

OUTBREAK OF TYPHUS OF THE MURINE TYPE

FIRST REPORT FROM THE ISTHMUS OF PANAMA*

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Murine typhus was diagnosed for the first time on the Isthmus of Panama on April 15, 1932. From then until January 15, 1947, the same clinical diagnosis, confirmed by the laboratory in each case, has been recorded on the records of forty-two patients in the Santo Tomas, Gorgas and Panama Hospitals.

In spite of the long interval elapsing from the first diagnosis, the disease heretofore has always been observed in sporadic form on the Isthmus of Panama, with a yearly average of 3 positive cases.

The purpose of the present paper is to report the first outbreak of typhus of the murine type on the Isthmus of Panama. This outbreak occurred from January 15 to February 5, 1947, and consisted of 13 cases in the city of Panama. Due to the care used in making the first diagnosis and the excellent cooperation between the Panama and Canal Zone Sanitary Departments, all of the 13 cases were traced to the same focus of infection.

The epidemiological study of the 13 cases diagnosed by us in the present outbreak shows that the focal point of infection was the feed storeroom of one of the cases in which were found dead rats. The first human case of this outbreak had been diagnosed shortly before discovery of this epizootic.

In fact, all the cases of this outbreak acquired the infection in this one storeroom; including the employer, eight employees and four more patients who reported having visited this commercial establishment to buy fodder on various occasions, within fifteen days before the onset of their illness.

The disease was observed in patients between 16 and 43 years of age. Eleven were male and two were female. Five were of the white race, four were mestizo and four were negroes. Seven were single and six were married. All lived in the city of Panama and worked in or had to visit the infected storeroom.

The study of the incidence according to *age, sex, race, civil status, origin* and *occupation* showed that, as Maxcy (1) has shown for endemic typhus, these factors were *not* of importance.

SYMPTOMATOLOGY

Subjective Symptoms

All of the thirteen cases studied by us exhibited *anorexia, asthenia, insomnia* and *cephalalgia* (with localization in the frontal, frontal-temporal and frontal-occipital or temporal areas) greatly accentuated during the course of the first

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† The author is indebted to Dr. H. C. Clark, Director of the Gorgas Memorial Laboratory, for his suggestions and support in the development of this work.

week, and persistent all during the illness. Some also reported a feeling of excessive sensibility of their hair, which annoyed them greatly.

No one complained of disturbances during *micturition*.

Constipation was reported in 92 per cent of the patients. In 36 per cent, we observed that constipation lessened during the course of the second week.

A mild *stuporous condition* was observed in 72 per cent of our cases but in only 30.7 per cent of this group was *stupor* obvious, and then it was of the type described by Kemp, in Texas.

Occasional *cough*, without expectoration, was reported in 54 per cent.

Chills during the course of the first three days were indicated in 46 per cent.

The symptom of *nausea* was positive in 46 per cent of the cases, in the first four days of the disease.

In 23 per cent of the group *vomiting*, *moderate photophobia*, *mild perspiration* especially during the first four days of illness, and *ocular ache* upon compression and movement occurred. In 15 per cent of the series, we noticed periciliary injection toward the 8th day of illness, which disappeared spontaneously 36 hours later.

Naso-pharyngitis was observed in 15 per cent of the cases.

Pain in the hands on clinching the first in 7 per cent.

None of the patients reported *deafness*.

The subjective symptoms are summarized below.

	<i>per cent</i>
Anorexia.....	100
Asthenia.....	100
Insomnia.....	100
Cephalalgia.....	100
Frontal-occipital.....	35.7
Frontal-temporal.....	21.4
Frontal.....	21.4
Temporal.....	14
Temporal-occipital.....	7.1
No trouble on micturition.....	100
Constipation.....	92
Improvement during the second week.....	36
Stuporous condition.....	72
Pronounced.....	30.7
Occasional cough.....	54
Chills during the first three days.....	46
Nausea.....	46
Vomiting.....	23
Moderate photophobia.....	23
Mild perspiring the first four days.....	23
Ocular ache upon compression and movement.....	23
Periciliary injection and pain which disappeared in 36 hours.....	15
Naso-pharyngeal cold.....	15
Pain in the hands on clinching the fist.....	7
Deafness.....	0

Fever was of the remittent type with an average duration of 15 days (12 days minimum and 17 days maximum).

The study of the febrile curve, of average and maximum daily temperatures (no patient came for consultation before the fourth day of disease), showed three periods in the evolution of the disease:

In the first period, until the fifth day inclusive, the fever was of the remittent type, with ascending average and maximum fever. The fever always descended during the morning and ascended in the afternoon about one half degree more than the day before. The difference between the maximum and minimum daily fever was never more than two degrees Fahrenheit.

