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ECONOMIC ADVISORY COUNCIL

East Africa Sub-Committee of the Tsetse Fly Committee

REPORT

*Presented to Parliament by Command of His Majesty
July 1935*

LONDON

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ECONOMIC ADVISORY COUNCIL.

EAST AFRICA SUB-COMMITTEE OF THE TSETSE FLY COMMITTEE.

Terms of reference and composition.

On the 23rd May, 1934, the Secretary of State for the Colonies communicated to the Economic Advisory Council the report of the Conference on Tsetse and Trypanosomiasis (Animal and Human) Research, held at Entebbe in November 1933; and on the 1st June, 1934, he forwarded a copy of a letter, with enclosure, dated the 16th May, 1934, from the Secretary of the Conference of East African Governors, reporting the conclusions of the recent Governors' Conference on the subject of tsetse and trypanosomiasis research. The Secretary of State asked that he might be furnished with the observations of the Council's Tsetse Fly Committee on these papers.

2. On the 3rd July, 1934, the Earl of Plymouth, Chairman of the Tsetse Fly Committee, appointed an East Africa Sub-Committee of that committee to prepare a report on these questions to be submitted to the Economic Advisory Council for transmission to the Secretary of State for the Colonies.

3. The sub-committee is composed as follows:—

Mr. Francis Hemming, C.B.E., Secretary, Economic Advisory Council. *Chairman.*

Dr. W. Horner Andrews, M.R.C.V.S., Director of Veterinary Research, Ministry of Agriculture and Fisheries.

Sir Arthur G. Bagshawe, C.M.G., M.B., Director, Bureau of Hygiene and Tropical Diseases.

Sir Guy A. K. Marshall, C.M.G., D.Sc., F.R.S., Director, Imperial Institute of Entomology.

Mr. F. G. Lee, Colonial Office.

Sir Thomas Stanton, K.C.M.G., M.D., F.R.C.P., Chief Medical Adviser to the Secretary of State for the Colonies.

Dr. C. M. Wenyon, C.M.G., C.B.E., F.R.S., Director-in-Chief, Wellcome Bureau of Scientific Research.

Mr. D. H. F. Rickett, Assistant Secretary, Economic Advisory Council. *Secretary to the sub-committee.*

*Trypanosomiasis : pp. 38 (593), 46.
C.A.H. : p. 36 (589)
Tsetse fly :*

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REPORT.

EAST AFRICA SUB-COMMITTEE OF THE TSETSE FLY COMMITTEE.

I.—INTRODUCTORY.

IN accordance with the duty laid upon us in our terms of reference, we have given careful consideration to the report of the Conference on Tsetse and Trypanosomiasis (Animal and Human) Research held at Entebbe in November 1933. In considering that part of the report which relates to the work of the Human Trypanosomiasis Institute, Entebbe, we have also had before us the report of the discussions which took place at the Governors' Conference at Nairobi in May 1934, transmitted to the Economic Advisory Council by the Colonial Office in a letter dated the 1st June, 1934. The following report embodies the observations which we recommend should be submitted on these two documents to the Economic Advisory Council for transmission to the Secretary of State for the Colonies.

2. Amongst the subjects which we have had to consider one of the most important has been the question of the future of the Human Trypanosomiasis Institute, Entebbe. We have received valuable assistance in this part of our inquiry from Dr. H. Lyndhurst Duke, O.B.E., the Director of the Institute, and Dr. W. H. Kauntze, M.B.E., Director of Medical Services, Uganda, who attended a meeting for the purpose of discussing this question with us, together with other matters arising out of the report of the Entebbe Conference. In addition, we are much indebted to Dr. Edward Mellanby, F.R.S., Secretary, Medical Research Council, for the assistance which he has given us in regard to the co-operation which might be obtained from the Medical Research Council in carrying out certain investigations suggested by the Conference.

