BRITISH MEDICAL JOURNAL

LONDON

SATURDAY JUNE 26 1948

THE EPIDEMIOLOGY OF YELLOW FEVER

In spite of the general interest aroused by many of the medical discoveries which were made during the war, few troubled to speculate how it was that Allied operations were never impeded by outbreaks of yellow fever. This freedom from yellow fever was the more remarkable, for never before in the history of the world have so many potentially susceptible European soldiers had to campaign in lands where yellow fever is endemic.

The yellow fever zone in Africa is now known to extend from the southern border of the Sahara to the Barotse Province of Southern Rhodesia and to Northern Bechuanaland, and from the Atlantic seaboard to the shores of the Red Sea and Indian Ocean. The East African campaign was thus fought out within the endemic yellow fever zone. Many hundreds of thousands of Allied soldiers and airmen tarried unwillingly in Freetown harbour, and at any rate in the earlier years of the war had ample opportunity of confirming the fact, originally demonstrated by Boyle[1] in 1831, that there was no berth in the harbour where one could be free from the ubiquitous mosquito.

From 1940 onwards the air route eastwards from the Gold Coast was one of the Allies' main lines of supply first for the Middle East and later for India and the Far East. To guard this air line as well as to train the quarter of a million West Africans who voluntarily enlisted in the Armed Forces some fifty thousand Europeans from the Navy, Army, and Air Force spent a part of their war service in West Africa. Among all these troops—British, French, American, and African—there were but four cases of yellow fever—one in an African sailor on the Gold Coast and three in European soldiers in Sierra Leone. Two of the four had almost certainly escaped inoculation against yellow fever. This freedom from yellow fever was not due to the disappearance of the disease from Africa. In 1940 there occurred the largest epidemic of yellow fever ever recorded, an outbreak in the Nuba Mountains in the Anglo-Egyptian Sudan involving probably some 30,000 Sudanese. Smaller epidemics also broke out in Spanish and Portuguese Guinea, though of the latter no clear account has yet been published. Sporadic cases likewise were seen in the Gold Coast and Nigeria, while immunity surveys among young children and monkeys indicated that the disease was in fact widely distributed during the years of war.

The freedom of the armed Forces from yellow fever must be attributed to the fact that they were very carefully and systematically immunized against the disease. At the same time immunization was also extended to civilian populations in areas where the new knowledge of the epidemiology of yellow fever indicated that outbreaks might be specially dangerous to the war effort.

The epidemiology of yellow fever in its broad lines is now clear. The fact that the disease is transmitted from man to man by the stegomyia mosquito *Aëdes aegypti* is seen to be only part of the picture. Yellow fever both in Africa and South America appears to be primarily an enzootic or in many cases an inapparent infection of monkeys, transmitted from one animal to another by forest-dwelling mosquitoes. Occasionally an infected forest mosquito may bite a human being, or an infected monkey approaching human habitations may be bitten by a house-haunting *Aëdes aegypti*. If the latter mosquito is common in a village a typical *Aëdes aegypti* outbreak may follow, provided a high proportion of the population is not already immune.

The role of monkeys in the spread of yellow fever was first suspected by Sir Andrew Balfour[2] in 1915, but it was not till 1936 that both in South America[3] and in Africa[4] primates were shown to be immune to the disease. Since then monkeys have been found with immune bodies in many countries of Africa. Durieux *et al.*,[5] for instance, have reported that a high percentage of the baboons on the north bank of the Gambia River are immune. As hordes of three to four hundred baboons not infrequently raid the unfortunate Gambian's farm, this monkey may well be responsible for maintaining infection in this area. In Uganda the lowland colobus monkey, *Colobus polykomos vellensis,* is probably the main species involved in the monkey-to-monkey yellow fever cycle in the uninhabited forest areas, while *Cercopithecus nictitans mpangae* plays an important part in bringing the virus into close contact with man.[6] In Barotseland and Northern Bechuanaland, however, no infected monkeys have been found.[7]

In South America the oecological picture differs again. Thus in an endemic area in Brazil the marmoset *Callithrix penicillata* has actually been found infected on four occasions at a time when an epizootic was occurring among these animals.[8] In Colombia the saimiri monkey, *Saimiri sciureus caquetensis,* is the most susceptible to yellow fever, except in a few areas where its place is taken by the marmoset *Oedipomidas oedipus.*[9] The evidence that marsupials play a part in maintaining infection is less complete.

