

TYPHUS FEVERS IN THE TROPICS*

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The title of the present discussion is "Tropical Typhus," but this name is obviously inappropriate, as the fevers with which we are dealing occur just as frequently in cold countries as in hot. A more suitable name is "Typhus Fevers in the Tropics," and although some experts are sure to object, I will adopt this until something better is suggested.

I propose to deal with the typhus fevers very briefly and in an elementary manner from the historical, clinical, and epidemiological points of view. I shall make little reference to the virus of the fevers: this omission is not due to any lack of appreciation of the very valuable contributions made by laboratory workers to our knowledge of these diseases, but to the fact that Dr. Fletcher and Dr. Felix, who have done so much to elucidate this aspect of the subject, are expected to take part in the discussion. My remarks are intended to provide a sketchy background to the very interesting observations which they are sure to make.

Typhus as an Epidemic Disease

"Every schoolboy knows" that the name "typhus fever" was originally applied to typhoid and relapsing fever as well as to typhus. In 1837 Still and Gerhard showed that typhoid fever was a distinct disease, and in 1843 Henderson differentiated relapsing fever. In 1862 Murchison emphasized the contagious nature of typhus fever. Nicolle and Conseil, in 1909, proved that the disease could be conveyed by lice. Between 1906 and 1910 Ricketts and Wilder suggested that the bodies now known as Rickettsia bodies were the causal organisms of typhus fever and Rocky Mountain spotted fever. In 1910 Wilson of Belfast discovered that the sera of typhus patients agglutinated organisms of the *coli* group which had been isolated from cases of the disease. He was careful to point out that he did not regard this agglutination response as indicating that the organisms caused typhus fever. Weil and Felix in 1916 described the reaction which is now known by their name; they used an organism called "*Proteus X 19*."

Until recently typhus exanthematicus was regarded as being essentially different from the other fevers which resembled it so closely in their clinical features; the reason being that these fevers were in sharp contrast with typhus in not being epidemic diseases associated with crowding, poverty, filth, and lice, and in not being directly communicable from man to man. Accordingly, even the spotted fever of the Rocky Mountains, which closely resembles typhus, was regarded by nearly all observers as belonging to a different disease group, until Wolbach, in his masterly monographs on the subject in 1916 to 1919, showed the essential similarity in the pathology of these two fevers. Sambon, however, had previously insisted that they were really the same as typhus fever.

So long ago as 1897 Brill of New York had discussed the relation between the disease which now goes by his name and typhus fever; he concluded that the epidemiological differences were so great as to make it impossible to place the two fevers in the same group, but in 1912 Brill's disease came to be regarded as an inter-epidemic form of typhus, because its virus was found to protect animals against typhus.

At this date the position was that typhus fever was regarded as a unitary disease, while the Rocky Mountain and Japanese fevers were considered as belonging to a different category; they were known to be communicated from rodents to man by ticks and mites respectively.

Insect Vectors in other Diseases Resembling Typhus

A brief reference must be made to some fevers, the aetiology of which was not known at first, but which are now recognized as belonging to the typhus disease group. In 1910 Smithson in Queensland described a fever resembling Brill's disease; he suspected that the vector was some insect living in sugar canes. The same year Conor and Bruch described a similar disease in Tunis, and called it "fièvre boutonneuse." In 1911 McNaught gave an account of an anomalous form of paratyphoid occurring in South Africa. In his report he makes a significant reference to a suggestion by Colonel Maher that the fever might be connected with ticks, since he found that some of the patients had been bitten by ticks prior to the onset. McKechnie, in 1913, wrote a very interesting report, unfortunately never published, of a fever prevalent in one locality in the Kumaon region of the lower Himalayas. He called this fever typhus, and suggested fleas, bugs, and mosquitos as possible vectors. Two years later, in 1915, Schüffner described a pseudo-typhus fever in Sumatra, and suspected a tick or mite of being the vector. The name given by Schüffner would probably be more correctly translated into English as pseudo-typhoid, as I understand he was thinking of typhus abdominalis rather than typhus exanthematicus.