In the second period, from the sixth to twelfth days inclusive, the fever was of the remittent type, with a matutinal descent of two degrees Fahrenheit. The study of the maximum temperature curve showed that it decreased slowly from one day to another, from 103.8 to 103 degrees F. The same was observed with the average fever which descended slowly from one day to another, from 102.6 to 100.8 degrees F.

The third period showed that both curves, in general, descended by lysis, in four days, with ample morning remissions.

The study in particular of this period showed that the fever came down in crisis the twelfth day, in 12.5 per cent of the cases. In 37.5 per cent the maximum evening temperature fell by lysis with ample morning remissions. In the other 50 per cent of the cases the maximum evening temperature came down by lysis, but with morning apyrexia.

Physical Examination

The study of the clinical histories of the seven hospitalized patients showed that the *palpebral conjunctiva* was slightly injected in all cases.

The *tongue* during the course of the disease was coated, with the dorsum yellow-tinged. Only in 25 per cent could we observe that the border of the tongue was red.

The *breath* had a strong offensive odor.

We did not find any pathology in the *tonsils, facial sinuses, pupils, thyroid gland and lungs*.

The *cardiac* sounds, in general, were faint; a hemic murmur could be heard during the febrile period. The rhythm was regular; there was bradycardia in relation to the temperature, as it only increased six points per degree F. of fever. The average blood pressure was 100-64 mm. mercury. Only one patient showed abnormal rhythm (with bi-, tri- and quadrigeminism) which became normal after 48 hours of hospitalization (the eighth day of the illness).

Abdominal palpation was done easily as there was no resistance. There was gurgling in the right lower abdomen in 62.5 per cent of the cases. Moderate sensitivity was reported in the direction of the ascending colon in one patient; and in the right upper quadrant, in relation with the hepatomegaly they all presented.

There was *hepatomegaly* of one or two centimeters below the costal border in 62 per cent and up to five centimeters in 37 per cent. The liver was of firm

consistency, moderately sensitive, rounded border and smooth surface. At the disappearance of the fever the liver returned to its normal size.

We had the impression that at the time of greatest hepatomegaly there was also the most marked stuporous condition.

The *spleen* was not palpable in 50 per cent of the cases and in the others it was felt only one centimeter below the left costal margin; none reported pain in the left hypochondrium.

There was no reaction of the *lymphatic system*.

There was no edema of the *skin*. Peripheral vaso-dilatation was observed in patients with light skin during the febrile stage.

We could not observe *rash* in two of the patients because of the color of their skin (they were of the negro race). In three of the six patients of the white or mestizo race the rash was very moderate. In two of this group it was limited to the flanks and dorsal aspect of the thorax; in the other one it was limited to the flanks, dorsal and anterior aspects of the thorax. In the other three patients the rash was generalized; in two of this group it covered all the body with the exception of the face, neck, palms of the hands and soles of the feet; in the third it covered all the body with the exception of the face and neck.

The rash was of the macular type in the first three cases. The color disappeared at pressure. It was not scaly or pruriginous, and the size varied between that of a pin-head and a disc of a centimeter in diameter.

In the cases of generalized rash, with the exception of the patient whose rash invaded the soles and palms, the rash was of the maculo-papular type with a range between the size of a pin-head and a disc of one and a half centimeters diameter. The papules were of irregular elevation and coloration.

Only on the patient whose rash invaded the palms and soles, did we observe that the maculo-papular rash developed to form true petechiae.

We had the impression that the extension of the rash and its dermatological type were in relation to the sharpness of the symptoms. In the case with petechial rash, for example, there was a marked stupor, of the type described in Texas by Kemp "clouding of consciousness without loss of orientation", with a higher febrile curve; this stupor was less in the other two cases, with a generalized rash but no petechiae; and there was no stupor in the others with localized rash.

The rash, which generally presented itself between the fifth and seventh day of the disease became less visible towards the thirteenth day and always disappeared at the fall of the fever with exception of the patient with the petechial rash who presented brown points in the place of the petechiae until the twelfth day of the post-apyretic stage.

Laboratory Examinations

The number of *red blood cells* ranged between 3.8 and 4.5 million per c.mm. In general they were below 4 million in the patients with generalized rash.

The number of *white blood cells* ranged between 1.3 and 9 thousand per c.mm.

The value of *hemoglobin* was between 79 and 86 per cent (13.4 and 14.5 grams).

The number of *polymorphonuclear neutrophils* varied from 64 to 79 per cent with an average of 70 per cent.

