

of the stomach in which temporary inhibition of peptic digestion is desired. This is particularly true in the prevention and cure of chronic gastric ulcer. By the use of certain foods, methods and time of feeding, and various alkaline substances, complete and continuous neutralization can be obtained.

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ENDEMIC TYPHUS FEVER IN THE PHILIPPINE ISLANDS

OBSERVATIONS BASED ON A STUDY OF TWENTY-THREE CASES OCCURRING AMONG FILIPINOS AT CAMP KEITHLEY, MINDANAO, P. I., WITH THE RESULTS OF ANIMAL INOCULATIONS *

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Endemic typhus fever has not been reported, heretofore, as occurring in the Philippine Islands. Reference to the Reports of the Director of Health,¹ from July 1, 1911, to Jan. 1, 1914, shows that occasional cases resembling typhus fever have occurred in Manila, but "not sufficient confirmatory evidence could be obtained as to the correctness of the diagnosis to warrant reporting them as typhus."

It is believed that sufficient data—clinical, laboratory and epidemiologic—are embodied in this report to show that typhus in endemic form unquestionably exists in the Philippines, at least in the Lanao section of Mindanao.

Twenty-three cases have been studied in the military hospital at Camp Keithley. The first case, erroneously diagnosed as malaria, was admitted Aug. 28, 1914. During September four additional cases were under observation, and it became evident that the disease was not one of those ordinarily encountered.

Tentative clinical diagnoses of typhus fever were made in these cases by elimination; but, in the absence of confirmatory laboratory evidence, the first positive diagnosis was not made until October 12.

The disease observed here corresponds to the acute infectious disease described by Brill² of New York which, subsequently, was proved by Anderson and Goldberger³ to be identical with the typhus fever of Mexico. In our cases the period of incubation appeared longer, the average leukocyte count was less and marked nervous manifestations—absent in Brill's cases—were not uncommon in ours.

* Submitted for publication March 19, 1915.

1. Ann. Rep. Bureau Health, Philippine Islands, Dec. 31, 1912, p. 94; *ibid.*, June 30, 1913, p. 131; *ibid.*, Dec. 31, 1913, p. 102.

2. Brill, Nathan, E.: An Acute Infectious Disease of Unknown Origin; a Clinical Study Based on 221 Cases, *Am. Jour. Med. Sc.*, April, 1910, p. 484.

3. Anderson, John F., and Goldberger, Joseph: The Relation of So-Called Brill's Disease to Typhus. An Experimental Demonstration of Their Identity, *Pub. Health Rep.*, Feb. 2, 1912.

Although in general our cases fall into the category of Brill's disease, an occasional case was encountered which approximated in severity the epidemic typhus of Europe. One case in particular was strikingly like a case of European typhus in an immigrant which I had the opportunity of observing clinically, and subsequently at necropsy at the Philadelphia Hospital for Contagious Diseases in 1906.

The disease does not coincide with the descriptions of the Manchurian typhus observed during the Russo-Japanese War, and the temperature curve, with its steep rise during invasion and abrupt decline, differs from the more gradual curve described as occurring in the typhus fever of Mexico.

The following general description fits the average case observed during this endemic. Variations from the usual picture were common and these will be considered as special features of the disease.

SYMPTOMS

The period of incubation in those cases in which it could be arrived at with any degree of certainty varied from ten to fourteen days. Prodromes were absent. The onset was abrupt, a chill ushering in the disease in twenty-one of our twenty-three cases. Headache, usually frontal, followed the initial chill quite constantly and invariably constituted the dominant symptom. In six cases vomiting occurred at the onset, and 25 per cent. of those observed complained of backache and pain in the extremities. Fever immediately followed the onset. The temperature rose rapidly to 103 or 104 F. and, reaching its fastigium on the second or third day, remained elevated, with morning remissions and evening exacerbations, for about a week. Defervescence, occurring in the usual case about the tenth day, was by crisis or rapid lysis through forty-eight hours. The pulse was full and bounding, relatively slow as compared to the fever and was not dicrotic.

The patient was seen within forty-eight hours after the onset as a rule. He was apathetic, and looked dull and stupid, but was not mentally confused. The face and neck were flushed or turgid, the temporal veins engorged and prominent and the conjunctivae injected. The bowels were either constipated or regular, there being no tendency to diarrhea. The lips were usually parched, sometimes fissured, and sordes on the lips and teeth was constantly noted in the severer cases. The tongue resembled that of typhoid fever, being coated along the dorsum and clean at the tip and edges. Early in the disease the tongue was swollen, moist and flabby, becoming dry and covered with a heavy brown coating later. The breath had a heavy musty odor not unlike that of typhoid fever. Nervous manifestations in the form of tremor of the hands, tongue and lips were present from the beginning.

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The following general description fits the average case observed in this epidemic. Variations from the usual picture will be considered as special features of the disease.

SYMPTOMS

The period of incubation in those cases in which it could be arrived at with any degree of certainty varied from ten to fourteen days. In some cases it was absent. The onset was abrupt, a chill ushering in the disease. In twenty-one of our twenty-three cases. Headache, followed the initial chill quite constantly and invariably as the most prominent symptom. In six cases vomiting occurred at the onset. In 5 per cent. of those observed complained of backache and pain in the extremities. Fever immediately followed the onset. The temperature rose rapidly to 103 or 104 F. and, reaching its fastigium on the second or third day, remained elevated, with morning and evening exacerbations, for about a week. Defervescence in the usual case about the tenth day, was by crisis through forty-eight hours. The pulse was full and rapid, but very slow as compared to the fever and was not dicrotic. The face was seen within forty-eight hours after the onset as a pale, anæsthetic, and looked dull and stupid, but was not cyanotic. The face and neck were flushed or turgid, the lips were gorged and prominent and the conjunctivæ injected. The bowels were either constipated or regular, there being no tendency to diarrhoea. The lips were usually parched, sometimes fissured, and the teeth and gums were constantly noted in the severer cases. The tongue was coated that of typhoid fever, being coated along the sides at the tip and edges. Early in the disease the tongue was moist and flabby, becoming dry and covered with a white coating later. The breath had a heavy musty odor not characteristic of typhoid fever. Nervous manifestations in the form of tremulousness, tongue and lips were present from the beginning.

