

## Original Articles.

### EPIDEMIC MALTA FEVER IN ASSAM— A SHORT PRELIMINARY NOTICE OF CERTAIN RECENT DISCOVERIES RELATING TO THE TRUE NATURE OF KALA-AZAR.

BY CHAS. A. BENTLEY, M.B. (EDIN.),

*Borjulié, Tezpur, Assam.*

In spite of the fact that *kala-azar* has been frequently investigated, it cannot be said that the nature of the condition is as yet at all clearly defined. It is true that both Captain Leonard Rogers, I.M.S., and Major Ronald Ross, I.M.S., came to the conclusion that the disease was malarial in character, but their respective reports differed so markedly in important details, that the one can hardly be said to offer much support to the other, except upon very general grounds.

Rogers states that the evidence of the malarial nature of the condition is so marked, from first to last, that it is scarcely necessary to discuss the possibility of any other infection.

Ross, on the other hand, fails to find many of the definite and generally accepted signs of paludism, in a large proportion of the cases he examined, and he appears to fully realize the objections to the malarial theory of the disease. Thus at page 22 of his "Report on the Nature of *Kala-azar*" he sums up the points for and against a malarial origin as follows:—

"For the malarial theory—

(a) The symptoms of *kala-azar* are almost, if not quite, identical with those of malarial fever.

(b) The disease occurs in malarious regions.

(c) Most of the cases contain yellow pigment.

Against the malarial theory—

(a) The high death-rate of *kala-azar*.

(b) The intractability to quinine.

(c) The existence of a low constant fever, not amenable to quinine and not like malarial fever, in the second stage of the disease.

(d) The apparent absence of the malarial parasites and the melanin of paludism from many established cases of the disease.

(e) The communicability of *kala-azar* from the sick to the healthy and its epidemicity."

On page 69, however, he states that the probability of *kala-azar* being a specific disease, distinct from malaria, is exceedingly unacceptable. "No observations of a disease exactly like malarial fever, but in which either the parasites or melanin have not been found in the early stages on exhaustive examination, are on record. It is highly improbable that two diseases should present such close pathological similarities, and yet be essentially different."

Finally the paragraph closes with the definite statement:—

"I think, then, with Rogers, that *kala-azar* is malarial fever."

An experience of some four hundred cases of *kala-azar*, in a recent epidemic in this neighbourhood, together with the results of certain investigations into the nature of the condition, have led me to challenge the idea that *kala-azar* is a form of malarial fever.

A visit which I paid to Nowgong, where I saw a number of cases of *kala-azar*, and recognized them as being of a similar character to the disease which had broken out in a portion of the district under my charge, and the evidence of several European and native medical practitioners familiar with the disease, sufficed to demonstrate the identity of the outbreak, with the epidemic fever, known as *kala-azar*. A careful study of a large number of cases of the disease, in their clinical aspect, convinced me that the disease was not ordinary paludism. Further investigation into the pathology and hæmatology of the condition now show that the epidemic is in all probability a very severe form of so-called "Malta" fever, complicated perhaps in a certain proportion of cases, with an intercurrent attack of malaria.

A reference to the earlier pages of Rogers' Report upon *kala-azar* shows that for many years medical men in Assam have not been entirely convinced of the malarial nature of the condition.

In fact those who are most familiar with the epidemic, Mr. McNaught in particular, have always urged the probability of a specific infection. It appears to me impossible for any one who has made a careful study of *kala-azar* and compared it with ordinary malarial fever, with the aid of a microscope, and after a careful perusal of the latest literature upon malaria, to accept any other conclusion, than that *kala-azar* is a distinct and specific disease.

Clinically *kala-azar* and malaria cannot nowadays be said to resemble one another any more than do typhoid fever and malaria. The only similarity is to be found in the presence of fever, with general enlargement of the spleen and occasionally the liver, and the production of a subsequent anæmia. Other conditions which used at one time to be confused with malaria, frequently show very similar characteristics. Until comparatively recent years, attacks of relapsing fever, cerebro-spinal fever and enteric fever were almost always diagnosed as malarial fever in this country. Reference to Craig's recent monograph upon the æstivo-autumnal fevers will show to what an extent typhoid fever was confused with malarial fever during the Spanish-American War. Malta fever, so-called, which has only very recently been shown to be prevalent in many other parts of the world, besides the countries

bordering upon the Mediterranean, has often been mistaken for malarial fever. Some of the names which have at times been given to it are of themselves an indication of this error. "Typhomalarial fever," "Fæco-malarial fever," &c., are terms indicative of the confusion that has frequently existed regarding the nature of this disease.