Non-Epidemic Typhus in India

My own experience of a non-epidemic typhus fever was thrust upon me rather than sought. In June, 1916, while in the near neighbourhood of the place where McKechnie had already reported his cases of typhus, I found a tick on my neck in circumstances which indicated that it must have attached itself about twelve hours earlier. Some twenty days later, after returning to Lucknow, I began to suffer from fever with a step-like rise in temperature; within four days an eruption appeared, which recalled to my mind the descriptions I had read of the Rocky Mountain fever. At that time no human disease was known to be conveyed by a tick in India, so I had light-heartedly thrown away a very interesting specimen which, within a few days, assumed considerable importance as being the only likely vector of my attack of fever.

I wrote an account of my case in the *Indian Medical Gazette* of January, 1917, in which I suggested that the tick must have been either *Rhipicephalus sanguineus* or *Hyalomma aegypticum*. This, I think, was the first case in which definite evidence was produced of a tick being the vector of a typhus-like fever outside the Rocky Mountain fever zone. I also suggested that McKechnie's Kumaon fever and the fevers described by Conor, McNaught, and others should be classed with the spotted fever of Idaho and Brill's disease as a subgroup of typhus fever, differing from that fever in being conveyed by ticks or fleas, in being place diseases, and in having no connexion with lice, famine, dirt, or overcrowding. I fell into one serious error in regarding the low virulence of these diseases as being an important feature in differentiating them from classical typhus, but apart from this I have nothing to retract from what I wrote nearly eighteen years ago.

Several readers of my note, including Major-General Sprawson and Colonel Chapman, sent me accounts of similar cases which they had observed in various places in India. On the strength of these reports and after further study of the subject, I felt justified in suggesting

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in a paper published in the *Indian Medical Gazette* of October, 1921, that a fever conveyed to man from an animal of the wilds by a tick was widely distributed in India and probably in other parts of the world; that this could not be clearly distinguished from the Rocky Mountain fever; and that it, with the other sporadic typhus-like diseases, should be classified as members of the typhus fever group. Accordingly, I suggested the classification "louse typhus," "tick typhus," and "mite typhus." In later papers I produced evidence of the frequent occurrence of tick typhus in various parts of India as well as in other countries, and added to my previously proposed classification another heading—namely, "typhus of unknown vector."

Fletcher's Work in the Federated Malay States

Apart from work in the Rocky Mountain, Japanese, and Indian areas, there was little evidence of interest in the sporadic typhus fevers until 1926, when Dr. William Fletcher described a number of cases of "tropical typhus" in the Federated Malay States. Dr. Fletcher was struck with the resemblance between his cases and those described by me in India, but he found no evidence of tick bite, and the agglutination response to *proteus* X organisms was quite different in his cases from that observed in India. In the Indian tick typhus the Weil-Felix reaction was usually negative, or positive only in such dilutions as 1 in 80 or 1 in 100 to *proteus* X 19, whereas Fletcher found two sharply contrasted groups of cases, one of which gave a strongly positive reaction to *proteus* X 19 and was negative to the Kingsbury strain of *proteus*, while the other reacted to the Kingsbury strain of *proteus* X but was negative to *proteus* X 19. At first the differences between the two forms of tropical typhus and tick typhus were rather puzzling, but recent work indicates that there really are three distinct types of sporadic typhus—namely, tick typhus, mite typhus, and flea typhus—and that each of these shows a distinct characteristic agglutination response towards *proteus* X organisms.

Apart altogether from its great intrinsic value, Dr. Fletcher's report was very important in attracting the attention of the medical world to these sporadic typhus fevers. Within the past few years a vast number of observations have been published showing that the fevers of the typhus group are very widespread in their distribution and of considerable practical importance.

It was not until 1930 that Durand, Conseil, and Brumpt demonstrated the conveyance of "fièvre boutonneuse" by a tick, *Rhipicephalus sanguineus*, which was one of the two suspected by me in 1916. Now we know also that the form of sporadic typhus which conforms to Brill's description is conveyed from rats to man by fleas, so that to my previous provisional classification there must now be added another subgroup—"flea typhus."