It seems that the mosquitoes involved also differ in different areas. Lewis,[10] for instance, divides the Anglo-Egyptian Sudan into a number of oecological zones with differing mosquito faunas. Around Malakal, Kaka, and possibly Tonga, on the direct air line from Alexandria to the Cape, *Taeniorhynchus africanus* appears to be the probable vector, for *Aëdes aegypti* has been kept well under control for many years, and none has been found there or in the surrounding country. Yet yellow fever has undoubtedly occurred in this area in recent years.[11] In the Nuba mountains during the great epidemic of 1940 infection was transmitted from man to man probably by *Aëdes metallicus.*[12] In Uganda, in the forest region, the most likely vector is the mosquito *Aëdes africanus,* whose favoured habitat is in the upper foliage of trees. *Aëdes africanus* is a crepuscular or night feeder, and transmission

of the infection to monkeys probably occurs at night when the animals are asleep rather than during the day. In East Africa man is rarely if ever infected in the forest after nightfall. Human infections in Uganda probably result from a secondary cycle in which *Aëdes simpsoni* functions as a vector. This mosquito is a plant-axil breeder and is found principally along the edges of forests and about human habitations.[13] Presumably *A. simpsoni* initially acquires the infection from marauding monkeys, but thereafter the virus may be transmitted from man to man through the medium of this mosquito.

In West Africa, where the extent of tropical rain forest is now somewhat limited, man would seem to be very rarely infected in the forest at night. Infection probably occurs more commonly through infected monkeys raiding farms in the vicinity of villages and thus passing on the infection to *Aëdes aegypti*, which exists in most West African villages. In South America the virus, according to Laemmert and his colleagues,[14] crops up in different places by direct extension through the forest zone. The haemagogus mosquito is the principal vector, and as it is a day feeder woodcutters and others who visit the forest are the victims. Very occasionally *Aëdes leucocelaenus* may transmit infection.

The whole problem of the epidemiology of yellow fever has been complicated by the fact that virucidal bodies have been found in the sera of certain animals which there is good reason to think have never been infected with the yellow fever virus.[15] In addition to cows and sheep, the sera of certain rodents have been found, both in Africa[16] and in South America,[17] to neutralize the yellow fever virus. Of 1,794 rodents tested in one endemic area in Brazil 449, or 25%, were positive, but, contrary to what would be expected of an acquired specific immunity, the proportion of positive reactors did not increase with age.

A further complication is the finding of virucidal bodies in the blood of certain birds in West Africa,[16] in an area of South Africa[7] where primates gave negative results, and in Brazil.[14] Of 114 birds examined in Brazil the blood of 3 inactivated virus, in South Africa 2 of 6, and in West Africa 4 of 40. Laemmert and Moussatché,[17] working with laboratory strains of yellow fever virus, have found that it will circulate in the blood stream of birds for several days after injection, but attempts to infect birds by mosquitoes have not been very successful. Elucidation of the origin and nature of these virucidal bodies, which are not found in every specimen but in only a small percentage of certain species of animals and birds, is a matter of considerable importance not only for the epidemiology of yellow fever but for the study of virus diseases in general.

