I lighted upon this postfebrile eosinophilia in numerous cases of fever in which malarial parasites and increase of large mononuclears were absent. I give here a few of the blood counts.

No. 1 Recruit. No previous admission for malaria. Fever lasted 5 days. No parasites.

1st Count, 3rd day—

Polymorphonuclears	... 19	per cent.
Large Mononuclears	.. 14	,,
Lymphocytes ...	... 60	,,
Eosinophiles ...	... 7	,,

2nd Count, 10th day—

Polymorphonuclears	... 62	per cent.
Large Mononuclears	... 12	,,
Lymphocytes	... 14	,,
Eosinophiles	... 12	,,

No. 2 Recruit. No previous admission for malaria. Fever lasted 3 days. No parasites.

1st Count, 2nd day—

Polymorphonuclears	... 78	per cent.
Large Mononuclears	... 14	,,
Lymphocytes ...	... 8	,,
Eosinophiles ...	... 0	,,

2nd Count, 9th day—

Polymorphonuclears	... 47·5	per cent.
Large Mononuclears	... 16	,,
Lymphocytes ...	... 16 5	,,
Eosinophiles ...	... 20	,,

3rd Count, 39th Day—

Polymorphonuclears	... 48·5	per cent.
Large Mononuclears	... 8·5	,,
Lymphocytes ...	... 17	,,
Eosinophiles ...	... 26	,,

No. 3. Rifleman, 2 years' service. No admission for fever for past 6 months. Fever lasted 4 days. No parasites.

1st Count, 2nd day—

Polymorphonuclears	... 79	per cent.
Large Mononuclears	... 10	,,
Lymphocytes ...	... 10	,,
Eosinophiles ...	... 1	,,

2nd Count, 9th day—

Polymorphonuclears	... 60·5	per cent.
Large Mononuclears	... 8 5	,,
Lymphocytes ...	... 17	,,
Eosinophiles ...	... 14	,,

3rd Count, 19th day—

Polymorphonuclears	.. 54·5	per cent.
Large Mononuclears	... 10	,,
Lymphocytes ...	... 22·5	,,
Eosinophiles ...	... 13	,,

No. 4 Recruit. No previous admission for malaria. Fever lasted 4 days.

1st Count, 3rd day—

Polymorphonuclears	... 49·5	per cent.
Large Mononuclears	... 10	,,
Lymphocytes ...	... 37	,,
Eosinophiles ...	... 3·5	,,

2nd Count, 12th day—

Polymorphonuclears	... 43·5	per cent.
Large Mononuclears	... 9·5	,,
Lymphocytes ...	.. 34	,,
Eosinophiles ...	... 13	,,

No. 5 Recruit. Fever lasted 3 days. Chart XIV.

1st Count, 4th day—

Polymorphonuclears	... 61·5	per cent.
Large Mononuclears	... 7	,,
Lymphocytes ...	... 30	,,
Eosinophiles ...	... 1·5	,,

2nd Count, 7th day—

Polymorphonuclears	... 55	per cent.
Large Mononuclears	... 6	,,
Lymphocytes ...	... 23	,,
Eosinophiles ...	... 16	,,

No. 6 Recruit. Fever lasted 3 days. Chart XV.

Count 6th day—

Polymorphonuclears	... 65	per cent.
Large Mononuclears	... 8	,,
Lymphocytes ...	... 20	,,
Eosinophiles ...	... 7	,,

No. 7 Recruit. Fever lasted 3 days. Chart XVI.

1st Count, 4th day—

Polymorphonuclears	... 82	per cent
Large Mononuclears	... 12	,,
Lymphocytes ...	... 6	,,
Eosinophiles ...	... 0	,,

2nd Count, 6th day—

Polymorphonuclears	... 64	per cent
Large Mononuclears	... 8	,,
Lymphocytes ...	.. 21 5	,,
Eosinophiles ...	... 6·5	,,

No. 8 Recruit. Fever lasted 4 days. Chart XVII.