3. In dealing with a subject involving the consideration of a large number of detailed items mainly technical in character, we have thought it convenient to preface our discussion with a general outline of the problem as a whole. In section II, therefore, of our report, we describe briefly the main characteristics of trypanosomiasis, both animal and human, and the principal methods available for controlling it. In the course of our account of these methods of control, we have found it convenient to include our recommendations in regard to certain items of research recommended by the Conference, which are directly concerned with the development of those methods. We have thus been free in section III to confine ourselves to the

discussion of items of fundamental research, the object of which is to obtain further knowledge of the causes of the disease. In section IV we discuss briefly the necessity for maintaining adequate contact between the scientific work on these subjects being carried out in Africa and similar research work in other parts of the world. In section V we give a summary of our principal conclusions and recommendations.

4. It will thus be seen that the arrangement of our report differs from that adopted in the report of the Entebbe Conference. The arrangement of that document corresponded with the order in which the various subjects appeared on the agenda for discussion at the Conference, in accordance with which items of research were dealt with in the report under two heads, the first containing subjects for inquiry suggested in the report of the Second International Conference on Sleeping Sickness, the second those subjects which had been suggested by investigators in the various East African territories. In a third section the report dealt with the future of tsetse and trypanosomiasis research generally in East Africa. This system of arrangement, while obviously convenient for the purposes of the report of the Conference, did not appear well adapted to the manner in which we ourselves desired to treat these subjects. In order, however, to facilitate reference between this report and the report of the Conference, we print as appendix 1 a summary of the programme of East African tsetse and trypanosomiasis research similar to that which appears on page 26 of the report of the Entebbe Conference, and we have added to it two further columns giving references to those sections of the report of the Conference and of our own report respectively in which the various items of research are discussed. We have attached also as appendix 2 to our report a note prepared for us by Sir Arthur Bagshawe, one of our members, on diagnostic methods in human trypanosomiasis, a subject which we regard as being of considerable importance and to which we refer in paragraph 76 below.

II.—THE CONTROL OF TRYPANOSOMIASIS IN MAN AND ANIMALS.

(a) General character of the problem.

5. In discussing trypanosomiasis in this report we deal only with the diseases known as sleeping sickness in man, and as nagana or tsetse-fly disease amongst animals. Both are endemic or chronic over a considerable part of Africa where their existence had been observed by at least the early part of the last century. Even in this form they are of considerable severity and a serious hindrance to the prosperous development of the areas affected. But at various times from causes which are still imperfectly understood, both in the Belgian, French and Portuguese territories in the Congo, and above all in the Uganda Protectorate in the years 1900–1909, epidemics of extreme violence have occurred decimating the whole population over a wide area. Epizootic outbreaks amongst domestic stock have been still more frequent. In many territories they render impossible the use of animals for transport. Moreover, amongst tribes for whom the ownership of cattle is both a source of wealth and the basis of social custom, losses of stock through trypanosomiasis have led to the moral degeneration as well as to the impoverishment of native communities.

6. As the name implies, the causal agent of the disease is the trypanosome, a protozoal germ or parasite with which the blood becomes infected. These germs are spread by the bites of the tsetse fly, and it is the presence of this insect in its various species over very wide areas which constitutes the special danger of trypanosomiasis to man and animals in Africa. Infection may be transmitted in one of two ways. The proboscis of the fly may become contaminated while feeding upon the blood of an infected subject, and the germs transmitted directly to the blood of a second host upon which the fly next feeds. This process of direct or so-called mechanical transmission was formerly supposed to be the only method of infection (see paragraph 15 below). It is still believed by some to be the normal process during the occurrence of epidemics. But investigation has shown that the most usual sequence is that known as cyclical or biological transmission. In this the germs are not transferred direct from host to host, but are absorbed by the fly, in the body of which they pass through various phases of development. At the conclusion of a period which varies from 14 to 28 days or longer the cycle of change is complete, and the trypanosomes, either in the proboscis or in the salivary glands, regain the form in which they were absorbed from the blood of the infected animal, and the fly then becomes a potential source of infection. It should, however, be added that in a very large percentage of the flies which absorb the germs into their system this cyclical process of development is never completed. These flies are incapable of transmitting infection.