The *lymphocytes* varied from 18 to 35 per cent with an average of 27 per cent. The *monocytes* within 1 and 5 per cent with an average of 2.7 per cent.

The *Wassermann* and *Kahn* test performed on different days of evolution of the disease were consistently negative.

The *urine* examination showed faint traces of albumin in 62.5 per cent of the cases, without relation to the day of the evolution of the disease.

No intestinal parasites or eggs were found in the *feces*.

The examination of the blood for *malaria parasites* was consistently negative in all the patients.

There was no *pulmonary* pathology or enlargement of the heart or aorta noted in the X-ray reports.

The *electrocardiographic* study showed no pathological characteristics (Wood-

TABLE 1

NAME	WEIL-FELIX AGGLUTINATION		COMPLEMENT FIXATION		RICKETTSIAL AGGLUTINATION	
	OX-19	OX-2	Epidemic	Murine	Epidemic	Murine
L. G.	1/320	1/40	1/10	1/320		
P. G.	1/320	Negative	1/160	1/320	1/320	1/1280
R. S.	1/640	1/160	1/40	1/320		
H. H.	1/5120	1/320	Negative	1/320		
B. M.	1/2560	1/80	Negative	Negative	1/160	1/1280
L. E.	1/640	Negative	Negative	Negative	1/1280	1/5120
T. H.	1/2560	Negative	Negative	1/20		
M. R.	1/2560	1/160	Negative	1/20		
P. R.	1/640	1/40	Negative	Negative	1/80	1/160
L. N.	1/5120	1/40	Negative	1/10	1/160	1/1280

ward and Bland (2), reported some abnormalities in epidemic typhus). There was no axis deviation in four patients; and to the left in one. The mechanism was always of the normal sinus rhythm. There were no abnormalities in the atrio-ventricular conduction or in the QRS intervals. The P wave, in general, was positive and of normal contour. The QRS segment was in relation to the electric axis, without anomaly. The ST segment was isoelectric in all cases. The T wave was of normal contour and positive.

Weil-Felix reaction: The diagnosis was confirmed in each case, with a positive Weil-Felix reaction.

Of the six patients in which diagnosis was made within ten to twenty days subsequent to recovery, Weil-Felix reactions done at the Canal Zone Board of Health Laboratory¹ gave strongly positive reactions (++++) in all. Sera of four patients were positive to proteous OX-19 in dilution of 1/320, of one patient in dilution of 1/160 and of one patient in dilution of 1/80.

¹ The author wants to thank Dr. L. B. Bates, Director of the Canal Zone Board of Health Laboratory, for his kindly assistance in the laboratory tests.

Seven patients were hospitalized and two or three reactions to Weil-Felix were performed during the course of the disease. In three patients of this group negative tests were observed within the fourth and fifth days of evolution of the disease. On the seventh day the agglutination was consistently positive in all of them and the agglutinin titre rose rapidly as the disease developed. None of these sera agglutinated with OX-K, according to the report of the Canal Zone Board of Health Laboratory.

Complement fixation and rickettsial agglutination: the sera of ten patients were sent to the Army Medical Center, in Washington D. C., from where we received the accompanying report² (Table 1) through the office of Lt. Col. J. C. Ellington, Health Officer, Panama.

These findings, according to Smadel, are consistent with a diagnosis of murine typhus.

COMMENTS

From an epidemiological standpoint, the focal point of the infection was the feed storeroom of one of the patients where dead rats were found (the cause of their deaths was unknown) before the onset of the human cases of murine typhus being reported.

It is logical that under these conditions, all the epidemiologic premises of Maxcy (1) were not observed here. Our outbreak of murine typhus was observed, in fact, only among people who had visited the infected storeroom or who had worked there.

We want to call attention to the fact that 30 per cent of the total number of cases were of the negro race which, in some respects, is in accordance with what was expressed by Baker, McAlpine and Gill (3), in contrast to what was reported by Maxcy (1). This outbreak was observed exclusively among those handling the feed, as was reported by Hone (4). And finally that the disease, according to Dyer (5), was observed in patients without any relation to their economic situation (in poor as well as in rich people) or social stratum (Rumreich (6)).

The diagnosis of the disease was made by the manner of its onset and the intensity of the symptoms; by the febrile curve and its duration; by the primary localization of the skin rash and its occurrence in relation to the onset of the disease; by the characteristics of the rash and the bradycardia, leucopenia, absence of pulmonary and blood vascular complications; and by the benign evolution of the disease (Manson-Bahr, Stitt-Strong, Napier) (7, 8, 9).

