EXPERIMENTAL INVESTIGATION OF "SIMPLE CONTINUED FEVER."

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LIEUTENANT-COLONEL J. J. GERRARD has drawn attention to the wide prevalence of undifferentiated fevers in Malta (JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, ix., 5, p. 487, November, 1907). The admission-rate for "simple continued fever," 1897-1905, was 142.4 per 1,000 of strength per annum. In 1907 there were no less than 548 cases returned under this heading in the Mediterranean area. This high figure cannot be explained by the well-known fact that the Micrococcus melitensis, typhoid and paratyphoid bacilli may give rise to transient illness with trivial febrile symptoms, though a proportion of the cases may be due to one or other of these infections. Thus in Malta in 1905, out of 750 admissions for Malta fever 100 were first returned as "simple continued fever." ("Report of Mediterranean Fever Commission," part vii., pp. 136 and 158). In an epidemic of enteric fever about 50 per cent. of the attacks are atypical. But as only sixteen admissions for Malta fever and fifty-eight for enteric are recorded for the year 1907, it is clear that another cause is at work to account for the 548 attacks of "simple continued fever."

An important paper by the well-known Austrian Army Surgeon R. Doerr has appeared in the Berliner klin. Woch. for October 12th, 1908, on "A New Invisible Virus." In 1886 Pick described a three-day fever accompanied with severe head- and backache and pain in the lower limbs, exceptionally with vomiting and diarrhoea, sometimes with a polymorphous fugitive rash. It was prevalent during the hot and dry summer months in South Herzegovina and on the Dalmatian littoral, and disappeared entirely in the cold season. It occurred amongst the troops during their first hot weather, and became known to them as "Hundskrankheit," on account of the subsequent weakness and depression. In the official returns it was shown as "endemic gastric catarrh." The mortality was nil. Of late it has been a fertile cause of disability in the Austrian army, and the War Minister ordered a commission to investigate it. Doerr now makes a preliminary report. He states the illness is common in Italy, where it is known as "summer fever," "climatic fever," "summer influenza," or "malarial influenza." In thirty-five cases he abstracted 10 to
20 cc. of blood with which to make cultures; all proved sterile. Serum tests with typhoid, paratyphoid, and Gärtner's bacilli were negative. No protozoa were to be seen by dark ground illumination, or in stained films of the blood. He then resorted to experiments on man, justified by the fact the infection never ends fatally. He took blood from a patient in Herzegovina on the first day of the illness, allowed it to clot, and despatched the serum to Vienna, where the disease was not endemic. Though the serum was three and a half days in transit, 0.5 cc., injected under the skin of his assistant, Dr. Raubitschek, induced a typical attack eight and a half days later. A second experiment with 1 cc. of blood subcutaneously resulted in fever on the fourth day. Blood drawn forty-eight hours after the onset of pyrexia was no longer virulent.

He concluded, therefore, (1) that the virus circulates in the blood on the first day of the fever and that it is also present in the serum; (2) that the blood is no longer infective at the end of the second day; (3) that the virus is resistant and retains its infectivity for three and a half days.

He next took blood from a patient during the first day of the attack, mixed it with physiological salt solution, and filtered some of it through a Berkefeld-Nordtmeyer candle and the rest through a Reichel filter. Two soldiers injected with the respective filtrates developed the disease six days later, though stationed in a non-endemic district.

Taussig had previously noted that stations at a high altitude were free from "Hundskrankheit" and that fresh cases appeared only in the first seven days after transfer from an infected area; dissemination by contagion or through excreta was thus excluded. He was inclined to attribute the diffusion to a species of Diptera known locally as "Pappatici," which are a veritable pest during the hot weather when the fever prevails. Doerr took up this clue. Twice only after many failures did he succeed in infecting men by these flies which had been fed on "Hundskrankheit" patients and conveyed to a healthy locality. He improved his methods of caging, and in a second series of experiments four persons contracted the illness out of eight on whom infected flies had fed. As in the case of yellow fever, the virus must undergo some development in the insect's body, for he found that the "Pappatici" did not become infective until eight days after biting a "Hundskrankheit" patient.