Tremulous speech was less constant but not infrequent. Prostration and profound anorexia developed early.

About the third day the spleen could be palpated. On the fourth day subcuticular mottling, most marked in the dependent parts, was noted. The eruption was observed on about the fifth day, beginning on the abdomen and chest and rapidly spreading to the extremities. The so-called tache cérébrale—the appearance of a red line on the skin when stroked with the finger—was demonstrated constantly. It appeared early and could be elicited for several days after the eruption had disappeared. The headache and other subjective signs usually ameliorated on about the sixth day, and the patient became comparatively comfortable.

The crisis could be looked for on about the tenth day. Preceding the crisis the patient became restless and nervous and the brow was usually moist. Profuse sweating and diuresis were almost invariably concomitants of the crisis, while diarrhea and vomiting occurred occasionally. Following the crisis all symptoms ameliorated, the spleen receded and the eruption faded rapidly. More or less prostration was usual for twenty-four hours after the crisis, following which the tongue cleaned, the appetite returned and convalescence was established with a rapidity that was striking and all out of proportion to the clinical picture preceding it.

SPECIAL FEATURES

The onset was characterized by chill in twenty-one cases, headache in nineteen and by vomiting in six. Lumbar pain and pains in the extremities occurred in eight cases and vertigo was recorded once. In two of the cases the onset was gradual and fever was the first symptom noted. There was intense pain in the chest in one case at the onset, probably due to pulmonary congestion.

The *facies* at the onset was that of intense congestion—face flushed, temporal veins prominent and conjunctivæ injected. The expression in some cases was anxious and in others dull and stupid. The color remained good until the crisis, after which pallor was evident for a variable time and the patient exhibited a "washed out" appearance.

The temperature rose rapidly during the stage of invasion, reaching the fastigium on the second to the sixth day. The average fastigium in twenty-one cases was 103.5 F., the lowest 102 F. and the highest 104.6 F. The fastigium was reached on the third or fourth day in 50 per cent. of the cases. In about two-thirds of the cases an initial drop or remission of from 3 to 5 degrees occurred on the second, third or fourth day. This single early remission occurred with sufficient fre-

quency to constitute a special feature of the temperature curve; and that it occurs, apparently, in typical cases of typhus fever, witness the temperature charts from Murchison,⁴ Wilson⁵ and Doty.⁶

After reaching the fastigium the usual curve was that of continued fever, with morning remissions of a degree or two, until defervescence. The fever was distinctly remittent in five of our twenty-three cases, remissions of over 2 F. occurring daily in these cases. An occasional case was encountered in which the fever was irregular and conformed to neither the continued nor remittent type. Defervescence was by crisis in fourteen cases, by rapid lysis in six, and in the remaining three cases the type was too doubtful to classify. A pseudocrisis followed by recurrence of fever occurred seven times. Pseudocrises were noted from the fifth to the twelfth days. Crises occurred from the fourth or fifth day, in mild or abortive cases, to the twelfth or fourteenth day in the severer cases. Lysis covered a period varying from forty-eight to ninety-six hours. The febrile period in this series of cases ranged from six to sixteen days, terminating from the tenth to the fourteenth day in the majority. The temperature was considered normal when the evening temperature reached 98.4 F. After defervescence the temperature usually oscillated for three or four days, remaining within a degree of normal, and then became subnormal for a period varying from two or three days to a week. Slight chills and chilly sensations, during the course of the disease, occurred in two cases.

The *skin* of the face, neck, upper part of the chest and of the back and shoulders was suffused during the early days of the disease. Sweating was unusual before the crisis, being noted but twice. Sudamina did not occur. Herpes labialis was observed in one case. The so-called tache cérébrale was a constant phenomenon. It could be elicited before the eruption appeared and after its disappearance. In eleven of the twenty-three cases the skin became mottled on the fourth or fifth day and the characteristic eruption followed.

The *eruption* occurred in sixteen cases, was absent in two cases and in the remaining five cases, which occurred during the first part of the endemic, the rash was either absent or overlooked. It appeared on the fifth day in two-thirds of the cases, but in isolated cases it was observed as early as the fourth day and as late as the eighth day. It appeared first on the abdomen and chest and, developing rapidly

4. Murchison, in Osler: Principles and Practice of Medicine, Ed. 8, New York, D. Appleton & Co., 1912, p. 354.

5. Wilson: Medical Diagnosis, Philadelphia, J. B. Lippincott Company, 1909, p. 642.

6. Musser: Medical Diagnosis, Ed. 5, Philadelphia, Lea Brothers & Co., 1904, p. 703.

the temperature curve; and of typhus fever, witness Wilson⁷ and Doty.⁸ The curve was that of continued fever for two, until defervescence in five of our twenty-three cases. An irregular and intermittent type. Defervescence in six, and in the remainder classify. A pseudocrisis seven times. Pseudocrises vs. Crises occurred from the cases, to the twelfth or covered a period varying febrile period in this series terminating from the tenth the temperature was con- cre reached 98.4 F. After lated for three or four and then became subnormal to week. Slight chills the ease, occurred in

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and not in crops, had extended to the back, shoulders, arms, hands, legs and feet and in two cases to the face within twenty-four hours. The lesions were discrete, slightly raised, rose-red to dark red, irregular in outline and measured from 2 to 8 mm. in diameter. Some of the spots were hyperemic and disappeared on pressure; others darker red, were modified but not entirely blanched by pressure, while an occasional spot here and there was distinctly petechial, fading gradually after the eruption had disappeared and leaving dirty yellowish stains in the skin. In individual cases the lesions numbered from a few dozen to many hundreds. In the average case the spots were much more profuse than the rose-spots of typhoid and less numerous than the lesions in the average case of measles. The eruption faded rapidly with the crisis and had disappeared by the tenth day. Desquamation did not occur.