In each case the laboratory finding confirmed the clinical diagnosis with a positive Weil-Felix reaction with proteus OX-19 (there was co-agglutination with OX-2. Negative reactions occurred with OX-K). The complement fixation test was positive, also, for murine typhus. And there was positive agglutination with the murine type of *Rickettsia*.

It is interesting from the clinical point of view, that in no case was there an

² The author thanks Dr. Joseph E. Smadel, Scientific Director, Department of Virus and Rickettsial Diseases, Army Medical Center, Washington D. C., for his kindly scientific assistance.

initial chill, although in 46 per cent of these cases there were chilliness sensations in the first three days of the disease. The maximum temperature occurred around the fifth day and the general symptoms varied according to the temperature, at the same time there was a correlation between the extensiveness of the rash and the fever. A more or less generalized rash, of a relatively short duration, was observed starting from the fifth to the seventh day in all the patients. It was always localized primarily over the sides of the chest. In only one patient were there frank petechiae associated with the rash. There was no pulmonary nor cardio-vascular complications. Wassermann and Kahn reactions were uniformly negative in all cases (performed in different days of the disease). The serum agglutination reaction was strongly positive with proteus OX-19, as well as having co-agglutination with OX-2; there was no agglutination with OX-K.

The course of the disease was generally benign. There were no deaths. There were no sequelae after the illness except for a temporary asthenia in all cases, which disappeared at the end of the second week of apyrexia.

Comparison of the clinical symptoms found in our series with those found by others elsewhere may be of some interest. With the exception of the reports by Hone (4), Sinclair and Maxcy (10) and Gardner and Brown (11), which refer, like ours, to the epidemic form of murine typhus, all the others refer to cases of the endemic type.

Boyd (12) and Sharma (13) refer to pulmonary complications in their cases in India (Bengalore), a feature not seen in our series.

Our series differ from the cases reported by Heilig and Naidu (15) in showing negative Wassermann and Kahn reactions, even though these were done at different stages, from the fifth to fourteenth days, of the disease. The same authors (14) report further cases from which ours differ in that the rash was of shorter duration and, with the exception of our single case with petechia, did not leave marks afterward. Our series also gave greater agglutination with proteus OX-19.

In the cases reported by Maxcy (16) from Alabama and Georgia the rash was localized primarily over the abdomen and flexor surfaces of the forearms, the borders of the tongue were red, 29 per cent of the cases showed delirium and 60 per cent showed nervousness. In our cases, on the contrary, the rash was localized primarily over the sides of the thorax, the borders of the tongue were red in only 25 per cent and none of our cases presented either delirium or nervousness.

In the cases reported by Kemp (17) from Texas, diarrhea was as frequent a symptom as constipation during the first week of illness and there was diffuse abdominal pain. Our cases presented only constipation, and abdominal tenderness was localized in the right hypochondrium, correlated with a moderate degree of hepatomegaly.

Rumreich, Dyer and Badger (18), reporting cases from the eastern part of the United States, observed marked conjunctival injection, pharyngitis and bronchitis and, in contrast to our series, the rash was primarily localized over the chest and abdomen.

In contrast to the cases reported by Blatteis (19) from Brooklyn, our series presented neither an initial chill nor signs of meningeal irritation. Splenomegaly, reported in 28 per cent of his cases, was not found by us. Furthermore the average duration of fever in his series was 12 days, ending by crisis in 60 per cent, while in ours the average duration was 15 days, ending by crisis in only 12.5 per cent.

In the report by Sinclair and Maxcy (10) on an outbreak of murine typhus in the Rio Grande valley region, the rash was localized primarily over the abdomen. Gardner and Brown (11), reporting cases from the same Rio Grande outbreak, again note rash primarily over the abdomen, with secondary extensions. They also report diarrhea following constipation in the majority of cases and a rapid pulse, all features not noted in our series.

The clinical aspects of the cases of endemic typhus reported by Musser (20) and Pullen et al. (21) in New Orleans, as well as those of Halverson (22) in California correspond with those we have observed in the present outbreak in Panama city.

According to this review we can finally say that the clinical form observed in this present outbreak of murine typhus in the city of Panama reproduced in every aspect the clinical description of the disease as reported in well known text books; and the minor differences found in some reports are not enough by themselves to change this conclusion.

SUMMARY

Murine typhus is reported for the first time on the Isthmus of Panama.

The epidemiological study of the cases diagnosed in the present outbreak of murine typhus showed that the focal point of the infection was the storeroom of one of the patients where were found dead rats shortly before the first human case had been diagnosed.

The study of the clinical form of the disease as observed in this outbreak of murine typhus showed that it reproduced, in every aspect, the clinical findings reported in well known text-books.

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