7. Though the tsetse fly is thus the immediate source of trypanosomiasis infection and an essential factor in the spread of the disease, the part it plays is limited to that of an intermediary. It transmits infection, but it is not itself the origin of it. Experiments on one of the principal species have shown that a fly retains its infectivity for upwards of 96 days. But since flies are incapable of infecting one another, it is clear that if all other sources of infection could be excluded from one area, the disease would after a short time disappear, and the country though not fly-free would be free from trypanosomiasis infection. When during the final stages of the great outbreak of sleeping sickness in Uganda in 1909 it was decided to evacuate the population (amounting to 24,000 persons) from the Buvuma and Sesse Islands and from the shores of lake Victoria, it was hoped not only that the epidemic would be stopped, but also that after a few years the fly would become non-infected and harmless, and that it would then be possible to allow the population to return to the lake shores. An examination however four years later of flies caught in the area showed that they were heavily infected with germs which were thought to be those of human trypanosomiasis. The most plausible explanation was that though the human population had been evacuated, the game population remained, and that the antelope served as a reservoir from which the fly drew infection. In the meantime laboratory experiments had shown that cattle and several different species of antelope could be infected by feeding an infected fly upon them and that these cattle and antelope in their turn could transmit the infection to a previously uninfected fly.

8. It thus became evident that in addition to the two principal elements of the sleeping sickness problem, man, and fly, there must be added a third in the game population (wild ungulates), together with the subsidiary element of domestic animals. It was from a proper inter-relation of these factors that a correct understanding of the propagation of the disease was to be derived. Unfortunately there were many complicating circumstances. In the first place it soon became known that the germs of the infection were not by any means the same in every case. Six years after the discovery in human beings of the trypanosome later named *Trypanosoma gambiense*, Dutton, 1902, a second species, subsequently named *Trypanosoma rhodesiense* Stephens and Fantham, 1910, was discovered. The latter is the causal agent of the Rhodesian form of sleeping sickness, which differs from the Gambian form in being of greater virulence and more resistant to treatment. It is moreover associated with a different species of tsetse fly, *T. gambiense* Dutton, being conveyed in East Africa by *Glossina palpalis* (Robineau-Desvoidy, 1830); and *T. rhodesiense* S. & F., by *Glossina morsitans* Westw., 1850, and by *Glossina swynnertoni* Austen, 1922. In addition to these two species of human trypanosome there are a number of trypanosomes which are responsible for the disease in animals. The principal of these are *Trypanosoma brucei* Plimmer and Bradford,

1899; *Trypanosoma congolense* Broden, 1904; and *Trypanosoma vivax* Ziemann, 1905. To each of these principal species must be added a number of closely allied but less important forms.

9. Accurate knowledge of the relation between these varying species of parasite is clearly of great importance to the understanding of the disease, the characteristics of which vary appreciably according to the species of germ producing it. Thus, as regards the relation of human to animal trypanosomiasis it is known that man is practically speaking immune to infection by two of the principal trypanosomes found in domestic stock, *T. congolense* Broden and *T. vivax* Ziemann. Similarly, it has been shown that *T. gambiense* Dutton, one of the two parasites which produce sleeping sickness, though it can infect animals both wild and domestic is not strongly pathogenic to them. The germs multiply in their blood but do not produce violent symptoms of disease. Much controversy however has developed over the question of the relation of the second of the two human parasites *T. rhodesiense* S. & F., to an important species of animal trypanosome, *T. brucei* P. & B. It has been asserted by British workers that these two species are in fact the same, while various foreign authorities have maintained the contrary view. The special importance of this controversy lies in its bearing upon the question not only of the relation of human and animal trypanosomiasis but also of the part played by game as a reservoir of infection. As we have already mentioned, it has been shown by experiment in the laboratory that game animals can be infected with both species of human trypanosome. For some years, however, no evidence had been obtained to show that the Rhodesian form of infection actually existed in game animals. In 1912, however, Kinghorn and Yorke claimed to have found that 16 per cent. of the game in the Luangwa Valley in Northern Rhodesia were infected with *T. rhodesiense* S. & F. This conclusion was questioned by German workers, notably Kleine, Taute, Fischer and others, who asserted that the trypanosome found in the game was *T. brucei* P. and B., and that this species, while closely related to *T. rhodesiense* S. & F., was not, in fact, the same. In particular, German workers claim to have shown by subsequent practical investigations involving human inoculations that *T. brucei* P. & B. cannot give rise to sleeping sickness in man.