The *blood* showed certain constant changes. The leukocyte count, in sixteen cases, varied from 4,000 to 18,000, the average count being 7,865. Differential leukocyte counts showed a rather consistent increase in the percentage of large mononuclear cells, with a corresponding decrease in the number of polymorphonuclears. Eosinophils were not present in appreciable numbers during the febrile period. These observations are in accord with those of Wilson⁷ at Belfast, who states that a relative increase in the large mononuclears, especially toward convalescence, was very characteristic and that during the febrile period eosinophils were absent or scanty.

The average differential count in sixteen cases showed polymorphonuclears 55 per cent., lymphocytes 25 per cent., large mononuclears 16 per cent., eosinophils 0.8 per cent. and basophils 0.2 per cent. Unfortunately, routine estimations of hemoglobin and red cell counts were not made. Clinically, however, there appeared to be anemia of varying degree following defervescence of the fever. In considering the blood changes, the fact should be mentioned that feces examination showed that the majority of the patients harbored intestinal parasites.

Blood cultures in fifteen cases gave negative results. Blood was taken from a vein, and flasks of plain broth or dextrose broth were inoculated at the bedside. Both aerobic and anaerobic cultures remained sterile after from three to ten days incubation at 37 C. In justice to the contention of Plotz,⁸ who recently reports having isolated an anaerobic organism from cases of typhus fever in New York, I confess that the technic employed in making anaerobic cul-

7. Wilson, W. J.: The Etiology of Typhus Fever, Jour. Hyg., August, 1910, quoted by Balfour and Archibald; Second Review, Wellcome Research Laboratories, Khartoum, 1911, p. 387.

8. Plotz, Harry: The Etiology of Typhus Fever and of Brill's Disease, Preliminary Communication, Jour. Am. Med. Assn., 1914, lxii, 1556.

tures here was, of necessity, crude. Tubes of dextrose-broth were heated to drive off as much oxygen as possible, cooled rapidly, inoculated, and the surface of the medium was covered with a layer of sterile oil to exclude oxygen. Obviously, the degree of anaerobiosis obtained by this method was only relative, but more approved methods could not be resorted to with the facilities at hand.

The *pulse* exhibited no characteristic features. Early in the disease it was of good volume and tension, relatively slow as compared to the temperature, and dicrotism was absent. A pulse rate over 100, with the temperature ranging between 102 and 104 F., was the exception rather than the rule. The critical fall in temperature was occasionally

TABULATED RESULTS OF LEUKOCYTE COUNTS

Case No.	Day of Disease	Leuko-cytes	Polymor-phonuclear Per Cent.	Lympho-cytes Per Cent.	Large Mononu-clears Per Cent.	Eosino-phils Per Cent.	Baso-phils Per Cent.
1	4th	11,500					
1	7th	18,000	72	12	15	1	
8	7th	5,000	61	20	18	0	
9	3d	6,600	68	23	15	1	1
10	3d	8,400	77	12	11		
11	2d	8,000	50	23	25		
12	3d	5,000	25	25	50		
13	2d	10,000	45	39	15		
14	2d	5,000	57	30	12	1	
15	5th	4,000	65	25	9		
16	4th	6,000	65	19	15		1
17	6th	8,600	67	23	11	1	
18	5th	6,800	58	32	16		
19	3d	7,500	55	35	10		
20	9th	6,000	57	29	11	3	
21	5th	8,500	63	29	7	1	
22	3d	8,200	51	24	19	6	

accompanied by a rise in the pulse rate to 120 or 130; but considered throughout the disease the pulse was a slow one like that of typhoid fever.

The *heart* showed no variations from the normal except in one case. A soft blowing systolic murmur was audible in this case following the crisis. The point of greatest intensity shifted and the quality of the murmur changed from day to day, and these peculiarities, in conjunction with the temperature curve of sepsis, led to a clinical diagnosis of acute endocarditis, which was confirmed subsequently at necropsy.

Digestive System.—Anorexia developed early and persisted throughout the febrile period. It was profound in 30 per cent. of the cases. The tongue was flabby, moist and swollen early in the disease, coated along the dorsum and clean at the tip and edges. Later

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the tongue became dry and the coating darker and thicker. In the severer cases the lips were parched and fissured and sordes collected on the teeth. Nausea and vomiting occurred at the onset in six cases and during the course of the disease in four cases. In one case it was so persistent that the patient could retain nothing but champagne. Intestinal symptoms were conspicuous by their absence. Meteorism, abdominal pain, tenderness or diarrhea were not encountered once in twenty-three cases. The spleen could be palpated below the costal margin in twelve of the twenty-three cases. The enlargement occurred early, being elicited on the second or third day in six cases, on the fourth day in three, while in the remaining three cases it was demonstrable on the fifth, sixth and seventh days, respectively. The liver was palpable in but one case. Scleral jaundice was observed once.

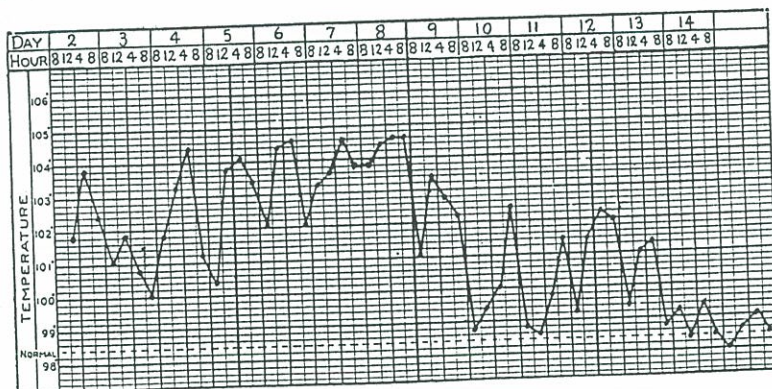


Chart 1.—Temperature chart in a severe case of typhus.