Count 5th day—

Polymorphonuclears	... 45	per cent.
Large Mononuclears	... 12	,,
Lymphocytes ...	... 32	,,
Eosinophiles ...	... 11	,,

No. 9 Recruit. Fever lasted 3 days. Chart XVIII.

Count 4th day—

Polymorphonuclears	... 63	per cent.
Large Mononuclears	... 9	,,
Lymphocytes ...	... 24	,,
Eosinophiles ...	... 4	,,

These few observations are the only ones that I have preserved in my notes The occurrence of eosinophilia appeared to me at the time to be of academical but of no particular practical interest, hence I did not follow up the point and establish it by a large number of observations. But when I found the same phenomenon in a series of cases of undoubted dengue, its bearing on the question of the identity of these fevers became at once apparent, and I publish these observations in the hope that they may be found to be of some use in the settlement of this question.

THE PROBLEM OF DENGUE, THREE-DAY AND SEVEN-DAY FEVER.

BY W. L. HOSSACK, M.D., D.P.H.,

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CAPTAIN KENNEDY'S paper on Dengue, which has just appeared in the *Indian Medical Gazette*, November, 1912, is of particular interest, not only on account of its intrinsic value, but still more because it affords an opportunity for all to put on record their impressions of a most striking epidemic. It also reopens, and in my opinion finally closes, an interesting controversy as to the relations of three Indian fevers which have been given distinctive names, three-day fever, seven-day fever, and dengue, whether they are three distinct diseases, or three interchangeable and inseparable expressions of one very variable disease A short resumé of the history of the controversy seems advisable, particularly as it may help to bring opinions to a focus. In 1905 Rogers added yet another to the many services he has rendered in the study of Indian diseases by publishing a detailed account of seven-day fever; he described it as an endemic fever confined to seaports and coastal regions and quite distinct from dengue. This was very shortly afterwards followed by a description of three-day fever in Chitral by MacCarrison. MacCarrison admitted the great similarity between the new disease and that described by Rogers, but decided after great hesitation that they were distinct because in three-day fever there was no tendency to have either rash or terminal rise of temperature.

Fooks now came on the scene with a description of an outbreak in Sialkot, in which three-day and seven-day types of fever, with intermediates, were present in the same epidemic. A rash was observed in some of the cases. He avoided stating conclusions, but the facts of his paper did this for him; it seemed clearly demonstrated that three-day and seven-day fever were slightly differing expressions of the same disease.

Contemporaneously and, as far as I remember, quite independently of any Indian work, Ashbourne and Craig described an epidemic in the Philippines which they named dengue. Amongst the fever charts published were charts identical with those of three-day and seven-day fever.

In 1908, Megaw entered the lists and collected and analysed the facts recorded by the various observers who have just been mentioned. As the result of his analysis he arrived decisively at the conclusion that all three were one and the same disease. Rogers failed to produce any arguments against the facts so ably marshalled by Megaw; in fact, he may be said to have retired behind the entrenchments of authority, and from that impregnable position he breathed reproaches on Megaw for his lack of reverence. All Megaw had done was to explain the greater severity of the dengue of the past, as judged by existing text-book accounts, by the fact that the old observers probably overlooked the slighter and less typical cases, and had a tendency to over emphasise the striking features of the class of cases they deemed typical.

It is certain that Verchere and Elliot drew much more harrowing pictures of the 1872 epidemic than did Edmonstone Charles, when he originally put his description on record. Quite possibly the disease increased in intensity and virulence as it progressed. One thing is certain that some of the text-books fail to emphasise, as did the old observers, the importance and frequency of slight and atypical cases and that the fact that the disease is a very variable one. Instead, they lay far too much emphasis on striking cases which by no means represent the most typical and common form of the disease.

