DOCTOR FREER AS AN ORGANIZER AND AN ADMINISTRATOR.

By Murray Bartlett,
President of the University of the Philippines.

It is a rare thing when the creative and executive faculties are united in one mind. Rarer even is the combination of scientific genius and business ability.

To see deeply into the laws underlying the mystery of nature, to follow the trace of unknown promise to a successful conclusion, then to apply the practical methods of efficient life to the results of scientific research is seldom achieved by one mind and will. It is this combination of human powers that has made possible the fame of an Edison, a Bell, a Westinghouse. In most cases, men, such as these, use their ability to capitalize for material value the fruits of their scientific investigation.

Doctor Freer was one of these rare men. Undoubtedly he could have devoted his extraordinary ability to amassing a large fortune. Indeed, he had more than one opportunity so to do. He might have erected upon the foundation of his genius for seeing nature's hidden powers a great business organization in his own land for his own enrichment. Instead, he built up about his research and the research of others a great institution for the practical benefit of humanity in a strange and far-away land. The Bureau of Science is, perhaps, not so much a monument to Freer, the Scientist, as to Freer, the Organizer. Truly could one of his friends say, "The Bureau of Science is Freer."

This is why there has been universal testimony to-day that his place can not be filled. If such a statement can be true of any man, it is certainly true of Doctor Freer, for where can be found one, not only preëminent in his own line of study,

but familiar with the details of every other phase of scientific investigation; possessing the practical ability of a captain of industry and inspired by a spirit of service for country and for humanity? To say, however, that Doctor Freer's place can not be filled is not to declare that the work of the Bureau of Science can not go on. His task was so well done, so completely organized that, with careful guidance, its many activities may continue unimpaired through the years.

Doctor Freer had all the qualities of a great organizer; untiring industry which keeps no office hours, knowledge of affairs in the broad sense which kept him in touch with the practical needs of the world of trade and commerce, and ability in choosing his assistants. Of these qualities, it is needless to speak. The organization he left behind speaks for him. In treating the subject of Doctor Freer as an organizer and an administrator, I wish to mention the characteristics which were peculiarly his own.

First, he was capable of rare unselfishness where an ideal was to be gained. All the way through, he sacrificed his own time and desire for investigation in order to guide the investigation of others for the good of his Bureau. It was to him a real deprivation to give up his own personal research in a field in which he had few peers and no superiors, yet there was no hesitation on his part in giving freely the results and the credit of his experience to men who were just beginning their scientific investigation.

Nowhere does this unselfishness appear more clearly than in Doctor Freer's relations with the College of which he was the executive head. The Philippine Medical School was very largely the creation of Paul Freer. Its thoroughness of instruction and its high as well as practical standards were made possible by his thorough acquaintance with medical instruction and his extraordinary knowledge of university affairs. He was thoroughly imbued with the idea of founding here, in these Islands, a great Medical College; to provide for the Filipino people a succession of competent physicians and surgeons who should protect and safeguard the health of their race. He had the

right to take pride in the success of this institution and to look upon it as his own. When, however, by operation of law the Philippine Medical School ceased to be an independent institution and became a constituent part of the University of the Philippines, he gave the same care, enthusiasm, and loyalty to the College of Medicine and Surgery, although he occupied, what might appear to be, a subordinate position. I sometimes think that I saw the biggest side of Paul Freer—the older man and the younger man, the man of long and rich experience and the man with little. If in future years any credit is given to the work of laying the foundation of this University in its early days, the larger part should be his.

This spirit of unselfishness enabled him to administer his trust, not for the benefit of his own Bureau, but for the larger cause of the Government as a whole, and for its work in these Islands. His outlook was broad and his vision clear. With him the Bureau of Science was simply one means of rendering a service to the Philippine people. His real aim was to make that service as perfect as possible. A favorite phrase with him was "we must play the game." To him, the game was not an opportunity for individual play, but for team work.