Respiratory System.—Epistaxis, so constant a feature in typhoid fever, occurred but twice in our series; once on the second day while the patient's face was almost purple from congestion, and in the second case on the ninth day, preceding the crisis. Irritative cough without physical signs to account for it was observed twice. Hypostatic congestion and edema of the lungs occurred as terminal features in one case. Pleurisy with effusion complicated one case.

Nervous System.—Signs referable to the nervous system were common, and it appeared to stand the brunt of the infection. Constant harrassing headache constituted the dominant symptom to the patient's mind. It developed at the onset and usually persisted until the sixth day. It was frontal as a rule, but in some cases the head ached "all over" and in one case the pain was occipital. Tremor of the tongue was observed in nineteen cases, of the lips in fifteen cases, of the hands in fourteen, and six of the patients had tremulous speech. The trem-

ors were course and of the intention variety, becoming apparent on voluntary efforts such as protruding the tongue, talking, or buttoning the pajama shirt. In two cases tremor of the tongue was incoordinate in character, and the patients instinctively held the organ protruded with the aid of the teeth. Delirium occurred in two cases. It was low and muttering without noisy manifestations in both instances and in both cases it preceded the crisis. Coma vigil, carphologia, subsultus tendinum and relaxation of the sphincters occurred in one case. Visual hallucinations were recorded once. Insomnia, ascribable to the constant harassing headache, occurred in 26 per cent. of our cases. Tinnitus aurium and partial deafness in both ears, transitory in character, followed the crisis in one case.

Urinary System.—Retention of urine occurred rather persistently in one case, necessitating frequent catheterization. Polyuria was an almost-invariable concomitant of the crisis. The urine was high colored and showed the usual febrile changes—concentration, high specific gravity, marked acidity and increase of solids. Albumin, sugar or casts were not demonstrated. The kidneys showed moderate parenchymatous degeneration at necropsy in one case.

Relapse.—A relapse, intercurrent in character, occurred in one case. During the initial febrile movement the temperature became subnormal on the morning of the sixth day, and then oscillated between 97 or 98 and 100 F. until the fifteenth day, the evening temperature never reaching normal. From the ninth to the fifteenth day the patient was up and about and desired to return to duty. On the sixteenth day he had a distinct chill, and the temperature suddenly rose from 97.2 to 102 F. Blood was negative for malaria, and careful physical examination failed to reveal any cause for the chill and fever. The fever of the relapse continued for twelve days. Constipation, backache, profound anorexia and nervousness accompanied the relapse. No eruption was observed.

MORTALITY

One death, due to acute ulcerative endocarditis following the crisis, occurred in the series of twenty-three cases, establishing a death rate of 4.34 per cent.

DIAGNOSIS

Sporadic cases of the disease observed here would have undoubtedly been diagnosed as cases of fever of undetermined type, as the teaching has been that typhus fever is a disease of cold or temperate climates, and one would think of the possibility of its existence in the Philippines only after having thoroughly eliminated every other possibility. Having established the identity of the primary cases, the diagnosis of subsequent cases was not difficult.

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Clinically, the striking features of the disease were intense head-ache, conjunctival injection, tremor of tongue, hands and lips, and the history of an initial chill followed by an abrupt rise of temperature. An eruption appearing usually on the fifth day, in conjunction with the foregoing features, clinched the diagnosis. The so-called tache cérébrale was a constant feature and, although it may be elicited occasionally in other diseases, its constancy was an aid to diagnosis in our cases. Negative findings of importance were the absence of plasmodia in the blood and the failure to cultivate any organism from the blood by ordinary methods. A history of living in, or having visited, an endemic center was also of value.

Isolated cases of this disease might be confounded with measles, relapsing fever, cerebrospinal meningitis, uremia, pneumonia, or in the

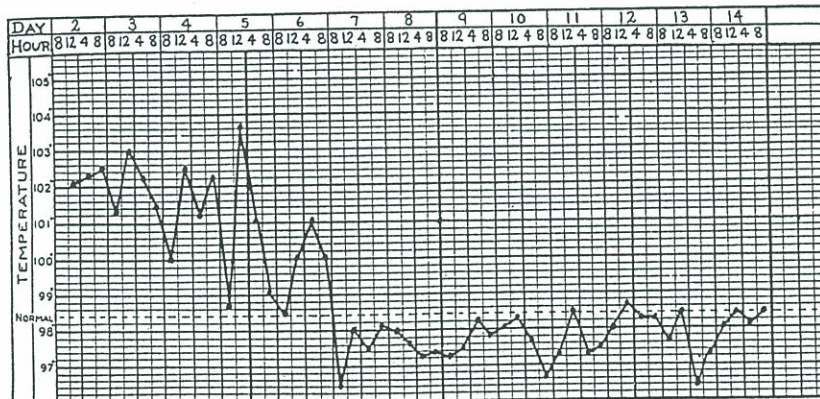


Chart 2.—Temperature chart in a mild case of typhus.

pre-ruptive stage, with smallpox. In reviewing the endemic, however, these diseases may be dismissed at a glance. The disease bore certain resemblances to other diseases which require more careful differentiation, and these will be considered seriatim.

Typhoid fever is characterized by a gradual onset, the course of the fever is longer, defervescence is by lysis and convalescence is not rapid. Abdominal symptoms, absent in our cases, constitute a prominent feature of typhoid. The eruption of typhoid appears on the seventh or eighth day and consists of rose-colored spots. In our cases the eruption could be looked for on the fifth day, and the spots were darker in color and more profuse than those of typhoid. The typhoid bacillus may be isolated from blood cultures in 90 per cent. of typhoid cases during the first week of the disease, while, in our experience, blood cultures were uniformly negative. An additional factor is that

our patients, with the exception of five civilians, had been immunized against typhoid by protective inoculation, and, although an occasional case of typhoid may be expected among those who have been immunized, the possibility of numerous cases occurring is extremely remote.