It appears strange that in the investigations of *kala-azar*, the possibility of the disease being analogous to Mediterranean fever should have been overlooked.

In this article I shall attempt to indicate the similarities that exist between the two conditions.

I shall first, however, enumerate the points which serve to distinguish *kala-azar* from malaria acute, or chronic.

(a) *Kala-azar* during its early stage never exhibits true pyrexial periodicity.

(b) During the second stage of the condition, quotidian periodicity is common, but the character of the fever is quite atypical of malarial fever, showing a very constant and limited diurnal variation.

(c) At all stages the fever is resistant to and almost unaffected by quinine, even in enormous doses, and for given very long periods.

(d) The examination of the blood fails to show the presence of malarial parasites in the majority of instances, and the frequent absence of pigment (melanin) and other signs of paludal infection, indicate that condition is most probably only an accidental complication.

(e) The morbid anatomy is typical only of chronic pyrexia and its accompanying chronic congestion of the internal organs.

(f) Recent investigation shows that the presence of a micrococcus may sometimes be detected in the spleen tissues.

(g) Reference to an accompanying table will show that *kala-azar* in seventy-five per cent. of cases exhibits the specific serum reaction to cultures of the micrococcus *melitensis*.

A short glance at the clinical picture of *kala-azar* shows that it commences as an acute attack of irregular fever, absolutely resistant to quinine. This primary attack is followed by a period of absolute or relative apyrexia, which is broken by a recrudescence of irregular fever. This history of recurring attacks of fever with intervals of apyrexia is repeated for perhaps several months, by which time the spleen and frequently the liver of the patient has become considerably enlarged. Anæmia and marked emaciation are frequently present also, while the skin takes on a peculiar greyish-earthly appearance.

Following upon the splenic and hepatic enlargement, a chronic low fever occurs, while joint pains, simulating rheumatism, and heavy sweats frequently manifest themselves. This stage may last for many months, apparently unaffected by treatment, and recovery may

occur, when the disease has worn itself out. More frequently death ensues, not often from the fever, but from some intercurrent affection such as dysentery, pneumonia or phthisis. Any one familiar with the characteristics of Malta fever cannot but be struck by the resemblance which that condition bears to the clinical pictures of *kala-azar*. I would suggest that those interested in the subject should compare the description of *kala-azar* as found in Rogers' and Ross's reports, with the article upon Malta fever, by Bruce, in Davidson's diseases of warm climates, or with Hughes' monograph upon "Undulant Fever." Until a few months ago, before I had carefully studied the matter, I took it for granted that *kala-azar* was of malarial origin, and as early cases were occurring frequently in my immediate neighbourhood, I treated them for malaria. I soon found how resistant the fever was to ordinary doses of ten and fifteen grains of quinine, and so I gradually increased the dose, until in some cases I have given grains sixty (1-drachm) at one time. Finding that doses of this amount did not stop an attack or prevent a recurrence of the fever, I commenced giving quinine in doses of grains 30, by intra-muscular injection. This failing, I tried methylene blue, tannic acid, and carbolic acid in large and increasing doses, but without avail. Aconite, opium, tincture of Warburg, as well as all the synthetic anti-pyretics were all tried in turn, but proved of little use. During this period I examined many blood films from cases of *kala-azar*, both in the fresh and stained condition but although I found certain changes present in the blood of very many of these cases, I failed to find true malarial parasites, or pigment in all but a few isolated instances. The changes most frequently observed were,—the presence of normoblasts, polychromatophilia—and increased number together with a peculiar reticulation of the blood plates, when examined after Nakanish's method of staining fresh films.

At the same time I made a careful study of all the available recent literature upon malaria, and thus I soon became convinced of the error of continuing to regard *kala-azar* as a manifestation of paludism.

About three months back, I happened to be examining some fresh films prepared from the spleen of a fatal case of *kala-azar*. Among the splenic cells, free in the plasma, I noticed a number of small bodies resembling micrococci in active molecular motion. In a dried film, I was subsequently able to stain some of these bodies, after a good deal of difficulty, but it was exceedingly difficult to distinguish them except in very thin films. Following up this discovery, I sent a series of blood samples to Major R. Semple, R.A.M.C., Director of the Pasteur Institute, Kasauli, who very kindly examined them for me by means of the serum agglutination tests for typhoid and Malta fever. The result of the examination

of some twenty-five samples is given in the annexed table. From this it will be seen that fifty per cent. of the bloods examined gave a complete reaction to Malta fever, in all of three dilutions, and another twenty-five per cent. showed a more or less partial reaction. Six bloods gave no reaction at all.