In our own relations, the unusual facilities of his Bureau were freely offered to the University, and I believe that in his dealings with other departments of the Government, his attitude was marked by the spirit of true coöperation. Thus he has left behind him a great lesson in administration to those of us who are administrators in this Government. His example entreats us to work not for the conspicuous success of our own Bureaus but for rendering a complete and perfect service by the whole Government.

The University of the Philippines will always revere the memory of Paul Caspar Freer; great as a scientist—greater, perhaps, as an administrator—but greatest of all as a man.

DOCTOR FREER AS A FRIEND OF THE FILIPINOS.

By Fernando Calderon,
Professor of Obstetrics, University of the Philippines.

There are three classes of Americans according to their feelings toward the Filipinos with whom they are in daily contact. First, there are those who maintain an attitude of *absolute indifference* with respect to the future of the Filipino people, when both races should thoroughly know and gladly help each other. These Americans, after spending some time in the Islands, return to the United States without having in any manner coöperated in the improvement of their brothers, the inhabitants of this beautiful Archipelago. Then, here are those who are absorbed by a feeling of *utter selfishness,* and whose sole desire is that this country be converted into a fit place for the satisfaction of their personal ambitions, thus forgetting entirely the economic welfare of the Filipino people. Lastly, there are those noble Americans who have come to the Philippines imbued with a kindly spirit toward the Filipino, whom they treat as brother and friend.

The object of these Americans, who are, after all, the real and proper representatives of the great American nation in the Far East, in coming to these shores, is neither to further their private interest nor to satisfy their greed for wealth, but to fulfil their sacred mission of service and usefulness and to set an example of righteousness to their fellow-countrymen here, so that we may justly call them the standard-bearers of a civilization which is based on the ethical and immutable principles of democracy and on that great ideal of history: the universal brotherhood of man. These are the Americans whose beneficent influence will infuse new ideas and new energies into our insti-

tutions and inculcate into the minds of the rising generation that wholesome spirit of democracy which will make the Philippines the most prosperous and progressive country which the world ever beheld in these far-away regions of the extreme Orient. To this group of worthy and self-denying citizens of America the late Dr. Paul C. Freer belongs, whose memory will ever be cherished by those Filipinos who have had opportunity to realize his untiring efforts for the advancement of science in the Philippine Islands.

I need not remind you, of course, to prove my assertion, that Doctor Freer was the one who created and established the Bureau of Science on a scientific basis, helped a great deal in the foundation of the Philippine Medical School and planned this beautiful building, and that he was, perhaps, the principal factor in the construction of that magnificent General Hospital where the College of Medicine and Surgery has its clinics. All of these institutions are admired by visitors and constitute a perennial fountain of blessings upon the Filipino people.

But there is still another feature of his work which deserves notice. Paul Caspar Freer was a solicitous protector of the Filipino youth. It was his desire that young Filipinos should participate directly in the scientific movement which, since the establishment of American government, has been initiated here. For this reason, both government and private students, upon their return from abroad, found the Bureau of Science an adequate field for their studies and the Director, Doctor Freer, a generous adviser who knew how to encourage the spirit of personal initiative and original research.

Paul Caspar Freer also entertained the salutary idea of putting as many Filipinos as possible in his Bureau. On account of this policy, the division of mechanics of the Bureau of Science is at present completely entrusted to Filipinos; and, in the majority of the other divisions, the work of young Filipino graduates is by no means small. Two of them, Messrs. Timoteo Dar Juan and José del Rosario, in the division of chemistry, after graduating in pharmacy from private schools in this city, were asked by Doctor Freer to practise in his office. Later on, Doctor

Freer recommended their being sent to the United States as government students, and now they are instructors in the College of Medicine and Surgery.

This true friendship on Doctor Freer's part toward the Filipinos also manifested itself in the College of Medicine and Surgery, of which he was the Dean. It was a real source of pleasure for him to work with so many Filipino members of the faculty.

In rendering my humble tribute to the memory of that great friend of the Filipinos, allow me to suggest that we, his fellow-workers and admirers, especially his Filipino friends, place a votive tablet on one of the walls of this building, as a sincere token of our enduring appreciation of his disinterested service and as an outward expression of our unswerving admiration of his ideals as a man and a scholar.

