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Dear Deborah,

I appreciated your sending me recently Kerr copies of two papers by Charles Nicolle and read them with care; I have also re-read relevant portions of "Rats, lice and History". Various circumstances have interfered with promptly summarizing my findings which might be of interest to you, a delay which I regret, but I hope the analysis will still be helpful.

In the article "Experimental Research on Exanthematic Typhus undertaken at the Pasteur Institute of Tunis during 1909" (published in Bulletin Pasteur de Paris, volume?, pp. 243-275), Nicolle states that, a) he had negative results in preliminary attempts to directly infect M. cynomolgus and M. sinicus individuals with the blood of typhus patients; b) he was successful in producing disease by inoculation of a chimpanzee with blood collected from another patient within a few hours after the appearance of exanthem; c) using human body lice collected from normal patients and fed on the chimp he was able to transmit the disease to bonnet monkeys; d) blood from the latter was infectious for other individuals of this species. In section IV of the paper (with Comte and Comte) he discusses in some detail the transmission of typhus by the body louse, pointing out that: the human louse feeds with equal voracity on man and monkeys, consuming blood rather than epidermal debris; lice must be fed daily if they are to be used for biting purposes; special methods must be employed to maintain lice in captivity. No mention is made here concerning head lice.

The second article is from Re Bull. Inst. Pasteur (Paris, 1920-21?, pp. 49-59). It is a review on the "State of Our Experimental Knowledge of Exanthematic Typhus - an outline of the methods used and problems remaining to be resolved". Nicoll presents his views, with few technical details or references to prior literature. The following points strike me as noteworthy.

1. Typhus exanthematicus is a single disease, world-wide. Reciprocal vaccinations (cross-immunity tests in animals) have shown the identity of typhus of Parisians with that of North Africans, Mexican typhus with that of Brill's disease, etc.

(update)

N.B. In "Rats, their History", Dr. Z. corrects this notion, saying (p. 173 in the Bantam Classics edition): "There are two distinct types of true typhus virus. The diseases they cause in man are identical and both are transmitted from one individual to another by human body and head lice .... they can be distinguished.... Before these distinctions had been recognized typhus had been regarded all over the world as a single disease perpetuated by man - louse - man transfer .... (p 174) most of the work we ~~have~~ discussing has been done since 1928, a good deal is hardly off the presses, and some of it is not yet up to date as these paragraphs are being written". Dr. Z. uses here and elsewhere the term "virus" as synonymous with "microbe".

2. In human typhus transmission, no other arthropod than the louse is implicated - not fleas, not bed bugs, not biting flies nor mosquitoes or ticks. Only lousy people are affected. It is linked to their skin and rags, goes with them and stays until they come to the threshold of the hospital where they find soap, water and clean clothing. Epidemic foci are linked with dirty people and the outbreak of epidemics is linked seasonally with the number of lice found on the person.

3. The louse does not become infective until several days after a blood meal. There seems to be proliferation of the typhus agent in the louse. At the time the

bite becomes infective, the agent is in the gastro-intestinal tract since the louse dejecta are infectious (for monkeys or guinea pigs). Hereditary transmission of the agent in the louse is not demonstrated, contrary to the situation in relapsing fever.

4. Two factors control typhus transmission - a) man, the sole reservoir in Nature, where the <sup>agent circulates in the blood</sup> ~~body~~ exists during more than the extent of the illness;
- b) the louse, of which the bite becomes violent at least 7-8 days after it has fed on a diseased person. The violence of louse dejecta permits a second, indirect mode of contamination — excoriation by scratching of skin soiled with louse dejecta.
5. Children play an important role in the etiology of typhus, since in them the disease is generally mild or inapparent.
- \*\* 6. "The head louse transmits typhus like the body louse". (Nicolle, p.55)
7. Patients freed of their lice are no longer dangerous for others. In well-maintained hospitals, cases of typhus contagion were not observed except in the personnel at the entrance who could not defend themselves against the vermin on patients and their rags which they were obliged to contact. However, cases of lab. contamination or accidents even among doctors have been recorded.
8. If instead of allowing them to bite, one injects infectious lice under the skin of monkeys or guinea pigs, the results are constantly positive; this non-natural route must be a more severe challenge. (Nicolle, p.54)

In "Rats, Lice and History" (Bayliss Classics edition), Tissier states: "The body louse and the head louse carry the infection from one human being to another" (p.165). He accepts and confirms Nicolle's claim (item 6, above), though I haven't yet located experimental data on this specific point. In speaking of the murine variety, H.Z. writes (p.166): From the bite of infected fleas, the human being contracts typhus. This is the sporadic or endemic case - If the victim is lonely, group infection may occur. If he lives in a louse-infected community, the consequence is an epidemic."

(4)

H.Z. conjectured (p.131) that ... "from the several head varieties arose the body louse, when naked man began to wear clothing" and he accepted (p.131) "the relatively recent discovery by Bacot that the head lice of man would intermingle with the body lice and give fertile progeny."

I hope you won't mind the above mention of matters beyond those specific issues on which you sought my thinking. I am convinced that Linssen in the early 1930's concurred with Nicoll's view, expressed more than a decade previously, as to the capability of human head lice to transmit typhus. Since both men believed strongly in the importance of the experimental method as the basis for scientific conclusions, I presume that they were aware of actual trials on this point, although I don't know where the pertinent data are recorded. Let's hope one or other of you will have a revelation —.

Sincerely,

M.F.S.