10. Whatever the outcome of this controversy, there still remain further questions which must be answered before it can be assumed that game plays an integral part in the spread of human trypanosomiasis. Even if it be admitted that game animals can and do become infected with the human species of trypanosome, and thus act as a reservoir from which tsetse flies, hitherto uninfected, may draw the virus, it is still doubtful for how long the germs thus stored up in the blood of the animals retain their power to infect man. We shall refer to this question in a later paragraph in discussing the

work which Dr. Duke has been pursuing at the Human Trypanosomiasis Institute, Entebbe (see paragraph 70 below). We have discussed this subject at some length here in order to illustrate the manner in which fundamental research of an apparently abstract character may not only throw light upon theoretical questions regarding the disease, but may also have a determining influence upon the methods of controlling it.

11. The development of measures to control trypanosomiasis has naturally been bound up with the advance of knowledge in regard to the cause of the disease. New discoveries in knowledge may therefore bring about important changes in the methods of control adopted. Broadly speaking, however, at the present stage of development, the methods of control are of three kinds: (i) administrative methods, such as the evacuation of population from an infected area, the control of movements of population (in search of work, &c.), the clearing of water places, and the concentration of settlement; (ii) the control of tsetse flies; (iii) control by chemotherapy, that is to say, treatment by means of various drugs. In succeeding sub-sections we discuss briefly these three types of control, and state our recommendations in regard to specific forms of research which we think should be carried out with a view to their improvement.

(b) Control by administrative measures.

12. In addition to the treatment of sleeping sickness by drugs and the launching of direct attacks upon the tsetse fly, there are various other methods by which the interaction of the factors leading to a spread of the disease may be altered or checked. These are usually referred to as administrative methods of control. Broadly they represent an attempt to prevent or eradicate infection by controlling the movements of population.

13. There seems to be little doubt that the spread of sleeping sickness in Africa has been largely assisted, if not caused, by the development of the means of communication which took place at the end of the last century. It is an obvious precautionary measure in restricting the incidence of the disease that infected persons should not be at liberty to migrate where they please in search of a market for their labour or their produce. It is equally plainly a wise precaution that fishing in lake areas which are known to be infested with fly should not be permitted except under close control, and access to watering places similarly endangered should only be allowed after clearing of the bush has driven back the fly.

14. Such measures as these may be looked upon as part of the routine to be observed in preventing the spread of infection. But administrative control in the wider sense has a larger scope than this. In its various phases the policy of controlling population movements has in most cases been designed to play a large part in furnishing

a solution of the sleeping sickness problem. Amongst the various ways in which the method can be applied, the most drastic and the most obvious is the evacuation of the population from an area affected by an outbreak of sleeping sickness. Frequent contact between man and fly is one of the first essentials in the transmission of infection. If all contact between the population and the fly is severed, the immediate result at any rate must be to cause a halt in the spread of infection.

15. In the great outbreak of sleeping sickness in Uganda the withdrawal of a large section of the population undoubtedly had the effect of preventing the further transmission of the disease. In the light, however, of the scientific knowledge existing at that time, it was expected to do more than this. At that time Sir David Bruce's theory of mechanical transmission of the trypanosomes still held the field (see paragraph 6 above). The process whereby tsetse flies themselves become infected was unknown; and the part which might be played by wild animals as a reservoir of infection was unsuspected. In these circumstances it was natural to suppose that complete severance of contact between fly and population would suffice to destroy infection in the fly almost immediately. It was anticipated that the population itself could be purged of all infection in at most three years. The withdrawal of the population would ensure, therefore, not only the interruption of the epidemic, but also the reclamation of the affected areas. At the end of three years it would be possible to re-occupy the tsetse areas with as little danger of infection as existed before the germ was first introduced into the tsetse in that area.