However, it is no longer necessary to work merely on the records of the past, or to be more accurate text-book description as we have just experienced a huge sweeping pandemic which in every way conforms to descriptions of the past, particularly the Calcutta epidemic of 1871-72 as described by Edmonstone Charles in the *Indian Medical Gazette*. The typical rash, both initial and terminal, has been less common in the present pandemic at least in the early stages of the epidemic; but even in 1872 Charles was unable to verify its presence in fully one-third of his cases. Cases of great severity have been observed, whether one regards the intensity of the pains, the high range of the fever, the liability to relapse, or the delayed and painful convalescence. The temperature charts agree with the descriptions and charts of the past, and also with those of three and seven-day fevers. It is true that in the "Lady Fraser" epidemic the continued type of fever, the three-day type, was chiefly observed; but it must be noted that Edmonstone Charles insists that relapses, and in them he includes terminal rise, are an accidental manifestation. It is difficult to avoid the conclusion that Rogers is confronted with two alternative courses: either he must contend that we have had three diseases or at least two simultaneously epidemic in Calcutta; or he must admit that Megaw was right and that alterations are necessary in his descriptions of both dengue and seven-day fever.

In a recent discussion on the dengue epidemic Rogers laid emphasis on the fact that the pulse observed by Dr. Dutt had been a rapid pulse as opposed to the slow pulse of seven-day fever, my own observations have led me to a contrary conclusion, a rapid pulse has been quite exceptional and when it occurred it was almost always associated with hyperpyrexia. In the classical descriptions of dengue there seem to be some divergence of opinion on this matter.

Edmonstone Charles emphasizes the lack of relation of the rapidity of the pulse to the height of the fever scheme with characteristic thoroughness describes it as sometimes rapid, sometimes slow. Erahan says it is not ordinarily a slow pulse. Clayton says it may be rapid or little affected. Manson, Jackson, and Castellani make it rapid at a rate increasing proportionately to the temperature.

The three main points that have to be settled are:—

(1) Is the dengue of 1912 in Calcutta the same as the dengue of 1872.

(2) Does the dengue of 1912 include individual cases and outbreaks indistinguishable from cases and outbreaks of three and seven-day fever.

(3) Is it possible that dengue is inseparable clinically from three and seven-day fever, but that these latter are nevertheless distinct diseases.

As to the first question I think there will be no disagreement. Dengue in 1912 practically does not differ at all from dengue in 1872.

As to the second I shall be glad to hear the points on which the outbreaks and cases of 1912, particularly the "Lady Fraser" outbreak, are to be distinguished from three and seven-day fever.

As to the 3rd question it may be suggested that it is true that this dengue epidemic in many individual cases, cannot be separated by clinical tests from three and seven-day fever, but nevertheless it is clear that dengue is something quite new to this generation from the fact that it has attacked all and sundry even those who were immune from seven-day fever, either from an inherited immunity as in Bengalis, or from an immunity acquired from previous attacks, as in Europeans. It seems to me that in such an argument a great fallacy is involved. It assumes that when a great pandemic of any disease occurs, the said disease cannot have previously existed in a community in a sporadic and endemic form, otherwise there would have been too much immunity to allow the disease to break out as a pandemic. But such an assumption is contradicted by many of the findings of epidemiology. It frequently happens that the origin of a pandemic is found in sporadic and endemic cases of the same infection and that this infection has suddenly undergone a great exaltation of virulence. How else are you to explain the devastating small-pox epidemic that swept Calcutta in 1909. It was so virulent that it not only broke down the protection afforded by vaccination, to a considerable extent, but even broke down the protection afforded by a previous attack of small-pox itself. Fatal results were recorded in cases well marked with small-pox. I cannot close this part of my argument more suitably than with a quotation from Verchere writing in 1879 of the Calcutta dengue epidemic of 1872. "The disease is endemic to a very small extent in Calcutta and other localities in tropical climates and it is then non-contagious. It is susceptible of acquiring epidemic exaggeration and it then becomes a true travelling epidemic." Now let us leave controversial arguments and deal with what, it must be admitted, are very fragmentary records of the epidemic as I have experienced it.

BEGINNINGS OF THE EPIDEMIC.