Need for Uniform Nomenclature

A few words must be said on the subject of the classification of the typhus fevers. Dr. E. W. Goodall objected to Dr. Fletcher's use of the name "tropical typhus," on the ground that all the typhus fevers ought to be called typhus pure and simple, irrespective of the vectors concerned and any other differences that exist between them. While I object to the name "tropical typhus," I object much more strongly to the position adopted by Dr. Goodall, for although the sporadic fevers are very similar to louse typhus in their clinical and pathological features, they are poles asunder in their epidemiology and in the measures that are called for in their practical management. If the name "typhus" were applied to all fevers of the group without further

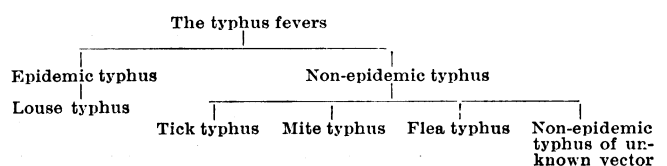
qualification a very misleading suggestion would be conveyed.

Disease nomenclature is intended to be helpful to the medical man, and should be as simple as possible, but if we attempt to secure simplicity by lumping together things that are essentially different the only result will be confusion. The classification of the typhus fevers is a matter of real importance, and I take this opportunity of appealing once more for the adoption of a uniform and rational nomenclature. The need for this step is evident when we consider that more than a dozen different names were given to the sporadic typhus fevers in a single recent issue of the *Tropical Diseases Bulletin*. Here is an incomplete list of twenty-seven names which have been used during the past few years for these fevers: spotted fever of the Rocky Mountains, fièvre boutonneuse, fièvre exanthématique, fièvre escharo nodularis, eruptive fever, macular fever, Marseilles fever, jungle typhus, spotted fever of the Eastern type, tick-bite fever, tick fever, Brill's disease, tropical typhus, endemic typhus, sporadic typhus, shop typhus, ship typhus, murine typhus, tabardillo, Mexican typhus, flea typhus, Manchurian typhus, Japanese river fever, tsutsugamushi, pseudo-typhoid of Deli, Mossmann fever, and mite typhus. This is an appalling list, the only redeeming feature of which is the growing tendency to use the name typhus. Place names are obviously unsuitable; they suggest that the disease is restricted to one locality—for example, I could not have described Indian tick typhus as Rocky Mountain fever. Names like "spotted" or "macular" are also unsatisfactory; there are so many fevers in which spots or macules appear that the name becomes meaningless.

My provisional suggestion that the word typhus qualified by the name of the vector should be employed was open to criticism, because the vector was often unknown or doubtful. This perfectly sound objection can only be met by a frank confession of ignorance when the actual vector is unknown or doubtful, and accordingly employing the non-committal general term "non-epidemic typhus" to indicate those fevers which are not conveyed from man to man by lice as contrasted with "epidemic typhus," which has a human reservoir of infection. The term "endemic" would be neater and better than "non-epidemic," but it has already been earmarked as a name for flea typhus, and therefore could not be used without risk of confusion.

Suggested Classification

Evidence is now accumulating to show that the specific agglutination response of each of the non-epidemic typhus fevers is associated with the vector concerned, so that we may soon be able to classify the fevers according to the vector, even when there is no direct evidence as to which arthropod is responsible in any given case. With the rapid accumulation of more knowledge of the geographical distribution of the fevers, difficulty in assigning each case to the appropriate vector should soon disappear. Until something better is proposed I therefore suggest the following modification of my original classification.



This classification is not ideal, since, apart from the occasional difficulty of determining which vector is concerned, we are not yet able definitely to state that there are four distinct types of virus. In louse, tick, and mite typhus the evidence is already fairly strong that each

virus is different from the others ; at any rate there is no case on record of direct communication of tick or mite typhus from one person to another, and, after all, the manner of conveyance of the diseases is by far the most important practical matter from the physician's point of view. Flea typhus is so closely related to louse typhus in its immunological and serological aspects that careful research will be needed to determine whether or not the virus of louse typhus can ever be transmitted by fleas. If this virus be transmissible by fleas it must be greatly attenuated in the process, since flea typhus is the one type which has never been found to be severe. There is no evidence that any of the non-epidemic typhus fevers has ever started in a louse-borne epidemic, so that although there may be some mental reservations regarding the relation of the fevers, practising physicians can safely base their action on the hypothesis that epidemic and non-epidemic typhus fevers are essentially distinct from each other.