16. Subsequent discoveries in regard to the transmission of the disease have shown that there is little prospect of success for such a policy, if unaccompanied by direct attempts to exterminate the fly. Indeed, experience has shown that temporary withdrawals of the population would tend too often in practice to become permanent. The resulting situation must necessarily exercise grave effects upon the industry of the areas concerned. Moreover, even as a means of escape from infection by fly, this policy, if adopted generally, would be futile. The outbreak in Uganda was caused by the parasite known as *T. gambiense* Dutton, which is transmitted by a species of fly, *G. palpalis* (Rob.-Desv.), found only on lake shores and the banks of rivers. In the case of this fly it is in consequence possible to withdraw population into regions where it cannot follow. But the distribution of other species is not similarly restricted. In particular, *G. morsitans* Westw., the fly which transmits both the parasite of the Rhodesian form of sleeping sickness and also one of the most important kinds of animal trypanosome (*T. brucei* P. and B.), is ideally suited to the type of bush which springs up wherever land previously cultivated has been abandoned. Moreover, the absence of population promotes the growth of bush and the spread and multiplication of game animals, and though in some

instances the second of these factors may neutralise the first,* they more usually operate together to assist the advance of fly.

17. Bush, game, and fly may thus be said to represent a hostile coalition before which retreat is unavailing, and the best method of defence is attack. We deal later with the methods which are being worked out for the reclamation of infested areas by the destruction of the fly. But in addition to direct attacks of this kind, experience has shown that the most effective means of holding up the advance of fly is by the concentration into closer settlements of scattered native populations. These measures are effective in meeting other problems besides that of tsetse fly. Small native communities living in proximity to unsettled areas suffer from the depredation of their crops by wild animals such as elephant and from loss of stock due to contagious diseases such as rinderpest and snotsiekte spread by game. But in addition to this it is beyond their power to keep the country surrounding them free from bush, from game animals, and hence from fly. They are constantly exposed to infection with sleeping sickness, particularly where they engage in primitive forms of agriculture such as the collection of gum and wild honey which take them far afield. Where their liberty of movement is not restricted they may easily become the means of spreading infection into more thickly populated areas.

18. All these dangers can be avoided by the policy of closer settlement. The principle on which it is based is that the movements of population and the course of agricultural development should be so directed as to restrict the distribution of the fly by destroying the environment which it requires for its existence. Concentration of the population in this sense is entirely different from a policy of concentration such as we have described above, which implied the withdrawal of the population to uninfected and more densely populated areas. The method which it follows is that the natives should seek safety in numbers and should live in settlements of sufficient size to keep back the fly. It has been found that a settlement with a minimum population of 3,500 to 4,000 is large enough to secure freedom from fly roughly two years from its establishment. Even where, however, settlements are smaller than this, concentration is of value in facilitating early treatment with drugs of any sleeping sickness cases which occur.

19. The Entebbe Conference devoted considerable time to the discussion of this method of control. Dr. G. Maclean, Sleeping Sickness Officer, Tanganyika, described the principles which had been worked out in applying it in that territory. He pointed out that these settlements were not mere expedients designed to facilitate treatment, or control a passing epidemic, but were intended to be

* *e.g.*, in the Sesse Islands, where the sitatunga increased in such numbers after the removal of the population that the bush was kept under and the breeding thickets of the fly were destroyed.

the basis of permanent settlements in which economic development could proceed unchecked and the general standard of living could be raised. The Conference as a whole accepted the view that organised settlement and development of this nature was ordinarily the most important general preventive measure which could be taken by administrations in the campaign against tsetse fly and trypanosomiasis. They were, however, agreed that such development, in order to be effective, must take into account many different aspects of human and animal environment and must include measures for the improvement of agriculture and animal husbandry as well as measures to safeguard the health of the population. They emphasised that this could only be achieved by the closest co-operation between the various departments concerned and the co-ordination of their activities. They therefore concluded their recommendations on this subject by appealing for "organised inquiry into the best means of carrying out such concentrations and settlements, and their subsequent development."

