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To cite this article: W. E. Deeks (1914) Six Day Fever in Panama, Annals of Tropical Medicine & Parasitology, 8:2, 357-365, DOI: [10.1080/00034983.1914.11687651](https://doi.org/10.1080/00034983.1914.11687651)

To link to this article: <http://dx.doi.org/10.1080/00034983.1914.11687651>

Published online: 24 Mar 2016.

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SIX DAY FEVER IN PANAMA

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(Received for publication 6 January, 1914)

SEVEN CHARTS

In the Journal of the American Medical Association of October 26th, 1912, the writer published 'A Preliminary Report of a Hitherto Unrecognized Six-Day Fever, in Ancon, Canal Zone.'

Since writing that report cases have accumulated, and up to the present time, fifty have been admitted. These have furnished sufficient data to enable us to give a more accurate account of this interesting fever, which is unique in the Western Hemisphere.

In the former report, it was stated that the epidemic first appeared in two mail clerks who exclusively handle the foreign mails. They sickened within an hour of each other, and no other cases appeared for ten days, which would indicate the incubation period of the disease. Since that time the affection has spread through the American colony in the vicinity of Panama, and also among the Panamanians, but has not been recognized among the coloured population.

In all, fifty cases have been treated in the hospital, and probably many more were treated outside. The mortality is nil, although some of the patients afflicted have been very ill.

As there have been no deaths, we are ignorant of the pathological lesions.

The disease appears to spread from certain centres. When one person in a household sickens, usually several in the same household or from the same vicinity soon acquire the disease, but not all. This suggests that either some are naturally immune, or that there is an infecting agent which does not convey the disease to all. Any sporadic case can always be traced to his or her having visited an infected focus, or possibly stayed over night, as was shown in the large bachelor quarters where the infection remained some time.

Several sporadic cases in neighbouring towns occurred, but these

had in all cases, as far as could be determined, visited an infected focus.

Whatever the nature of the infection, it is interesting to note that none of the attendants on the patients in the hospital ever contracted the disease, though no special precautions were taken to guard against such infection. This argues that either the disease can be communicated in the pre-febrile stage only, or else if there be an infecting agent, this was not present in the hospital.

SYMPTOMATOLOGY

There are no prodromata; patients apparently well are suddenly seized, frequently with chills, and the temperature promptly rises to from 100° to 103° F., depending upon the severity of the disease.

Giddiness and vertigo are occasionally complained of, and intense frontal headache about the eyeballs is very persistent, as are also dull aches in the back, loins and legs. Occasionally these are severe enough to necessitate alleviation by medication. There are no joint pains.

Anorexia is constant and continuous throughout the febrile stage, and very frequently vomiting during the first two or three days.

PHYSICAL SIGNS

The tongue is usually coated, but not markedly, there is no sore throat. The eyes and face are usually injected, and sometimes markedly so.

The pulse is normal, or for the degree of fever, slow. Respirations are not altered. The spleen is usually enlarged and generally palpable, its free border projecting two or three fingers breadth below the costal margin.

The liver has not been found to be enlarged, as is so common in malaria.

The skin is frequently mottled or erythematous soon after the onset, but there is no characteristic or constant skin rash early in the disease.

The urine has frequently a faint trace of albumin, and a few hyaline and granular casts like most febrile albuminuriae. Sometimes, however, the nephritis is very severe, as was seen in three of our cases. The nephritis was of the diffuse type, with a great deal

of albumin, hyaline, granular and epithelial casts, but never generalized oedema as in the nephritis of scarlet fever. In all cases the urine became practically normal before the patients were discharged. In severe cases the albumin disappeared within a week after the fever subsided, and only a few hyaline casts remained at the end of the second week.

The blood findings are interesting. In my former report there seemed to be some variance as to the leucocyte counts. This was due to the fact that some were taken early, and others late, in the course of the disease.

The following counts were taken within the first three days of the onset, and show how constant this feature of the disease is, and it has, in consequence, considerable diagnostic importance:—

LEUCOCYTES	POLYNUCLEAR	LARGE MONONUCLEAR	SMALL
5600	91	7	2
7600	80	18	2
5000	89	6	4
4800	91	5	4
3300	72	22	6
—	88	5	7
7800	84	6	10
5400	83	8	9
Leucopenia	78	10	12
7200	80	5	15
3500	80	3	17
—	90	5	7
6000	90	8	2
6360	88	8	4

Unfortunately, a number of other leucocyte counts were taken so late in the course of the disease that they are very variable, and of no value.