PAUL C. FREER, CHEMIST.

By H. D. Gibbs,

Chief of the Division of Organic Chemistry, Bureau of Science, and Associate Professor of Chemistry, University of the Philippines.

In 1887 Paul C. Freer received the degree of doctor of philosophy in Munich. It is astonishing to note the number of great chemists who have received their first inspiration in chemical research in Professor Adolf von Baeyer's laboratory in Munich, and who have absorbed and later radiated the teachings of this great master. This period in v. Baeyer's work was largely devoted to the study of the structure of ring compounds and very soon afterward he published his classic series of articles on the structure of the benzene ring and the reduction of terephthalic acid.[1]

For some years before Doctor Freer received his degree, W. H. Perkin, jr., son of the Perkin who founded the industry of the manufacture of coal tar dyes, had been working in v. Baeyer's laboratory on the synthesis of ring compounds. In 1885 the first part of the article "On the Synthetical Formation of Closed Carbon-Chains" [2] was published. The continuation of this article [3] was published by the joint authorship of Freer and Perkin and was a further study of the construction of the ring compounds from open chains. Parts II and III were published by Perkin alone and in Parts IV and V Freer [4] again appears as

[1] *Ann. d. Chem.* (Liebig) (1888), 245, 103; (1889), 251, 257; (1890), 256, 1.

[2] *Journ. Chem. Soc. London* (1885) 47, 801, Part I. On some derivatives of trimethylene.

[3] The synthetical formation of closed carbon-chains, part I (continued). The action of ethylene bromide on the sodium-derivatives of ethylic acetoacetate, benzoyl-acetate and acetone-dicarboxylate, by P. C. Freer, Ph. D. and W. H. Perkin, jr., Ph. D., *ibid.* (1887), 51, 820.

[4] The synthetical formation of closed carbon-chains, part IV. Some derivatives of hexamethylene, by Paul C. Freer, Ph. D. and W. H. Perkin, jr., Ph. D., *ibid.* (1888), 53, 202; Part V. Experiments on the synthesis of heptamethylene derivatives, by Paul C. Freer, Ph. D. and W. H. Perkin, jr., Ph. D., *ibid.*, 215.

the senior author. The work commenced in v. Baeyer's laboratory was later carried on in the laboratory of Professor Dixon, Owens College, Manchester, England.

This research with Perkin is a valuable contribution to the knowledge of the tetra, penta, and hexamethylene rings and the derivatives of tetrone, pentone, and hexone. Efforts to synthesize the heptamethylene ring determined that the methods attempted were not feasible.

About this time Doctor Freer was offered a commercial position in the dye manufacturing industry and it became necessary for him to choose between this and an academic career. He chose the latter and, although knowing that the former meant greater financial reward, I know he never regretted his decision.

To my intimate knowledge there are two things which Doctor Freer carried through life as a result of his association in Munich. The first was his intense interest in the discussions of the structure and behavior of the benzene ring. Less than ten days before his death, we were at the Country Club in Baguio discussing some phases of the work described in an article which I had just presented to him for publication in the Philippine Journal of Science, when he enthusiastically said: "This throws more light on the benzene ring. We must further elucidate the structure of the benzene ring." The second was his generosity with his ideas and assistance to the younger chemists. Only we chemists of the Bureau of Science know how much of Doctor Freer's keen mind, inspiration, and editorial ability there is in the chemical articles originating in the Bureau, for his name seldom appears. We know that a person of less lofty ideals, less ability, and more self aggrandizement would have felt himself privileged, at least, to take the credit of a joint authorship in a large proportion of the published chemical research.

The next period of his research, extending from 1887 to 1902 during his residence in America, principally at Ann Arbor, Michigan, was largely concerned with the sodium derivatives of various ketones and aldehydes, their formation and behavior. In 1890 Doctor Freer contributed an important piece of research which did much to settle the mooted question of the constitution

of aceto-acetic ether, when he found that acetone, a substance containing no methylene group, was capable of forming a sodium derivative, the reactions of which were similar in nearly every respect to those of sodium aceto-acetic ether. This reaction proved to be a general one shown by other ketones as well as acetic aldehyde.