20. It will be clear from all that has been said in this section of our report that we fully share the view of the Conference regarding the importance of the concentration of population as a means of combating sleeping sickness. Like them, we believe that such measures are amongst the most important methods which can be employed in the campaign against tsetse fly and trypanosomiasis. Moreover we can well understand that the application of this policy and its working out in detail is a task which requires constant co-operation between the many departments interested. We are, however, in some doubt as to the intention of the Conference in recommending organised inquiry into these matters. If it is suggested that some central body should be set up either in Africa or in the United Kingdom to conduct a general investigation into the principles to be adopted in applying the method of closer settlement, we should feel considerable doubt as to the wisdom of such a course. The task of controlling native settlements and securing for them a permanent basis upon which sound economic development can proceed must clearly in our view vary greatly according to the nature of the area and the characteristics of the native tribes concerned. Nor are we satisfied that the many individual problems of adjustment which arise in the course of working out a smoothly running scheme of inter-departmental co-operation are such as to be capable of being discussed in general terms which will be uniformly applicable.

21. If, however, it is the intention of this recommendation that within each administration and within its various sections the occasion should be taken as and when opportunities offer to set up small *ad hoc* bodies to secure an adequate machinery for consultation and discussion of problems as they arise, that is a course which would appear to us to have many advantages.

(c) The control of tsetse flies.

22. Important as is the part played by the concentration of native settlement in checking the incursions of fly and preventing the spread of trypanosomiasis infection, it is not in itself a sufficient defence against this danger. In the first place, even where such settlements are planned upon a liberal scale, the need for expansion will in course of time make itself felt. The native will require more land for cultivation or to provide grazing for his cattle. Moreover the mere fact of concentration, involving as it does removal of the population from scattered contact with the fly, entails greater freedom of advance for the fly even though it provides greater safety for the population. The concentration of population must, therefore, if it is to succeed, be coupled with active measures for reclaiming areas already infested and for holding up the advance of the fly over a wide front.

23. The problem of tsetse fly control is one which affects in varying degree every territory in East Africa which is subject to infestation. From the outset, however, the main part of the research work directed to the discovery of methods of control has been concentrated in a single specialist department established in the Tanganyika Territory. Much valuable work is being carried out on tsetse research at the same time in other territories. In view, however, of the leading part played by the Tsetse Research Department in Tanganyika, this section, dealing with the control of tsetse fly, is in large measure devoted to an account of the results and progress of the work proceeding in Tanganyika under the direction of Mr. C. F. M. Swynnerton, Director of Tsetse Research in that territory.

24. How large the areas of infestation may sometimes be may be judged from the fact that in Tanganyika the biggest fly-belt is 500 miles at its longest by 300 miles at its widest point. It is evident that a problem of this magnitude can only be dealt with if means are found whereby these great tracts of territory can be split up into areas of a more manageable size. Once the fly-belt has been subdivided by means of suitable barriers into a number of small compartments from which the flies cannot escape, the task of eradication will be greatly simplified. Moreover, such barriers, combined with suitable measures for preventing the reintroduction of flies by human beings or by wild animals, serve to guard against the danger of the reinfestation of areas which have already been reclaimed.