Dengue, as remarked by Manson, "bursts upon a place" and the majority of those in the community are stricken with certainty and rapidity following the introduction of the first case. The disease is characterized by a two-phased fever, marked arthritic and muscular pains, constant leukopenia and a tendency to slow convalescence during which rheumatic stiffness and twinges in the muscles and joints are common. In contrast to this picture, our cases showed no tendency toward pandemicity, the temperature curve was that of continued fever, pains in the muscles and joints were not harassing, the leukocyte counts frequently showed slight or moderate leukocytosis, and convalescence was rapid and uninterrupted.

Influenza, another pandemic disease, may be dismissed because of the endemic character of our cases and the absence of catarrhal symptoms.

Malaria may be eliminated in view of the uniform absence of plasmodia in the blood of our cases, the character of the temperature curve, and the negative results of therapeutic tests with quinin.

EXPERIMENTAL TYPHUS IN ANIMALS

Three monkeys and ten guinea-pigs were inoculated with blood from various cases of the series—mild and severe—during the febrile period.

The blood was drawn directly from the median basilic, or median cephalic vein and, without being defibrinated, diluted with saline solution or otherwise treated, was injected intraperitoneally at the bedside. The amount of blood injected was uniformly 3 c.c., and the intraperitoneal route was the one invariably chosen.

Brief protocols of the experiments follow:

MONKEY 1 (Mike).—Male; nativity, Samar, P. I.; species undetermined but one that is common in the Philippines; weight, 5½ pounds. Inoculated intraperitoneally with 3 c.c., of blood from Case 14. The patient was in the third day of the disease at the time the blood was taken and was extremely ill. The eruption was just appearing. The monkey was in robust health. His normal temperature, taken morning and evening for three days prior to inoculation, ranged between 101 and 102.2 F. Following inoculation there was a gradual daily fall in temperature for six days; but the animal was responsive, appetite was normal and there was no evidence of illness until the tenth day. In other words, the incubatory period of nine days was silent. On the tenth day following inoculation, the animal sat huddled up, his fur was ruffled, and, in contrast to his previous behavior, he lay perfectly quiet while the temperature was taken. As the attendant expressed it, he was "droopy." The tem-

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perature began to rise, reaching its fastigium — 103.4 F. — seven days after the onset of illness. On the following day, the eighth day of illness, the temperature dropped 4 degrees by crisis. The animal was weak and unresponsive for several days following the crisis, and emaciation, which became evident at that time, persisted for several weeks. No eruption was noted.

MONKEY 2 (Pat).—Male; nativity, Samar, P. I.; same species as Monkey 1; weight 9½ pounds. Inoculated intraperitoneally with 3 c.c. of blood from Patient 15, at the time in the fifth day of his illness, with eruption out all over the body and symptoms marked. The course of the disease in this animal was essentially the same as in Monkey 1. The period of incubation was approximately eight days, during which the animal remained well. During the febrile period of seven days signs of illness—huddled posture, ruffled fur, anorexia and lassitude—were evident. The temperature reached its fastigium—103.6 F.—within thirty-six hours of the onset, remained elevated four days and declined by rapid lysis, the entire febrile period occupying about seven days. The normal temperature of this animal lay between 101 and 102 F. during the three days preceding inoculation. Emaciation became evident after the fever declined. No eruption was detected.

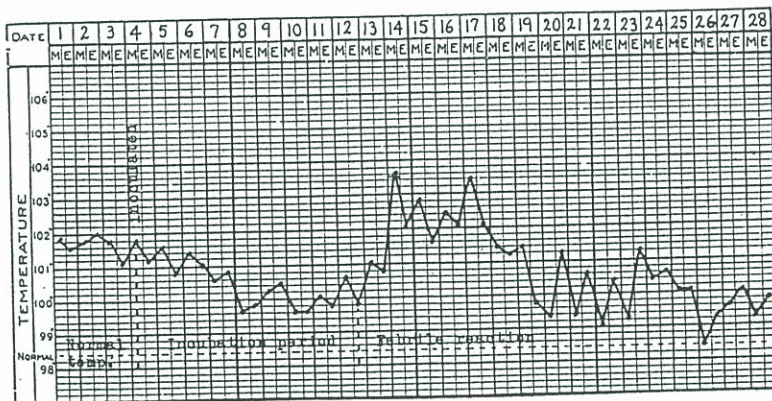


Chart 3.—Febrile reaction in Monkey 2, following intraperitoneal inoculation with blood from a typhus case.

MONKEY 3 (Moro).—Male; nativity, Mindanao, P. I.; species common in Mindanao, but different from that of Monkeys 1 and 2; weight 6 pounds. Inoculated intraperitoneally with 3 c.c. of blood from Case 17 on the seventh day of illness. Patient was not severely ill. In this animal no palpable evidences of illness were detected. During the second week following inoculation there was questionable fever, but the reaction was too doubtful to classify as positive.

GUINEA-PIG 1.—Inoculated intraperitoneally with 3 c.c. of blood from Case 8. Blood taken on the seventh day while the disease was at its height. Reaction doubtful.

GUINEA-PIG 2.—Inoculated in same manner as previous animals with blood from Case 9, the one case of the series which terminated in death. Reaction questionable.

GUINEA-PIG 3.—Inoculated in the usual manner with blood taken from Case 10, one of the mildest clinically of the series. Blood taken on the sixth day of the disease. In this animal there was a well-marked incubatory period of ten days during which the animal showed nothing abnormal. On the eleventh

day the temperature began to rise, reaching 103.6 F. on the seventeenth day. During the night the temperature dropped sharply to 100 F., and the animal lay huddled in a corner, obviously ill. Respirations were rapid and shallow and the animal refused to eat. The temperature again rose sharply to 103.8 F. and then declined, the animal dying the following afternoon, eighteen days after inoculation and about eight days after the onset of illness. Necropsy showed congestion and edema of the lungs. No other gross changes were demonstrated.