In 1898 he completed a most interesting piece of work on the constitution of phenylhydrazones. Some of the compounds prepared were very difficult to handle and were made in Michigan during the winter when the thermometer was about 20° below zero. The oxidation of acetone p-bromphenylhydrazone to p-brombenzene azo-isopropylene was especially troublesome, requiring careful handling even at this low temperature, and on several different occasions when our laboratories in the Bureau of Science were unusually warm, Doctor Freer brought up this subject with me and took delight in discussing the difficulties we would experience in trying to produce this reaction in Manila.

During this period, before his arrival in Manila, in addition to the 14 articles on ketones and aldehydes referred to, Doctor Freer also published papers on "The Saponification of Substituted Acetic Ester, Tetrinic Acid, The Constitution of Some Derivatives of Formic Acid, Distillation in Vacuum, Formamide, Jamaica Dogwood, Organic Peroxides, the Action of Acids on Metals, and Halogen Substitution Products of Aliphatic Acids," and two textbooks, one The Elements of Chemistry and the other Descriptive Inorganic General Chemistry. These books are very highly regarded both from a chemical and literary standpoint.

From 1901 to 1912, a period of a little over ten years spent in the Philippines, Doctor Freer found that, on account of his administrative duties in connection with the Bureau of Science and the Medical School, and his editorial work on the Philippine Journal of Science, his personal application to research was impossible, a fact which he regretted deeply. Nevertheless he found time to write a number of articles descriptive of the work of these institutions, and his address given at the commencement exercises of the Philippine Medical School, Feb-

ruary 27, 1909, and later published in the Philippine Journal of Science, is an inspiration to all workers in science. His editorial work was most conscientiously performed and I have known him to read many articles three times before the final appearance in print. During the last four years of his life, he developed the keenest interest in the studies of sunlight and sunlight reactions carried on in the Bureau of Science, and through his wide acquaintance and scientific reputation, he obtained the coöperation of various colleagues in America, Europe, Africa, Asia, Australia, and some of the most important islands outside of the Philippine Archipelago. This work was beginning to bear fruit at the time of his death, and he had already published two articles summarizing the results. It promises to throw much light upon several mooted questions concerning sunlight and its effects upon man, and in a few years would have resulted, I believe, in such an indisputable mass of valuable evidence that Doctor Freer and his friends would have regarded it as his crowning achievement.

LIST OF PUBLICATIONS.

Ueber den Acetyltrimethylencarbonsäureäther, by W. H. Perkin, jr., and P. C. Freer. *Ber. d. deutschen chem. Ges.* (1886), 19, 2561–2569.

The synthetical formation of closed carbon-chains. Part I (continued). The action of ethylene bromide on the sodium-derivatives of ethylic acetoacetate, benzoyl-acetate, and acetone-dicarboxylate, by Paul C. Freer and W. H. Perkin, jr. *Trans. Journ. Chem. Soc.* (1887), 51, 820–853.

On the action of ethylene bromide on the sodium derivatives of the ethers of acetoacetic, benzoyl-acetic and acetone-dicarboxylic acids, by Paul C. Freer and W. H. Perkin, jr. *Am. Chem. Journ.* (1888), 40, 446–457.

Synthese von Hexamethylenderivaten, by Paul C. Freer and W. H. Perkin, jr. *Ber. d. deutschen chem. Ges.* (1888), 12, 735–737.

The synthetical formation of closed carbon-chains. Part IV. Some derivatives of hexamethylene, by Paul C. Freer and W. H. Perkin, jr. *Trans. Journ. Chem. Soc.* (1888), 53, 202–215.

The synthetical formation of closed carbon-chains. Part V. Experiments on the synthesis of heptamethylene derivatives, by Paul C. Freer and W. H. Perkin, jr. *Trans. Journ. Chem. Soc.* (1888), 53, 215–222.

Zur Kenntniss des Heptamethylenringes, by Paul C. Freer and W. H. Perkin, jr. *Ber. d. deutschen chem. Ges.* (1888), 21, 738–739.