The above, however, gives one a good idea of the blood picture, as it shows, generally, a leucopenia with a high polynuclear differentiation.

The febrile stage of the disease varies from five and one-half to six days, and is very constant.

When the date of the onset is known, the defervescence of the fever can always be predicted within a few hours.

The temperature curve is of the characteristic saddle-back variety, as has been described by Rogers and Crombi, and also by Castellani. The intervening period between the onset and the fall of temperature is lower than at the beginning and the end of the febrile stage.

The accompanying charts show these characteristics (see pp. 362-365). The temperature usually falls by slow crisis; generally falling in twenty-four hours between the highest point of the febrile stage to normal. Sometimes this is accomplished in twelve hours.

In one instance only have we seen the fever last over six days. On the sixth day there was a pseudo-crisis, as in pneumonia, and the temperature reached normal and remained so on the seventh. In two instances, after the crisis a slight post-febrile temperature of from one to one and a half degrees persisted for three days longer.

THE RASH

This is almost always present, and is very characteristic. It usually makes its appearance on the dorsal surfaces of the feet, and the radial surfaces of the forearms, either the first or second day after the temperature reaches normal. The appearance of this rash may be delayed to the sixth day after the drop in temperature. It is finely petechial in character, and may be spread so as to involve all of the extremities. Rarely is it seen on the body.

In a recent case the petechial rash covered completely the body surfaces. Over the shoulder blades and buttocks, where there was closer contact with the bed, it was so thick as to give a vivid red colour to those parts.

The rash does not disappear on pressure, but when it begins to fade, gives to the skin involved a general dark bluish or cyanotic tinge. I have never seen any rash that resembled it.

In the cases above referred to, though the rash was so general and so severe, no desquamation followed.

It frequently is accompanied by a general erythema, which may

involve the whole body. This blotchy erythema is intensely itchy, and frequently necessitates narcotics, in order to obtain rest. The rash remains out from one to three days, when it gradually fades. When the petechial form of the rash is very marked, it occasionally is followed by desquamation.

The petechial form of the rash is practically constant, but sometimes so slight that it may be overlooked, unless carefully sought for on the first and second days following the fall of the temperature.

In order to determine the nature of the infection, cultures of the blood, urine and stools were repeatedly taken by Drs. Samuel T. Darling, H. C. Clark, and Lewis B. Bates at different stages of the disease, and all proved negative.

The Widal reactions have all been returned negative.

Efforts were also made to transmit the disease to animals, without result.

The disease undoubtedly is a distinct entity, probably related to the exanthemata. If there be a transmitting agent, it has not been found here. It certainly is not a mosquito, as a great many cases have occurred here in mosquito-proof houses.

The infective agent is probably transmitted over long distances, as we have every reason to think that the first two cases derived their infection from sorting mails from India destined to Hindoo labourers here.

The disease is probably identical with the seven-day fever referred to by Castellani in his 'Manual of Tropical Medicine.' It has been described by Rogers and Crombi as occurring in the sea-port towns of India and Ceylon during the months May to September.

Leonard Rogers describes cases with a duration of seven and more days, and says that blood cultures in six of his cases were positive for a bacillus related to the *B. coli* group. As Dr. T. R. Brown and I have shown here, it is not unusual to have paratyphoid with seven and eight days of fever. I am inclined to believe that Rogers has included some of these in his description of seven-day fever.

The disease can readily be differentiated from malaria by the absence of parasites in the blood, and the differential leucocyte

count, also by its failure to yield to quinine; from dengue by the absence of joint pains, by its being a single phase fever, and by its large spleen, which is never present in dengue, and the characteristic rash, also the time it occurs in relation to the fever; from influenza, by the absence of coryza and pulmonary symptoms, the blood picture and the definite course; from typhus, by the febrile course, rash and milder manifestations; from typhoid and the paratyphoid group by the cultural blood findings.

In conclusion, it may be stated that we have at present a distinct disease, running a characteristic febrile course accompanied by a rash, probably allied to the exanthemata, which made its appearance in Ancon Post Office last April, and which is still with us. It has not been recognized hitherto or described in the Western hemisphere.

The nature of the infection is not known.

Day of Disease : First.

Day of Disease : Second.

Day of Disease : First.

Day of Disease : First.