25. The creation of these barriers will often be assisted by natural features such as a patch of wood unsuited to the fly or an unbroken stretch of thicket. Concentrated settlement such as we have already described should also play an important part in their formation. But in addition to this, various methods of creating artificial barriers have been devised in recent years. These methods are essentially the same in principle as those employed for the

general eradication of the fly. Both depend upon the artificial creation of conditions which are known to be unfavourable to the fly, as for example, by the cutting down of bush, the planting of deciduous thickets, or the production of natural thickets by protecting selected strips of land from grass fires. In general, it may be said that one of the most important developments which have been taking place recently in tsetse research is the employment, as a means for controlling the movements of flies, of methods which were originally conceived as methods for the wholesale destruction of flies. Thus, the fly barriers we have described may often be useful not only for the sub-division of a fly-belt as a preliminary to a general attack on it, but also for the purpose of isolating an infested area the reclamation of which is not considered to be an immediate necessity. In view of the vast size of the problem, and of the expense and other difficulties connected with bush-clearing upon a large scale, the evolution of methods of control on these lines represents a development of great value in the field of anti-tsetse work.

26. Of the methods for the actual eradication of flies within a given area, one of the first to be adopted was wholesale clearing of bush. From the outset it was known that if the bush in which the flies lived were cut down, they would disappear. But clearing on a large scale with paid labour was impossible owing to the prohibitive cost. This obstacle has in part been overcome in the Tanganyika Territory where Mr. Swynnerton, working with the Administrative Officers, has succeeded in persuading some thousands of natives to co-operate voluntarily for a short period each year in schemes of reclamation by clearing. This method is, however, of limited application, since it can only be employed in areas peopled by cattle-owning tribes who are both willing and able to work together in combination.

27. Moreover, the results of felling the bush present at once a series of subsidiary difficulties. If the clearing is not occupied by cultivation, vegetation springs up again and the resulting coppice is ideally favourable for some of the most dangerous kinds of tsetses. To dig up the tree stumps is not feasible on account of the high cost, and it is only after numerous experiments over a period of years that various successful measures for killing the roots have been evolved in Tanganyika, such as burning, poisoning, or ring-barking. Even the activities of white ants have been utilised, since no one of these methods is applicable to all the different kinds of trees.

28. A more serious limitation of the possibilities of this method lies in the danger of erosion. In areas of comparatively low rainfall, clearing on a large scale is attended by grave disadvantages owing to the fact that it affects water supplies adversely and leads to the erosion of the soil. In such areas as these, therefore, the effect of wholesale clearing is even more disastrous than that of infestation by fly. Since, however, these areas are at the same time specially

suited to the cattle tsetses, the development of alternative methods of eradication is an important object of research.

29. At the present time in Tanganyika, the great Shinyanga fly-belt has been divided up by corridor clearings into a number of blocks in which different methods for eradicating tsetse are being tested. Of these the following may be mentioned: (1) organised grass fires; (2) differential, as opposed to wholesale, clearing; (3) fly and game barriers formed by dense strips of thicket; (4) fly traps; and (5) eradication of the fly by protecting blocks of bush from grass fires.

30. The value of properly organised grass burning has now been demonstrated in two blocks of about 12 and 15 square miles respectively, the flies having been completely eliminated in these areas by this means alone, without destruction of the bush. This is at present the cheapest method of getting rid of tsetses on a large scale. Unfortunately it can only be used where the grass is of a suitable type, neither too short nor too long. Moreover, it requires skilful planning, to guard against the possibility of re-infestation, and there are obvious practical difficulties in preventing the grass from being burnt too soon. As a result of the Shinyanga experiments, the method has recently been adopted in South Ankole by the Uganda Veterinary Department with very encouraging results. Good fires, however, for four or five successive years will probably be necessary for complete success.

31. The experiments with trapping are as yet far from complete. The method is one that requires special skill and technical knowledge, since in order to be successful, the operator must be acquainted with the normal movements of the fly and with its special breeding and feeding places. In the case of the cattle tsetses it seems probable at present that this measure will prove useful only as a secondary line of attack. But with *G. palpalis* (Rob.-Desv.) the results are much more promising, and already a small island in lake Victoria has been cleared of fly by this means.