Uber die Einwirkung von Jodwasserstoffsäure auf die Krotonsäuren, by Arthur Michael and Paul C. Freer. *Journ. f. prak. Chem.* (1889), 40, 95–96.

The action of sodium on acetone. *Am. Chem. Journ.* (1890), 12, 355–357.

Ueber die Einwirkung von Natrium auf Aceton. *Journ. f. prak. Chem.* (1890), 42, 470–472.

The action of chlor-carbonic ether on acetone-sodium, by Paul C. Freer and George O. Higley. *Am. Chem. Journ.* (1891), 13, 322–326.

The constitution of aliphatic ketones, and the action of sodium on acetone. *Am. Chem. Journ.* (1891), 13, 308–322.

On the saponification of the substituted acetic esters, by Paul C. Freer and F. L. Dunlap. *Am. Chem. Journ.* (1892), 14, 366–376.

Some reactions with acetoacetic ether and with salicylic ether. *Am. Chem. Journ.* (1892), 14, 407–422.

Ein Vorlesungsversuch, die Effusion der Gase betreffend. *Ztschr. f. phys. Chem.* (1892), 9, 669–670.

Zur Kenntniss des Acetessigesters. *Journ. f. prak. Chem.* (1892), 45, 414–416.

The action of metals on nitric acid, I. The reduction of nitric acid by copper, by Paul C. Freer and George O. Higley. *Am. Chem. Journ.* (1893), 15, 71–81.

2. The reduction of nitric acid by copper and by lead, by George O. Higley. *Am. Chem. Journ.* (1895), 17, 18–26.

3. The reduction of nitric acid by silver, by George O. Higley and W. E. Davis. *Am. Chem. Journ.* (1896), 18, 587–590.

4. The reduction of nitric acid by silver, by Paul C. Freer and George O. Higley. *Am. Chem. Journ.* (1899), 21, 377–392.

On the action of sodium on acetone. *Am. Chem. Journ.* (1893), 15, 582.

Descriptive inorganic general chemistry. Boston (1894), 550 pp.

Ueber die Einwirkung von Natrium auf Aceton. *Ann. d. Chem.* (Liebig) (1894), 278, 116–140.

Zur Kenntniss des Acetone. Ueber die Einwirkung von Chlorkohlensäure-äthylester auf Natriumaceton. *Ann. d. Chem.* (Liebig) (1894), 283, 380–391.

Derivatives of tetrinic acid. Experimental work by E. R. Miller. *Am. Chem. Journ.* (1905), 17, 792–796.

The elements of chemistry. Boston (1895), 289 pp.

On the action of chlorcarbonic ester on sodium acetone. *Am. Chem. Journ.* (1895), 17, 1–18.

On the action of sodium on the esters of aconitic and nitric acids. Preliminary notice. *Am. Chem. Journ.* (1895), 17, 31–33.

Tetrinic acid. *Am. Chem. Journ.* (1895), 17, 779–792.

The action of sodium on aldehyde. *Am. Chem. Journ.* (1896), 18, 552–562.

Notes on new apparatus. 2. Distillation in a vacuum. *Am. Chem. Journ.* (1896), 18, 585–586.

3. The demonstration that two volumes of hydrogen and one volume of oxygen form two volumes water vapor. *Am. Chem. Journ.* (1896), 18, 562–584.

On the constitution of some derivatives of formic acid. First paper, by Paul C. Freer and P. L. Sherman, jr. *Am. Chem. Journ.* (1896), 18, 562–584.

The action of sodium upon methylpropylketone and acetophenone, by Paul C. Freer and Arthur Lackman. *Am. Chem. Journ.* (1897), 19, 878–890.

Die Einwirkung von Natrium auf Aldehyd. *Ber. d. deutschen chem. Ges.* (1897), 29, 1147.

Ueber die Constitution einiger Derivate der Ameisensäure, by Paul C. Freer and P. L. Sherman, jr. *Ber. d. deutschen chem. Ges.* (1897), 29, 1148.

Ueber die Constitution einiger Hydrazone. *Ber. d. deutschen chem. Ges.* (1897), 30, 736–738.