1 *A Practical Medico-Historical Account of the Western Coast of Africa*, 1831. S. Highley, London.
2 *Trans. roy. Soc. trop. Med. Hyg.*, 1915, **8**, 75.
3 Soper, F. L., *Quart. Bull. Hlth Org. L.o.N.*, **5**, 19.
4 Findlay, G. M., *et al.*, *Trans. roy. Soc. trop. Med. Hyg.*, 1936, **29**, 419.
5 *Bull. Soc. Path. exot.*, 1947, **40**, 111.
6 Haddow, A. J., *et al.*, *Trans. roy. Soc. trop. Med. Hyg.*, 1947, **40**, 677.
7 South African Institute for Medical Research, *Annual Report for the Year ended December* 31, 1946, p. 21. Johannesburg, 1947.
8 Laemmert, H. W., Jr., and Ferreira, L. de C., *Amer. J. trop. Med.*, 1943, **23**, 227.
9 Bates, M., *Scient. Monthly*, 1946, **63**, 42.
10 *Bull. Ent. Res.*, 1947, **37**, 543.
11 Findlay, G. M., *et al.*, *Ann. trop. Med. Parasit.*, 1941, **35**, 121.
12 Lewis, D. J., ibid., 1943, **37**, 65.
13 Smithburn, K. C., and Haddow, A. J., *Amer. J. trop. Med.*, 1946, **26**, 261.
14 Ibid., 1946, **26**, Suppt., p. 23.
15 Findlay, G. M., *Trans. roy. Soc. trop. Med. Hyg.*, 1941, **35**, 51.
16 Findlay, G. M., and Cockburn, T. A., *Nature, Lond.*, 1943, **152**, 245.
17 Laemmert, H. W., Jr., and Moussatché, H., *J. infect. Dis.*, 1943, **72**, 228.

GOLDEN JUBILEE OF R.A.M.C.

This week the R.A.M.C. celebrates the Golden Jubilee of its foundation in 1898, when Queen Victoria signed the royal warrant stating: "Our Will and Pleasure is that the officers below the rank of surgeon-major-general serving in Our Army Medical Staff shall be formed into a corps, together with the warrant officers, non-commissioned officers, and men of Our Medical Staff Corps; it is Our further Will and Pleasure that the designation 'Medical Staff Corps' shall be abolished, and that the corps formed as above-mentioned shall be styled 'The Royal Army Medical Corps.'" Before the standing Army was raised in 1660 medical men engaged in warfare were the personal attendants of high officers. In that year the few medical officers and orderlies incorporated in the Regular Army wore the uniforms of their regiments, and except for some garrison and general hospitals the medical service was regimental. Apothecaries and a number of lay officers for administration and supply swelled the ranks, but the medical arrangements in the field were often disorderly, though during the Napoleonic wars the sick and wounded received considerably more attention than formerly. Not until 1854 was the Hospital Conveyance Corps formed—solely to evacuate the wounded. It proved to be a failure in the Crimean war, chiefly because it consisted of old and feeble pensioners, and it was incorporated in the Land Transport Corps the following year, thus in effect being a predecessor of that part of the R.A.S.C. that has always co-operated so well with the R.A.M.C. In 1855 the Medical Staff Corps was created by royal warrant; its personnel had neither military titles nor badges of rank, and the sole officer appointed to it (a regimental officer) lived at the depot at Chatham. Naturally enough, this corps was not a success either, and two years later the Royal Will and Pleasure ordered the Army Hospital Corps to be raised forthwith. Its ranks were serjeant-major to private, and were filled chiefly by volunteers from the line and from the Medical Staff Corps. Subsequently some medical and other officers were appointed to it, though their duties were strictly limited. Only inferior medical men presented themselves for service in the Army,[1] and a B.M.A. deputation therefore waited on Lord Lansdowne on Jan. 20, 1898, to advocate the formation of a medical corps with proper ranks. He welcomed the proposals, and the royal warrant appeared on June 23.

It is sometimes said that the Forces' medical services developed as man became more humane. There is little evidence that he has, and in any case there were other more important causes of their growth. Healthy soldiers fight better than ill-nourished and diseased men inspired only by enthusiasm for fighting. Morale is better sustained when men know that they receive early treatment if they are wounded and that they have a high chance of recovery; and the healed can be returned to battle or some other war-winning occupation. Moreover, medicine itself has developed so much in the last 50 years that it is now indispensable for waging war efficiently. A century ago military surgeons could do little to help the sick and wounded

1 *British Medical Journal*, 1898, **1**, 236.
2 Ibid., 1947, **2**, 219.
3 *Jubilee Scrapbook of the R.A.M.C.*, 1948. Aldershot: Gale and Polden.