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DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

ON THE ETIOLOGY OF TYPHUS FEVER

[Following is a translation of an article by H. da Rocha Lima which appeared in the German-language periodical Berliner Klinische Wochenschrift (Clinical Weekly of Berlin), No 21, 1916, pages 567-569.]

A part of the results of the experiments conducted by Prowazek and myself in the prison camp at Cottbus in the early months of the year 1915 on behalf of the War Ministry were made public by me, after new important factors for a better interpretation of the results was obtained, in issue No 2 of the 1916 Archive fur Schiffs- und Tropenhygiene (Archives of the Institute for Maritime and Tropical Hygiene).

Despite the fact that in about 95% of the typhus fever lice which were examined, microorganisms uniform in appearance were found in unbelievable numbers, not only in the contents of the digestive tract, but also principally as parasites of the epithelial cells of the stomach and intestines, and that, on the other hand, in more than 100 lice from an area free of typhus fever (Hamburg) which were examined in the same manner a similar finding was not made once, I was still at that time unable to bring myself to express an opinion as to the importance of these microorganisms in the etiology of typhus fever. The fact that I am doing so now is due to the finding of new and important elements of proof during the most recent epidemic in Wloclawed. [Note: Comment during the course of proof-reading. In the meantime, the results given here were the subject of an address which I gave before the German Pathological Society in Berlin on 26 April. Until this date, there had been no reports of any checking on the numerous experiments of mine in connection with the finding of the characteristic features and the importance of the rickettsia provazckii. The fact that similar small bodies occur in smear slides prepared from typhus fever lice was of course mentioned by Prowazek and other authors before me. Recently Toepfer also saw bodies near a spirochaeta in a smear slide which are said to be very similar morphologically to rickettsia.]

In the course of the past year, H. Sikora has, with much patience and skill, worked out the technique of experimentation with lice practically to perfection. As I was now given the opportunity to continue my typhus fever experiments in Wloclawek, I was able to let lice of various origin, and in any desired numbers, suck on typhus fever patients, then to observe them under various conditions and in this way to answer the key question as to whether the microorganism found in typhus fever lice in Cottbus was perhaps an incidental finding -- i.e., an epizoon which occurred in the Russian lice independently of typhus fever -- or whether it is the typhus fever blood which has the capability to cause the infection of the louse with the body in question.

If this were to be the case, then the lice experimentally infected in this manner must also show the same findings as those infected by natural means. And this was also found in the fullest degree. In healthy lice which had been allowed to suck on typhus fever patients, the microorganism in question was found to develop regularly as a parasite of the stomach and intestinal cells, whereas lice which were kept under like conditions but allowed to suck only on healthy persons or those who had recovered from typhus fever were not infested. This microorganism which enters the louse only through drinking of typhus fever blood settles in the cells of the intestinal walls and multiplies rapidly. It probably also reaches the salivary glands of the typhus fever transmitter. Furthermore, the characteristics of the typhus fever virus and of these parasites, insofar as they are known, are identical. And since the only shapes which can be found with the microscope in the blood of typhus fever patients have the same shape and size as our bodies, no other logical conclusion can be drawn from the results of my experiments than that the microorganisms with which we were occupied are none other than the long-sought causative agents of typhus fever. (Illustration 1.)

Its exterior form is suggestive of a bacterium, but the characteristic difficulty in staining, the resistance to culturing and the tendency to gather together in sharply defined parts of the protoplasm of the affected cell much in the same manner as chlamydozoa suggest rather a strongyloplasm or chlamydozoa. Whether bacteria or strongyloplasm, the variations from known types are great enough to allow the assumption that it is a special species. As to the question of order, we do not yet have sufficient information. This remains an open question, and the required name for this microorganism which has until now been referred to as "body" might be most practical if a possibly prejudicial terminology were avoided. Therefore I should like, in honor of the great researchers who have fallen as victims of typhus fever -- Rowasek and Ricketts -- to suggest the name *Rickettsia Prowasekii*. (Illustration 2.)

