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COLLABORATIVE STUDIES ON THE BIOLOGICAL PROPERTIES OF  
DIFFERENT STRAINS OF THE MALARIA PARASITES.

The Medical Director has the honour to communicate a Progress Report on work at the Ministry of Health's Malaria Laboratory at Horton on strains of malaria parasites from Roumania by

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P. vivax. The strain of benign tertian malaria which has been used during the last 8 years for the practice of malariatherapy in England is cultivated in mosquitoes (*A. maculipennis*) at the Ministry of Health's malaria centre at Horton. It came originally from Madagascar. Since 1925 it has undergone 112 passages through mosquitoes (*A. maculipennis*) at the Ministry of Health's malaria centre at Horton. It came originally from Madagascar. Since 1925 it has undergone 112 passages through mosquitoes with which more than 2000 patients in different hospitals in England have been infected. The characters and properties of the strain in the human and insect hosts in England have been described in various publications and are now so well known that they can be used as a standard with which the characters and properties of other strains of the same species may be compared.

Early in 1933 opportunity was taken of the arrangements for co-operation organised by the Malaria Commission of the League of Nations to visit the Socola malariatherapy centre in Roumania and to bring back to Horton mosquitoes infected with a benign tertian strain indigenous in that country. It was obtained at the time of our visit (May 1933) from a child ("Apostol") who contracted the infection naturally in a village. The strain was brought to Horton in the stage of oocysts in mosquitoes. It is known at Socola and Horton as the B.T. Ap strain. At Horton between May 1933 and April 1934 it has undergone nine passages in mosquitoes and is now established as the strain of benign tertian malaria which will replace the Madagascar strain for the routine practice of malariatherapy in England.

This being so it will now be possible to commence and to carry on continuously a series of studies with this strain which will enable its characters and properties to be compared with those of the Madagascar strain already studied.

Difficulty of establishing the strain in English mosquitoes and patients. It is surprising that nearly a year elapsed before we were in a position to decide that we could maintain the strain in English mosquitoes and patients with the same ease and confidence as we experienced with the Madagascar strain. The long period was due to the fact that hardly any patient who was infected with the strain during the first few months after we brought it to Horton developed more than a very few gametocytes in the peripheral blood. The consequence was that never more than three or four oocysts could be found on the stomachs of mosquitoes fed upon patients. For a long time it seemed as if this paucity of gametocytes would prove to be an important difference between the Roumanian and the Madagascar strains. However, after the strain had undergone two or three passages through mosquitoes some of the patients bitten developed a larger number of gametocytes and by carefully selecting the best time for feeding mosquitoes upon these patients we were able gradually to obtain a batch of mosquitoes with an average of 102 oocysts on the stomach wall. Since then we have had no difficulty in maintaining the strain because large numbers of gametocytes appear in the blood of patients bitten by those heavily infected insects. The clinical course of the disease has also become more regular thus facilitating comparison with the clinical course in patients infected with the Madagascar strain.

It is of interest to note that Dr. Chelarescu, using precisely the same technique at Socola, has not as yet obtained heavily infected mosquitoes with this strain. She writes: "I find it difficult to keep this strain going: gametocytes are so rare that only a few of my anopheles become infected, and, even when they do, only very few oocysts are present".

If this difficulty continues the question will arise whether it is to be attributed to a biological property of the strain or to the fact that Roumanian patients already possess some degree of immunity to the indigenous strain. The experience at Horton is that gametocytes develop in greater numbers in non-immune patients than in those who possess even a feeble immunity. In the Madagascar strain of benign tertian malaria at Horton they are most numerous between the 7th and 15th day of the primary attack. Then their numbers gradually diminish even when fever and asexual parasites persist. In a relapse they reach their maximum number about the third day of fever and then their number quickly falls. In chronic cases they are seldom or never found.

Thus a possible explanation of the continued lack of gametocytes in patients at Socola may be that all the patients hitherto inoculated with the strain already possessed some degree of immunity to it prior to their inoculation.

The problem is sufficiently important to justify a repetition of the procedure of transporting the strain again to Horton (or to some other centre in a country free from local malaria) where it can be ensured that patients who are completely non-immune will be available.

P. falciparum. Of this species the Roumanian strain which was being used in the routine practice of malariatherapy at Socola and was in its 82nd passage was brought to Horton in defibrinated blood and inoculated into a patient on 27th May, 1933. The attack began on the 9th June. A second patient was inoculated

from the first on the 15th June and from this patient a batch of mosquitoes (*maculipennis*) was infected. Since then the strain had been successfully maintained in mosquitoes (5 batches) and has been used for infection in 40 cases of which 25 were for the purpose of testing quinine, atabrin and plasmoquine as true causal prophylactics.

The number of patients who were permitted to continue their malarial attack for more than a very few days is not yet sufficient for comparison of the clinical course with that caused by other strains or with the effects as observed in Roumanian patients at Socola. It is probable, however, that the strain will prove to be less virulent than the Italian strains which we studied but perhaps more virulent than the West African and Indian strains. Up to the present the numbers of crescents in the peripheral blood of different patients have been very variable. There have been many in the blood of some patients, none in others. From patients whose blood contains crescents our mosquitoes (*maculipennis*) readily become infected. In this respect the strain resembles our strains from Italy and differs from our Indian strains.

Remarks. For unavoidable reasons (particularly the small number of patients and lack of separate laboratory accommodation for insects infected with different species of parasites) we have been obliged to give up endeavouring to carry on various other species or strains which we brought from Roumania as well as some other items of the collaborative work which was initiated during interchange visits between workers at Horton and Socola. Our intention at present is to continue to use the Roumanian B.T. Ap strain cultivated in mosquitoes as the routine malarial therapy strain at Horton and elsewhere in England for several years until sufficient information has been obtained about it to enable its characters and properties to be described in the same manner as has been for the Madagascar strain.

Our study, of course, will be concerned with the characters and properties of the strain in English patients and mosquitoes. A similar study of the characters and properties of the strain in Roumanian patients and mosquitoes is being made at Socola.

Our Madagascar strain which we have ceased to use at Horton will be continued at Socola to enable a description to be written of its characters in Roumanian patients and mosquitoes.

With the same objects in view we shall also continue to carry on at Horton the Roumanian strain of *P. falciparum* as long as possible.