The earliest case that I came across, one that I failed to recognise at the time, was that of a topaz on the P. & O. "Sardinia," by name Francis Fernandez. He was found on the ship as she was going to sail on 4th May 1912. He had a temperature of 103, pulse 120—he was walking about—had marked headache and pain in the back and had a profuse brick-red macular rash on arms and chest, showing up clearly though the skin was very dark. I sent him to the Campbell Hospital, as possibly a case of small-pox with abnormal prodromal rash. He was discharged from hospital three or four days later

with a diagnosis of "simple fever with some prickly heats." (*sic*).

OUTBREAK ON THE DREDGER "SANDPIPER."

On the 9th May, 1912, the dredger "Sandpiper" came into port from down the river with 11 cases on board which I diagnosed as dengue. I put her into quarantine as I had no knowledge that the disease was then prevalent in Calcutta. The patients were suffering from short fever of two to four days duration, the temperature running up to 102 and 103. In this first batch there were only one or two with a slight rash. Dr. Elmes was put in medical charge and on the 12th and 13th Major Rogers visited the ship and confirmed the diagnosis. By that time two Europeans and 30 natives had been attacked and 14 were convalescent. On the 14th I released her from quarantine as I had found out that dengue was prevalent in the city. I found the gunner on that date suffering from fever with a profuse red rash all over the body. On the 17th when she had returned to work down the river one European and four natives were attacked; one of the natives was a relapse case, having been already attacked in the first batch. Pains were not a predominant feature in this outbreak; there was nothing comparable to the bone-breaking fever of text-book descriptions, so much so that the diagnosis of dengue which I had given was a guarded one.

OUTBREAK ON P. V. "LADY FRASER."

The vessel had been lying in port for over a month when on 30th May 1912, I received intimation of an outbreak of infectious disease, which had broken out three or four days previously amongst the firemen. On this date there were seven cases and between this and the 7th June, 18 cases in all developed, these cases constituting the first half of the epidemic. The position of things on the 7th of June was that two of the 18 cases had been sent to hospital, one with pneumonia and another with doubtful chest symptoms—he was discharged well in two or three days—and the rest were convalescent and for three days there had been no fresh cases. It proved impossible to detain the ship any longer as her consort was out of coal, so on the 8th she went down to the Sandheads. On the 10th she reported by wireless three fresh cases, and when I went down to her on the 13th June, I found 11 fresh cases. From the 14th to the 17th seven more cases occurred, making 18 in all in the second batch. I must apologise for the very scanty records I have to give; Dr. Elmes was in medical charge of the first batch and as for the second batch, well the monsoon was coming in, the "Lady Fraser" is a notorious roller and to put the truth plainly I was not in a position to make very full or accurate records, but still I recorded in my visits two or three times a day any departure from the average in pains or temperature or presence of rash. "No rash" was particularly noted. The best thing I can do is to quote from my official medical report.

MEDICAL REPORT.

The medical aspect of the outbreak is of some interest. Though the epidemic was diagnosed as dengue, the cases were by no means very typical. Rash was almost completely absent. In 7 cases of the first batch seen on the 31st May only one had a doubtful rash, one subsequent case of the batch of 18 had a fairly marked rubeoloid rash, while none of the 18 of the second batch shewed any rash at all. Temperatures were taken morning and evening, but only one or two of the cases shewed any tendency to terminal rise. The average duration of the fever was only two days. The average maximum temperature was 102 F., while 4 cases had 104, one rising to 104·5. The pulse tended to be slow, about 90 or less. One man was found in a somewhat collapsed state on the second day of fever, with a pulse of only 50. In the first batch joint-pains were not very marked in some of the cases; but in the second batch nearly all complained bitterly of these sometimes for a day or two after the fever had gone. A burning pain in the chest was complained of by several. The typical double attacks of dengue as described by Manson were almost completely absent. There was only one case of relapse—Mahomed Ali, Fireman. He had an attack in Calcutta, went to sea cured on the 8th, but got ill again on the 14th June with pulse 100 and temperature 104·2. On 15th June his morning temperature was 101 and on 17th he is noted as recovered. Only two of the extra firemen imported on the 19th June subsequently developed the disease. The first got ill on the 22nd June. This would point to an incubation period of only three days. Another one got ill on 25th June, which gives an incubation period of six days.