The only identifying characteristic of *rickettsia prowasekii* presently known is its ability to penetrate to the digestive tract cells of

the louse and there to multiply rapidly. Organisms similar in appearance can therefore be identified with certainty as rickettsia only if, in addition to morphological characteristics, this activity is also demonstrated. This postulate of course applies for all investigations which are conducted in an effort to answer any basic question. The monotonous and trying examination of sectional slides of the respective lice is absolutely necessary. The mere determination of similar bodies in smear slides from typhus fever lice cannot be taken as a sure confirmation of our investigation, nor can the same finding in normal lice be considered as a reliable argument against them. For in my first publication, I have already pointed out that similar shapes sometimes occur in smear slides of normal lice. (Illustration 3.)

This is not to say that the examination of smear slides has no importance, but only that special care must be taken in the interpretation of findings. This caution is particularly important in the absence of sufficient experience in the observation of fine morphological details; for small round shapes which now and then are seen to lie in pairs can be found in just about any slide preparation and actual microorganisms of spherical shape always seem to like to lie in pairs. The finding of small double bodies, or perhaps rods with pol-coloring, does not suffice to speak of "similar bodies" in the sense of an apparent identity.

The morphological characteristics of rickettsia prowazekii can only be recognized clearly on heavily stained Giemsa preparations at about 1500 times magnification. They are somewhat smaller than the smallest bacteria (*M. melitensis*, *M. prodigiosus*) and take on a red color and tone similar to chromatin red. The shape is not spherical but rather bluntly elliptical, olive-shaped. They often lie together in pairs, bound by substance of much lighter color which surrounds them. Exceptionally short or long individuals occur now and then, but in spite of having given particular attention to finding other shapes which might indicate a different kind of development and multiplication other than simple division, I was never able to observe them.

Breeding these microorganisms has as yet failed to succeed either under aerobic or anaerobic conditions, in spite of the addition of albumen-rich ascites, fresh blood, rabbit organs and lice extracts to the culture. Further experiments are still in progress.

Isolated single individuals in tissue or blood smears are presently hardly recognizable with certainty, for they are easily confused with other shapes. Slides in which they occur in very thin concentration are therefore to be looked upon with doubt. In the naturally, as well as in the experimentally infected lice, they are present in tremendous numbers and therefore easy to recognize. The smear slides present the appearance of smears of bacteria cultures.

In the blood of sick persons, I have seen objects with the shape and color of rickettsia prowazekii only within the leukocytes. Without wishing to identify these with certainty, I consider it not improbable that they represent the seeds of the disease slowly circulating in the blood stream. This agrees with the observations of Prowazek, the first to believe that he recognized the causative agent of typhus fever in the "giemsa-carmin-red-colored, distinct, elongated or round bodies and double bodies with fragile bonds." In any case, the prowazek bodies -- and only in the strictest sense of their discoverer -- are the only microorganisms of all those found in typhus fever which can be considered with, albeit an uncertain, probability to be identical with rickettsia in organisms of the louse, the histological examination of the large amount of material which I preserved for this purpose will first give any indication. My investigations have yielded the noteworthy fact that the temperature at which the lice are kept is of great importance in this connection. This discovery might also be a reason for the head louse's not playing as great a role in the transmission of typhus fever as does the body louse, which exists usually only under more favorable conditions of warmth.

When I kept the lice which were fed twice daily on persons sick with typhus fever at about 23°C, no rickettsia developed and these lice proved to be not infected in experiments with animals (guinea pigs). In lice which were fed on typhus fever cases in the same manner but kept at a temperature of 32°C, rickettsia did develop and guinea pigs injected with them became sick almost without exception. Until the fourth day after the initial feeding of lice on patients, the tests for rickettsia, as well as the experiments with animals gave negative results. After the fifth day, both tests gave positive results.

Experiments dealing with the inheritance of the infection in the louse, which are partly still in progress, have already yielded positive results. Here the larvae from eggs laid on the sixth day of the female's infection have been shown to be infected also.

Experiments conducted to date concerning the possibility of the transmission of the infection via the excretions of the louse, which also contain the germs, has as yet yielded no single positive indication.

The methods which I used in these investigations enable me to explain the required amount of blood, the optimum time for extracting blood from patients for the infection of lice, and the time at which the typhus fever patient is most infectious. Later reports will deal with the as yet unfinished experiments dealing with the production of a vaccine from the intestine of an infected louse which is maintained in the form of a culture and with obtaining a serum.

We see that there is still a series of important questions concerning the etiology of the causative agent of typhus fever which must still be investigated. As shown by the progress of my experiments up to this time, work with lice will furnish the best possibility of success in this effort.