The "Pappatici," or *Phlebotomus papatasii*, belong to the family *Psychodidae*. The genus *Phlebotomus* is characterised by
the body and wings being densely clothed with long hairs, which gives the "owl midge," as it is sometimes named, somewhat the resemblance of a minute moth. The antennæ, palps and legs are long. The proboscis is straight and projects vertically beneath the head. The abdomen of the female is red when distended with blood. It is very small, 1·5 to 2 mm. long, of active and nocturnal habits. Only the females are blood-suckers. The larvae live in water and rotting vegetable matter. They are cylindrical, with a short terminal stigmatic tube. The pupæ have two long tube-like anterior stigmata. Phlebotomus occurs in tropical and sub-tropical climates; Austen does not include it in his "British Blood-sucking Flies." It is found in Southern Europe and the Mediterranean, in Egypt, West and Central Africa, South America and India. Giles states Phlebotomus is most pestilential in the Himalayas during the rains and is equally as troublesome in the plains. This fact may explain the prevalence of short fevers of uncertain origin, 2,553 cases of which appear in the British Army Indian returns for 1907, which entailed a loss of 36,600 days service. In India and Egypt, Phlebotomus is often styled incorrectly a "sand-fly." Rondini says that P. papatasii is found on the higher slopes of hills, as well as in marshy districts. He has observed that the males are often abundant on the windows, the females less so. Giles gives an engraving of Phlebotomus on page 5 of the second edition of his well-known work on mosquitoes. Grassi has published a monograph on the genus ("Ricerche sui Flebotomi," Roma, 1907). Doerr observed that there were few culicæ and no anopheles in the summer at Mostan and Trebinje, where the fever was very prevalent, but that there were swarms of P. papatasii. He experimented with bugs without success. He concludes that the Dalmatian and Herzegovina three-day fever is caused by an invisible virus conveyed by P. papatasii.

Doerr's researches recall to mind those of Ashburn and Craig on 800 cases of dengue at Manila (Journal of Infectious Diseases, June 15th, 1907, p. 440). Their results were as follows: No microorganisms can be demonstrated in fresh or stained blood specimens. The red blood count is normal, and there are no morphological changes in the red or white cells. There is leucopenia, with a relative increase of lymphocytes. Blood cultures are sterile. The intravenous inoculation of dengue blood, either filtered or unfiltered, induces the disease in man. The cause of the disease is, therefore, probably ultra-microscopic. Dengue can be transmitted by Culex fatigans, which is probably the common mode of transmission.
The incubation period of experimental dengue averages three days and four hours. Dengue is not a contagious disease, but is infectious in the same manner as yellow fever and malaria. Certain individuals are immune to dengue.

The points in common between "Pappataciefieber," as it is now known in Austrian army returns, and dengue cannot be overlooked, but the identity of the two diseases is not complete, Doerr's claim for the discovery of a new invisible virus appears substantiated. The list is growing apace; foot-and-mouth disease, horse sickness, hog cholera, rinderpest, pleuro-pneumonia of cattle, yellow fever, are all due to some agent which can pass through a Pasteur-Chamberland filter, and is therefore invisible.

We must now point out the resemblance between "Pappataciefieber" and the Mediterranean "simple continued fever." In the first place we note, on referring to the charts of seasonal prevalence of "simple continued fever" in Malta ("Report of Mediterranean Fever Commission," part vii., p. 140), that it is a disease of the summer months like "Pappataciefieber." Secondly, we note that it occurs chiefly among troops during their first hot weather ("Report of Mediterranean Fever Commission," part vii., p. 142), thus agreeing with the incidence of "Pappataciefieber" mentioned previously. Thirdly, the charts given by Gerrard on p. 490 of the *Journal of the Royal Army Medical Corps*, November, 1907, are similar to those of "Pappataciefieber."

The loss to the army during the year 1907 in the Mediterranean area was nearly 6,000 days service. An experimental investigation is then of economic importance. A small monetary solatium would in all probability induce a number of individuals to submit to the inoculation of a virus which causes no more disastrous effects than three days fever. By this means the etiology of the disease would be unfolded, rational preventive measures could be carried out, and considerable financial loss prevented.