GUINEA-PIG 4.—Inoculated in the routine manner from Case 11 during the third day of the disease. Temperature rose sharply to 104 F. in twenty-four hours. It declined gradually to 101 F. and, running a continuous course between 101 and 102 F. for two weeks, suddenly dropped to 99 F., the point at which it had registered when the animal was inoculated. In the absence of a definite incubation period in this case, the reaction was classified as doubtful.

GUINEA-PIG 5.—This animal received intraperitoneally 3 c.c. of blood from Case 12, taken on the fourth day of the disease. The temperature curve was readily divided into three parts—incubation, febrile period and postfebrile period—at a glance. The period of incubation was ten days. The fever reached its fastigium on the second day following the onset, ran a continuous course for seven days, and defervescence occurred by rapid lysis in thirty-six hours. The febrile period occupied approximately ten days.

GUINEA-PIG 6.—Inoculated in the usual manner with blood from Case 13. Blood taken on the fourth day. Except for an abrupt rise in temperature to 103 F. on the sixth day following inoculation, which may have heralded an abortive attack, nothing significant was noted, and the result was classified as questionable.

GUINEA-PIG 7.—Inoculated from Case 14, together with Monkey 1, during the third day of the disease. Result negative.

GUINEA-PIG 8.—Received intraperitoneally 3 c.c. of blood from Case 15 during the fifth day of the disease. The temperature of this animal had been taken morning and evening for five days preceding inoculation, and the incubation period and febrile movement that followed were clearly defined. The period of incubation occupied nine days, and the fever, abrupt in onset and ending by crisis, lasted five days.

GUINEA-PIG 9.—This animal was inoculated intraperitoneally with 3 c.c. of blood from Case 16. Blood taken on the fifth (?) day of the disease. Temperature ranged between 99 and 101.4 F., and this being within the limits of normal in the guinea-pig, it was believed that the result was negative. On the twenty-sixth day after inoculation, however, the animal died. Necropsy showed the entire thoracic cavity filled with fluid blood and recent clots. The pericardium was intact and contained no blood. The right lung was atelectatic and the lymph nodes at the root of the lung were enormously enlarged, pale, and breaking down. Source of intrathoracic hemorrhage, although searched for diligently, could not be found. Hemorrhage probably occurred from erosion of a pulmonary vessel embedded in the mass of glands at the root of the lung. The liver and kidneys showed slight parenchymatous degeneration. Smears from the lymph nodes stained with Wright's stain, and by approved methods for the demonstration of tubercle bacilli, were negative for bacteria. Cultures remained sterile for ten days.

GUINEA-PIG 10.—Received intraperitoneally 3 c.c. of blood taken from Case 17 on the seventh day of the disease. The animal died suddenly ten days after inoculation. On opening the chest at necropsy the pericardium was distended with blood, on removal of which rupture of the right ventricular wall was revealed. The myocardium showed moderate parenchymatous change. There was intense pulmonary congestion.

Summarizing the results of the experimental inoculations recorded above, it will be noted that a definite febrile reaction occurred in 53.8 per cent. of the inoculated animals, while in the remaining 46.2 per cent. the reaction was negative or too questionable to be classified.

The incubation period varied from eight to ten days, during which the animal remained well. This was followed by an abrupt or gradual rise of temperature, the fastigium being reached on the second to the seventh day. The febrile period occupied from five to ten days, and the temperature defervesced by crisis or rapid lysis through forty-eight hours. In addition to fever, two monkeys and one guinea-pig exhibited loss of appetite, ruffling of the hair, huddled posture and "droopiness." An eruption was not observed. Emaciation was evident in two monkeys for a considerable time after recovery. Death terminated the infection in three instances.

In comparing these results with those of others, notably Nicolle and Conseil,⁹ Anderson and Goldberger,¹⁰ and Ricketts and Wilder,¹¹ it is believed that our attempts to infect monkeys and guinea-pigs with the virus of endemic typhus fever were successful.

Anderson and Goldberger¹⁰ outline the typhus reaction observed in monkeys as follows:

Following an inoculation with virulent material the monkey continues for a period varying from five to twenty-four days as if nothing had happened. . . . In about 90 per cent. of the cases the incubation period varies between six and ten days.

At the end of this period the temperature of the susceptible animal rises fairly rapidly as a rule, sometimes gradually or at times very abruptly. The fever reaches its fastigium in thirty-six to forty-eight or seventy-two hours; it then continues for a variable period of one or two to five or more days, then defervesces. The defervescence, like the invasion, is variable; although usually gradual, it is frequently rapid or even critical. In brief, the course of the fever in the monkey is essentially like that of the fever in man.

The fever may be accompanied by loss of appetite, thirst, a ruffling of the hair, and a drooping posture; very commonly, however, even with a well-defined febrile reaction, the animal except for some slight listlessness shows hardly any outward manifestations. In other words, the fever is the only definite index of a reaction. . . . In about 76 per cent. of the cases the fever varies in duration between six and ten days.

At the termination of the fever there is almost always manifest some degree of emaciation.

They state, further, that in their experience a very large proportion—22.5 per cent.—of monkeys possess at least a transitory immunity to

9. Nicolle and Conseil: *Ann. de l'Inst. Pasteur*, April and May, 1912; *abstr.*, *Progr. Med.*, March, 1913, p. 225.

10. Anderson and Goldberger: *Natural and Induced Immunity to Typhus Fever*, *Tr. Fifteenth Internat. Cong. Hyg. and Demography*, ii, Part 1, p. 17.

11. Ricketts and Wilder: *The Transmission of the Typhus Fever of Mexico (Tabardillo) by Means of the Louse (Pediculus Vestimenti)*; *Jour. Am. Med. Assn.*, 1910, lv, 1304.

the injection of virulent typhus blood from infected monkeys, and that inoculation of virulent blood from man, whether New York or Mexico City cases, was successful in only a few cases. This explains the apparently negative result following inoculation in our Monkey 3 (Moro).