However, it is very difficult to be definite as to the incubation period, considering the fact that the disease started in Calcutta amongst the firemen about the 27th May, and it was not until 16th June that the last case developed. No cases developed amongst them from 5th June until 10th June, and from this date until 16th June no less than 11 cases were found, all amongst the men who had been on the ship from the beginning of the epidemic. It should be noted that firemen and lascars share one common forecastle. In the first outbreak, lascars predominated, in the second outbreak, firemen. In port the lascars had hard work and exposure to heat, while painting and cleaning up. At sea the engine-room staff had most of the work and exposure to great heat. This seems to point to the fact that there is such a thing as partial immunity, *i.e.*, an immunity that breaks down only after prolonged exposure to infection, and then only when the general conditions of work and circumstances are unfavourable to the patient. The captain is a notable case of delayed infection. It was not till the vessel had returned to port, after he had been exposed to infection for over a month, that he developed the disease.

It has been suggested in the Philippines that dengue or seven-day fever is conveyed by mosquitoes (Culex), and in India and Europe by sandflies (Phlebotomus). The facts of this outbreak are rather against such a theory. During my four days' stay on the ship I saw no mosquitoes, but the Chief Engineer informed me that the ship was not quite free of them; he had seen one or two in his cabin on 16th June, the ship having reached Sandheads on the 8th June. At the Sandheads she lay quite 40 miles from the land, and was being scoured by a strong landward breeze (the first advance of the monsoon) so most of the stegomyia that swarmed on her in port must have been blown out of her, for it must be remembered that she was cruising about and presenting every quarter to the wind in turn. It is certain at least that conditions were extremely unfavourable for the conveyance of the disease by either phlebotomi or mosquitoes, as the disease developed in at least 7 of the cases, of the second batch subsequent to the 14th of June. The ship sailed on the 8th, so that reckoning on an incubation period of three to six days, most of those 7 must have been infected at sea. In the case of the extra firemen, who developed the disease on the 22nd and 25th June, it is practically certain that their infection was obtained at sea under conditions which made insect infection at least unlikely. It should be noted that pilot vessels are kept as clean as a Man o' War, so that phlebotomus-breeding is almost out of the question on board these vessels.

Individual Cases.—I wish to quote one or two cases which have come to my knowledge privately, as cases indicating that in individuals at least, the maximum severity of dengue as given in text-book descriptions has been fully equalled in this epidemic.

Case 1.—Major A., 36th Jacob's Horse, Alipore. Presumably one of Captain Kennedy's cases. He had three attacks in seven weeks; was invalided to Darjeeling and returned limping with recurrent shifting

pain in the joints. I saw him again on the 25th November, 1912, and he informed me that he still was not clear of pains, about five months after his first attack.

Case 2.—Miss J. had an attack of dengue in July. Had agonizing pain so that she could not move in bed without crying out. It hurt even to breathe. No relapse and speedy convalescence. Compared her pain to rheumatic fever, which she had seen.

Case 3.—A bearer in 10, Belvedere Road, treated by me. This was a case in which the pains were negligible and only a doubtful erythema about the face was present in the latter stages and a tendency to hyperprexia was the leading symptom. The original attack lasted six days and his temperature starting at about 103 kept high, and on the fourth day rose to 105 For nearly 30 hours it kept at from 104·5 to 104·8, and I was ready all the time for sponging and cold pack. On the sixth day it came down to 103 and on the seventh he had a subnormal temperature. That very day he went back to his own residence. but two days later he returned for further treatment with a temperature of nearly 104. In two days this had gone down and then he rapidly recovered. He was a typical case of relapse with tendency to hyperprexia. The pains were almost negligible and the rash (a terminal rash) was almost imperceptible. His pulse was at first slow about 90 but eventually reached 120 and resembled a plague pulse.