Differential Diagnosis

I have already referred to the error into which I fell eighteen years ago with regard to virulence ; the truth is that tick typhus and mite typhus may be very mild or very severe. The same applies to a lesser extent to louse typhus, which is sometimes quite mild. Flea typhus alone has a consistent record of mildness so far, although severe or even fatal cases have been recorded. Another point which is sometimes relied on for differential diagnosis between the various forms of non-epidemic typhus is the presence or absence of local necrosis at the site of infection associated with lymphangitis. This feature is sometimes present and sometimes absent, both in tick typhus and mite typhus ; it cannot, therefore, be relied on as a point of distinction between the two fevers. Agglutination and animal inoculation tests are not always conclusive, so that when there is no positive evidence regarding the vector difficulty may arise at times in individual cases in distinguishing between the three types of non-epidemic typhus.

On the other hand, there will seldom be any difficulty in deciding whether any given fever belongs to the epidemic or non-epidemic group if all the circumstances of each case or outbreak are investigated. After all, the chief concern of the medical man is to decide whether he is dealing with a disease which calls for extremely careful precautions to prevent spread to other human beings or with a disease not communicable from man to man.

Serological tests against two or more varieties of *proteus X* organisms will often be of great help in diagnosis, and knowledge of the local conditions will usually make it possible to be reasonably certain of the particular vector which is concerned.

We are now at an interesting stage of the investigation, and with so many intelligent observers at work throughout the world we seem to be rapidly approaching the time when the non-epidemic typhus fevers will be completely rescued from the small and rapidly diminishing group of fevers of unknown or doubtful aetiology. The most astonishing feature of the non-epidemic typhus fevers is that they escaped recognition so long in many parts of the world, in spite of their striking and characteristic features.

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THE MEDICINAL TREATMENT OF CHOREA (CALCIUM ASPIRIN)

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Discussion will be confined to chorea of Sydenham's type in children. Debatable cases of adult hysteria, pregnancy chorea, and conditions such as Huntington's chorea with gross structural changes in the central nervous system have been excluded.

General Considerations

The anatomical basis of the disease is still uncertain, and such changes as have been described are attributable to pyrexia, capillary emboli from coincident endocarditis, or confusion in diagnosis with the choreiform varieties of epidemic encephalitis. The basal difficulty is that in its typical form Sydenham's chorea is not fatal. Practically all recorded post-mortems have been carried out on cases of rheumatic endocarditis and pericarditis complicated by chorea, and not on patients dead from chorea itself. The most careful histological research, with modern methods on a typical case, by Shaw²⁸ did not reveal any morbid changes other than simple hyperaemia. It can be assumed, therefore, that the anatomical changes are negligible, and not such as to preclude complete recovery. If the patient is suitably rested and cared for, the spontaneous recovery rate approaches 100 per cent., so that the effect of a drug can only be assessed in terms of its ability to lessen the duration or severity of the attack. The average duration is usually accepted as six to ten weeks, but some cases drag on for months.

For greater discrimination some method of grouping is essential.

1. Mild chorea, in which speech is not definitely affected and the patient can feed and dress himself with more or less difficulty.
2. Moderate chorea, in which coarse voluntary movements can still be performed, but the patient cannot feed or dress himself.
3. Severe chorea. Violence or pseudo-paresis now prevent all purposeful voluntary action. Bed boards and other protective measures are required.

Adopting a somewhat similar grouping Sutton²⁹ records sixty-three undrugged cases.

Group	Average Duration	Extremes
1. Mild	35 days	10-65 days
2. Moderate	46 ..	19-120 days
3. Severe	67 ..	30-180 days

The general average was 47 days.

There is no reason to believe that the general characteristics of the disease have undergone any material change in the last eighty or ninety years. Already by 1846 H. M. Hughes⁷ had dealt with the matter at Guy's. A few years later Sée²⁷ recorded an extensive clinical and aetiological analysis in Paris, and Trousseau discussed it at the New Sydenham Society. In 1874 Pye-Smith²⁴ reviewed the Guy's Hospital figures again, and in 1897 Morley Fletcher¹⁸ did the same at St. Bartholomew's. The chief clinical features have remained constant throughout. The disease has persistently occurred about three times as commonly in females as in males. The age of maximum incidence has always been between eight years and puberty. Urban districts have been more affected than the country, and the association with articular rheumatism and inflam-