It is evident then that in Assam we have a severe type of Malta fever, which exists in an epidemic form, and which is probably very much more virulent than the analogous fever of the Mediterranean coast. Whether this fever was originally endemic in India, and has been introduced into Assam among its immigrant population, it is difficult to say. It is a significant fact, however, that *kala-azar*, which (as Rogers shows) was a continuation of the Rungpur epidemic of the sixties and seventies, and was also analogous to the famous Burdwan and Mauritius epidemics of a slightly earlier date, should have occurred so soon after the Indian Mutiny.

It is well-known that many of the thousands of British troops engaged in the Crimea were invalidated by attacks of fever, which was exceedingly common in that part of Europe. Many of these men were subsequently drafted to India, after the outbreak of the mutiny, and it is not beyond the bounds of possibility that the disease was first introduced into India by them.

Gradually gaining a hold among a susceptible population, it swept in a wave, through many parts of the country, increasing in virulence and intensity. Where populations were dense, its advance has been rapid as in Burdwan and Rungpur. In Assam, with its scanty population, it has taken many years to pass from one portion of the province to another.

This is of course purely hypothesis, but it appears to me to afford a reasonable explanation of many of the peculiarities of *kala-azar*,—its communicability and epidemicity.

The fact that when once the disease was introduced into Assam, it was the *indigenous population* who suffered the *first and the most severely*, and that after them, it was old and long acclimatized coolies who had settled down away from the gardens, who were the next to suffer. These people introduced it among the old coolies on the tea gardens, and so the disease gradually spread. This history is altogether different to what we know of the incidence of malaria.

In malaria-infected countries, such as Assam, was known to be, before the occurrence of *kala-azar*, the indigenous population and acclimatized inhabitants possess a relative immunity to the attacks of paludism, and it is the new comer who suffers severely. Can we imagine that this experience would be reversed for one small part of one malarious country in the world? There are many other considerations involved in the discovery to which I have called attention in this paper, but these must be left for some future

occasion. All I will now add is the prophecy that future investigation will show, that a large percentage of the fevers of India will prove to be of similar origin to the endemic fever of the Mediterranean sea-board. I may add that I am arranging to seek for bacteriological and experimental confirmation of the micro-coccal origin of *kala-azar*, and I shall hope shortly to publish some further notes upon the matter, together with the results of an exhaustive study of the hæmatology of the condition.

I am greatly indebted to Major D. Semple, R.A.M.C., who has, by his kindness in examining samples of blood for me, given ample confirmation of the correctness of this new theory regarding the nature of *kala-azar*.

TABLE OF AGGLUTINATION REACTIONS FOR MALTA FEVER.

No.	1 in 10.	1 in 20.	1 in 40.	Remarks.
1.	Complete.	Complete.	Complete.	Diagnosed as K. A. recently.
2.	Nil.	Nil.	Nil.	Very ill.
3.	Nil.	Nil.	Nil.	Dead.
4.	Complete.	Complete.	Complete.	
5.	Partial.	Partial.	Nil.	Dead.
6.	Complete.	Complete.	Complete.	Not diagnosed K. A. Dead.
7.	Complete.	Complete.	Complete.	
8.	Complete.	Complete.	Complete.	
9.	Feeble.	Feeble.	Nil.	Very ill.
10.	Complete.	Complete.	Partial.	Dead.
11.	Complete.	Complete.	Nil.	Dead.
12.	Complete.	Complete.	Complete.	
1a.	Complete.	Complete.	Complete.	
2a.	Complete.	Complete.	Complete.	
3a.	Nil.	Nil.	Nil.	Dead.
4a.	Sample damaged.	...	...	
5a.	Sample damaged.	...	...	
6a.	Nil.	Nil.	Nil.	Dead.
7a.	Complete.	Complete.	Partial.	Very ill.
8a.	Nil.	Nil.	Nil.	Very ill.
9a.	Complete.	Complete.	Complete.	
10a.	Complete.	Complete.	Partial.	Also gave reaction to Typhoid in 1-10.
11a.	Complete.	Complete.	Complete.	
12a.	Complete.	Complete.	Complete.	
13a.	Complete.	Complete.	Complete.	
14a.	Complete.	Complete.	Partial.	
15a.	Nil.	Nil.	Nil.	Dead.