CONCLUSIONS.

(1) *Identity of the* 1912 *Calcutta epidemic with previous Calcutta epidemics of Dengue.* I think this is generally admitted.

(2) The 1912 epidemic comprised cases and particular outbreaks, notably the "Lady Fraser" outbreak, clinically distinguishable from three-day fever, and as at present exemplified only by Captain Kennedy's paper, indistinguishable from seven-day fever.

(3) The evidence recorded in Captain Kennedy's recent paper is against the theory that dengue is carried solely by phlebotomus and the facts of the "Lady Fraser" outbreak, are against the necessity for a specific insect carrier of any kind. In the Alipore epidemic phlebotomus was not found at all in what was evidently a family extensive and complete insect survey. In the "Lady Fraser" epidemic, the conditions in the later stages of the epidemic were such as almost to preclude insect carriers.

(4) The recent pandemic seems to be an expression of a very variable disease caused by an ultra microscopic organism which is endemically present in Calcutta and evinces its presence by giving rise to what have been described as three-day and seven-day fevers

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A TELEOLOGICAL WORKING THEORY OF THE ASYMBIOTIC RELATIONS OF THE MALARIAL PLASMODIUM TO ITS ALTERNATIVE HOSTS—MAN AND THE ANOPHELES MOSQUITO. *

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[*Communicated to the Burma Branch, British Medical Association, December, 10th* 1912.]

THE varying epidemiological and endemiological phenomena of malaria in a single locality from year to year, and coincidently in different localities under varying local conditions, are so complex, that speaking for myself I have long felt the need of a working theory of some kind to give direction to investigation.

The consideration of facts at first sight apparently irreconcilable has gradually led me to definite conclusions, which I now venture, gentlemen, to lay before you, as providing that rational basis for investigation which the complexity of the problem demands.

We start with the fact that the malarial plasmodium passes its sexual phase in the anopheles mosquito as alternation host, and that certain anopheles of definite species act so frequently in nature in that capacity that they are regarded as definite malarial carriers. On the other hand we know that certain anopheles of species which do not carry malaria under natural conditions, have been found to do so under the artificial conditions of human experiment.

These facts are well-known; others of more recent discovery do not yet appear to have attracted the attention they deserve.

During considerable epidemics of malaria which have occurred in India within recent years, common and widespread local carriers—such as Culicifacies and Listoni—examined in large numbers for their direct incrimination, have failed to exhibit sporozoit infestation.

In the Andamans during 1911 Major Christophers found that of local potential carriers Ludlowi alone was active in that capacity; while coincidently at Kyaukpyu on the Burmese littoral—a place whose local conditions differ but little from those which characterised the field of Major Christophers' investigations, my investigations revealed that Fuliginosus was active as a malarial carrier while Ludlowi was not. Elsewhere in some localities Fuliginosus has been incriminated as the principal carrier; while it has been found to act but rarely in that capacity in others.

Myzorhynchus Barbirostris has occasionally been found to act as a carrier in nature, though at one time supposed not to subserve that function.

It will be seen therefore that the facts of mosquito-malarial inter-relation instead of being simple and fixed as has been thought, are really complex and fluctuating.

As regards the malarial plasmodium in the human body and the phenomena—individual and general—to which it gives rise, we need an explanation of the following facts:—(1) The periodic recrudescence of the disease at intervals in a single locality of three, five or even ten years, (2) The effect as regards intensification of malaria of the sudden addition to a malarial community by immigration of any considerable number of people who are either perfectly healthy or severally malaria-stricken, (3) The operation of poverty, defective housing and insufficient food, in intensifying malaria in localities where such conditions do not represent the normal state of the population, (4) The gradual lessening of malaria observed to follow the clearing of jungle and the establishment therein of those civilised conditions

* *Note.*—The author announced the theory developed in the following address on the 18th of November 1912, at the All-India Malarial Conference in Madras.