In 1912, Nicolle and Conseil⁹ demonstrated that the guinea-pig is susceptible to infection with typhus when inoculated intraperitoneally with from 2 to 4 c.c. of blood from man or monkeys. The incubatory period varied from seven to sixteen days. This was followed by fever lasting from four to eleven days, with an average of about a week. Toward the end of the febrile period there was a small loss in weight. They conclude that unless the temperature be taken, the infection may pass unobserved; in other words, the temperature curve is the only index of infection.

Results similar to these have since been reported by Anderson¹² and by workers¹³ in the Research Laboratories of the New York Department of Health.

EPIDEMIOLOGY

Climate.—Camp Keithley is on the north shore of Lake Lanao, Mindanao, P. I. It is 8 degrees north of the equator. Reference to the Medical History of the Post shows that the annual rainfall during the year July 1, 1908, to June 30, 1909, was 98.46 inches. The highest monthly rainfall was 22.14 inches and the lowest 3.22 inches. There is practically no dry season. According to the geographic definition, the post is in the heart of the tropical zone; but owing to the altitude and the proximity of a large body of water fed by cold mountain streams, the climate is temperate rather than tropical. Palms, the presence of which constitutes "the truest expression of the tropical climate," do not flourish. The heat is never sufficient to cause one the slightest discomfort while, on the other hand, blankets at night are not only desirable but necessary for comfort.

Typhus fever is preeminently a disease of cold and temperate climates. As Castellani and Chalmers¹⁴ point out, the disease appears in the tropics at high altitudes, principally, and it quickly dies out with the onset of hot weather. We are told that the typhus of Mexico (tabardillo) occurs constantly on the great Mexican plateau, while in the coast towns the disease is rarely encountered.

12. Anderson, John F.: The Problem of Typhus in the United States, Jour. Am. Med. Assn., 1913, lx, 1846.

13. Nicoll, Krumweide, and others: Collected Studies, Bureau of Laboratories, N. Y. Dept. of Health, 1912-1913, vii, 132.

14. Castellani and Chalmers: Manual of Tropical Medicine, Ed. 2, New York, William Wood & Co., 1913, p. 1094.

In view of the recently acquired knowledge that the disease is transmitted by the louse, it is difficult to connect its occurrence in the tropics with the peculiar climatic conditions incident to altitude. The louse is omnipresent—in the lowlands as well as in the hills. The explanation may lie in the fact that the coast natives, unaccustomed to the chilly night air of the highlands, hermetically seal their quarters and huddle together for greater warmth, thus not only creating filth, overcrowding and bad ventilation—predisposing factors which lower their resistance to infection—but, by more intimate contact, augmenting the passage of the transmitting agent from one to the other.

Season.—The twenty-three cases studied during the present endemic were evenly distributed, practically, over the months of September, October and November, the latter part, roughly, of the so-called rainy season.

Sex.—Males constituted 82.62 per cent. of the patients, while 17.38 per cent. were females.

Age.—Practically all the cases occurred in the third decade of life. Not a single case was seen in a child, and this is remarkable because of the large number of children exposed in the endemic foci from which the majority of the cases came. It is in harmony, however, with the experiences of Nicolle and Conseil¹⁵ at Tunis. They found that nursing infants are immune to infection, and that older children may have the disease in so mild a form that it may escape detection. This emphasizes the importance of recognizing mild cases of typhus in children which, unrecognized, may act as missing epidemiologic links and cause the continuance of an outbreak.

Endemic Foci.—Two distinct foci from which the disease disseminated were detected in connection with this endemic. The primary focus was a corral that had been converted into living quarters for families of enlisted men of the twenty-fifth and twenty-eighth companies, Philippine Scouts. The building is 170 feet long and 36 feet wide and is divided into twenty-six stalls, 14 feet deep by 10 feet wide, with two small rooms at each end. The building was converted into living quarters by closing in the stalls with sheets of iron roofing and building floors of scrap lumber. No provisions for lighting or ventilation existed, and the quarters were damp, dark and poorly ventilated. Twenty-seven compartments in this building were occupied by 103 persons—thirty men, thirty-one women and forty-two children—living in filth and squalor. Superficial examination showed the heads of many of these people infected with pediculi. That many of the

15. Nicolle and Conseil: *Gaz. d. hôp.*, April 9, 1911, p. 609; abstr. *Progr. Med.*, March 1913, p. 228.

Quick
Index
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women and children were ill-nourished needs no emphasis when it is remembered that they were dependent for their subsistence on native soldiers whose monthly wage is \$7.50.

Filth, overcrowding, poor ventilation, ill nourishment and vermin combined to form exact conditions for the spread of typhus fever.

Two of the occupants gave a clear-cut history of recent attacks of fever, which undoubtedly was typhus in view of the information subsequently received from a typhus patient infected by these people. Three other women looked ill, and one of these may have been convalescing from typhus, as her husband was subsequently under observation with well-marked symptoms.

The second endemic focus was the so-called barrio of Bungalow just beyond the limits of the military reservation and under the jurisdiction of the civil authorities of Dansalan. This barrio is composed of native shacks, tenanted by scout soldiers and their families.

The first three cases encountered were in married men who, when not on duty, slept at the corral. The fourth case was in a recruit who had not been away from the reservation and as he gave a history of having visited the corral, and other possibilities were not elicited, the assumption was that infection had been contracted on one of these visits. The fifth, sixth and seventh cases were, like the first three, in married men who lived at the corral. The information elicited from the eighth patient, an officer's servant, stamped the corral as the undoubted source of infection. She stated that she frequently visited the wife of a corporal of the Twenty-Eighth Company, who lived at the corral, and that she invariably visited there on Saturdays and Sundays. September 21 and 22 she slept at the corral and stated that the corporal's wife was ill with calentura (fever) at that time; that the woman was taken ill, September 8, and that her illness lasted two weeks. The corporal, who nursed his wife, was taken ill September 22, and was ill ten days. The officer's servant became ill October 5, fourteen days after sleeping at the corral.