Formamide and its sodium and silver salts, by Paul C. Freer and P. L. Sherman, jr. *Am. Chem. Journ.* (1898), 20, 223–228.

The action of benzoyl chloride on the phenylhydrazones of benzoin. *Am. Chem. Journ.* (1899), 22, 396–402.

On the constitution of the phenylhydrazones. *Am. Chem. Journ.* (1899), 21, 14–64.

On the constituents of Jamaica dogwood, by Paul C. Freer and A. M. Clover. *Am. Chem. Journ.* (1901), 25, 390–413.

Ueber halogensubstituirte aliphatische Säuren. *Ann. d. Chem.* (Liebig) (1901), 319, 345–357.

On the formation, decomposition and germicidal action of benzoyl acetyl and diacetyl peroxides, by Paul C. Freer and Frederick G. Novy. *Am. Chem. Journ.* (1902), 27, 161–192.

The preparation of benzoyl-acetyl peroxide, and its use as an intestinal antiseptic in cholera and dysentery. Preliminary notes. *Pub. Bur. Gov. Labs.* (1902), No. 2, (Second printing, 1904).

On the organic peroxides, by Paul C. Freer and Frederick G. Novy. *Contrib. Med. Research* (Vaughan), Ann Arbor, Mich. (1903), 63–127.

The spirit of organic chemistry by Arthur Lachman, with an introduction on the growth of the science of organic chemistry by Paul C. Freer, 6 pp. New York (1904).

The work of the Bureau of Government Laboratories of the Philippine Islands. *Science* (1904), n. s. 20, 105–109.

I. Description of the new buildings of the Bureau of Government Laboratories by Paul C. Freer. II. A Catalogue of the Library of the Bureau of Government Laboratories by Mary Polk. *Pub. Bur. Gov. Labs.* (1905), No. 22, 320 pp., 28 pls.

Plague and late cholera epidemic in the Philippine Islands. *Ill. Med. Journ.* (1905), 7, 346.

Accidental inoculation with the virus of plague. *Journ. Am. Med. Assoc.* (1907), 48, 1264–1265.

The action of sodium on acetone, by Raymond Foss Bacon and Paul C. Freer. *Phil. Journ. Sci., Sec. A* (1907), 2, 67–76.

A consideration of some of the modern theories in relation to immunity. *Phil. Journ. Sci., Sec. B* (1907), 2, 71–81.

The new Philippine Medical School established by the Government of the Philippine Islands. *Science* (1907), 26, 600–602.

The free dispensary of the Philippine Medical School. Editorial. *Phil. Journ. Sci., Sec. B* (1908) 3, 352–353.

The Philippine Islands Medical Association. Editorial. *Phil. Journ. Sci., Sec. B* (1908), 3, 183.

Address at the commencement exercises of the Philippine Medical School. *Phil. Journ. Sci., Sec. B* (1909), 4, 71–75.

The Philippine Medical School. *Journ. Am. Med. Assoc.* (1909), 52, 271–272.

Commencement address, Philippine Medical School. *Bull. Manila Medical Society* (1910), 2, 72–73.
Interesting things to see and do in the Philippines. *The Manila Times.* First annual edition (1910), 22, 23.
Threading the Archipelago. *Philippine Resources* (1910), 1, 17–21.
The study of Manila copal. *Phil. Journ. Sci., Sec. A* (1910), 5, 171–172.
The tropical sunlight. *Phil. Journ. Sci., Sec. B* (1910), 5, 1–20.
The Bureau of Science. *Merchants' Asso. Rev.* (1911), 1, No. 5, 1–5.
Medical education in the Philippines. *Manila Times.* Second annual edition (1911), 30–31.
The result of the past two years' work in the study of tropical sunlight. *Phil. Journ. Sci., Sec. B* (1912), 7, 1–28. [Abstract in *Med. Rec.* (1912), 81, 682.]
Tropical sunlight. *Pop. Sci. Month.* (1912), 80, 521–529.

BUREAU OF SCIENCE, MAIN BUILDING.