Patients 10, 11 and 14 lived at the corral and were infected there unquestionably. The source of infection in Cases 13 and 15 was not ascertained with certainty. They had visited the corral eleven and twenty-four days prior to the onset of illness, respectively, and although an incubation period of twenty-four days is unusual, it is possible that both were infected at that time. Patient 16 had a family quarantined at the corral, and it is possible that he—as occurred in two other instances—had broken quarantine and was infected during a clandestine visit.

Patient 18 was admitted to the hospital on the fifth day of the disease. She lived at Bungalow and was the first case from that endemic

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focus. She had formerly lived at the corral but denied having visited there for several months. Patient 19 was a recruit who probably contracted the disease while visiting a brother living in the house in Bungalow from which Case 18 was taken. Patient 23, the brother whom Patient 19 had visited, was admitted subsequently. Patients 20 and 21 were both married men who lived at Bungalow, and it seems reasonable to connect them with the other cases of infection there.

The source of infection in Cases 12, 17 and 22 could not be ascertained.

Origin of the Endemic.—Efforts to trace this endemic to a single original case have been unsuccessful. The clinical records of the last thousand cases admitted to the hospital at Camp Keithley have been reviewed, and from them six cases of fever have been culled which resemble cases of typhus observed during this endemic. The first of these cases was admitted May 28, 1913, another occurred in June, a third in July, and two more in December. The sixth case was admitted in February, 1914. Diagnoses of malaria were made in four of the cases, one was diagnosed intestinal autointoxication, and the sixth was diagnosed as paratyphoid fever. The malarias exhibited courses of fever similar to that of typhus, plasmodia were not demonstrated and quinin in large doses did not influence the temperature curve. The clinical records show no other instances of paratyphoid infection, and, as the diagnosis of paratyphoid fever in the sixth case was made in the absence of confirmatory evidence from the laboratory, it is believed that it should be viewed with considerable mental reservation. The diagnosis "intestinal autointoxication" is very frequently open to suspicion.

If we accept these instances of probable cases of typhus fever, the history of the disease extends back to May, 1913, at least.

My predecessor, Captain Pipes, of the Medical Corps, informed me that he had encountered cases of fever in Moros identical with the first case of typhus observed here, and was very anxious that the identity of the disease, the nature of which had not been determined at that time, be established. Information from various sources is in accord with Captain Pipes' statement. Mr. Moore, at the time acting provincial fiscal, recently related the occurrence of a fever similar to ours among the Cotabato Moros, and Captain Fletcher, P. S., states that the Moros of Romain Valley, in this province (Lanao), who live in old overcrowded cottas, report many cases of a fever that is attended with high mortality.

It is probable that typhus has existed in endemic form in Mindanao for an indefinite period, being looked on by the native, as all fevers are, as a form of malaria.

Whether the disease was originally introduced by religious pilgrims returning from Mecca, where typhus occurs in epidemic form, or whether it may have followed the lines of commercial intercourse from Japan are matters of conjecture.

Transmission.—Experimental transmission of the disease to monkeys by means of the louse, along the lines pursued by Anderson and Goldberger,¹⁶ Ricketts and Wilder,¹¹ and others was not attempted. In the absence of proper facilities for safeguarding such experiments, there would have been constant danger of infected lice escaping, and the attempts would have been foolhardy.

The epidemiologic data point, however, to the louse as the probable transmitting agent, and the evidence is strengthened by the fact that preventive measures aimed at ridding patients and contacts of lice broke up two proved endemic centers, and resulted in the disappearance of the disease.

A striking characteristic of this endemic, in connection with the theory of louse transmission, which is in accord with the experiences of those who have followed epidemics of typhus in Tunis, Belfast and Mexico City, is that the disease has been connected invariably with squalid environment. Our cases did not come from the families of officers, from the quarters of American noncommissioned officers, or from company barracks, although these places are not immune to the visitations of measles, malaria or dengue when such diseases are prevalent. On the other hand, the disease occurred constantly among those having more or less intimate daily contact with native women. The explanation may be that the louse occurs in the former places only under most exceptional circumstances, while it is as indigenous to the native woman as the flea is to the dog.

Entomologists state that the body louse (*Pediculus vestimenti*) is not found in the Philippines.¹⁷ This is interesting, as it is the louse that is commonly believed to be the transmitting agent in typhus fever. However, Anderson and Goldberger¹⁶ have recently demonstrated that the head louse (*Pediculus capitis*) is also capable of transmitting the disease, and the fact that the body louse is not found here does not weaken my conviction that the louse was the means of transmission during the recent endemic.

Flying insects, such as the mosquito or fly, may safely be ruled out as possible transmitting agents, as the disease remained restricted to

16. Anderson and Goldberger: The Transmission of Typhus Fever, with Especial Reference to Transmission by the Head-Louse (*Pediculus Capitis*), Pub. Health Rep., March 1, 1912.

17. Insects and Disease, Health Bull. No. 11, Bureau of Health, P. I., 1913, p. 15. Ann. Rep. Bureau of Health, P. I., June 30, 1912, p. 95.

areas beyond which it would have been carried with certainty by such intermediaries. No evidence was adduced that would inculpate the bedbug or flea. Transmission by food or drink is too remote a possibility to consider. That aerial transmission or fomites played no part in the dissemination of the disease seems evident in view of the fact that neither attendants nor other patients became infected at the hospital, where contact with fomites from typhus patients was more or less unavoidable for a period of three months.

I believe that consideration of the data outlined above justifies the opinion that the disease described is typhus fever. Further investigation along the line of experimental transmission by means of the louse would be interesting, and it is believed that the identity of this fever and Brill's disease might be established by cross-immunity tests with animals inoculated in the United States.

Anomalous fevers are common in the Philippines, and it is unfortunate that research workers confine their activities so largely to Manila, while interesting fields for investigation in the provinces are neglected. Field work similar to that prosecuted by officers of the Public Health Service in the southern United States would illuminate the medical geography of the Philippine Islands.