32. The most recent advance has been the discovery of the practical value of what is known as densification of the vegetation. If a patch of tsetse-infested bush is protected from grass fires for several seasons, it has been found that the growth becomes so dense as to be highly unfavourable to certain species of tsetses. In one block of four square miles which has remained unburnt for three years the numbers of *G. swynnertoni* Austen, have been reduced by nearly 90 per cent., although the numbers of the game in the area have slightly increased in the same period. At the same time, in a second block where grass burning has proceeded normally, the flies have increased by over 300 per cent. A smaller experiment with *G. morsitans* Westw. has also yielded encouraging results. We regard the results obtained in these latter experiments as being of great importance. We consider that further investigations on these lines.

but on a considerably larger scale would be highly fruitful in testing the possibilities of this method of control. We are aware that the need for economy during the last few years has imposed strict limits upon the funds available for tsetse research in Tanganyika. It is, however, in our opinion a matter for regret that the resources of the Tsetse Research Department are not at present sufficient for the purpose of further experiments on these lines. The method which is thus being developed is one which could be used at comparatively small cost in large areas where clearing and grass fires are not feasible, and it has the great advantage that it will help to conserve both the soil and the surface water.

33. The brief outline which we have given of the work being done by the Tsetse Research Department in Tanganyika gives but a small idea of the difficulties and complexities which are inherent in the task. At every turn, subsidiary problems arise, some of which are described in the very full statement submitted by Mr. Swynnerton to the Entebbe Conference and printed as appendix III to their report. We have given careful consideration to the programme of investigations there set out and we are satisfied that it represents a carefully planned series of investigations well directed to the main objects in view. We fully endorse the recommendation of the Conference that these investigations should be included as item (l) in the programme of research on these subjects to be carried out in East Africa. In the circumstances we feel that the Department is to be congratulated on the substantial progress it has achieved. It has succeeded in demonstrating that in certain types of country, tsetse flies can be controlled by measures the cost of which on a full scale would not be too high to permit of general application. Furthermore, considerable advances have been made in devising methods which will be applicable in areas where the natural conditions which prevail are of a different character.

34. In the third portion of their report (section C, pp. 23-25) the Entebbe Conference discussed the future of trypanosomiasis and tsetse fly research generally in East Africa. With regard to tsetse fly research the conference reached two conclusions. In the first place it expressed "its appreciation of the great practical importance of the work of the Tanganyika Tsetse Research Department to all three territories as regards the control of both animal and human trypanosomiasis." Secondly, it recorded "its conviction of the need, not only for this work, but also for every facility being given by the respective Governments to continue and extend the present opportunity for personal co-operation and collaboration without regard to inter-territorial boundaries."

35. With both these expressions of opinion we find ourselves in full agreement. Research for improved methods of tsetse control is in our view of primary importance. The solution of the tsetse fly problem is in fact the key to the future prosperity of the East African

territories, and will more than repay the time and money devoted to its investigation. Development expenditure of this kind represents in the broadest sense the conservation of the essential capital resources of the country, and its curtailment must always therefore in the long run prove to be a false economy.

36. We do not propose to examine here in detail the financial basis of the tsetse research work in Tanganyika. We feel, however, that some general comment is called for in regard to the adequacy of the funds at present available for this work. We realise that the present position is the outcome of exceptional financial circumstances, and does not in any sense reflect the view which is taken regarding the scientific merits of these investigations. We feel bound, however, to point out that as matters stand the provision made for this research is quite out of proportion to the importance and magnitude of the problem which is being attacked. We have already referred to important developments in the work, progress in regard to which is hampered by lack of funds. At the present time the staff of the department is hardly adequate to keep going the existing series of experiments, for which continuous observations over a period of years are essential. Yet in work of this nature the scope of the investigation must inevitably expand if valuable indications are to be followed up and their possibilities fully tested.

37. We may illustrate this difficulty further in relation to the second of the conclusions of the Entebbe Conference referred to above, in which the conference emphasised the importance of inter-territorial co-operation amongst tsetse workers. In addition to carrying out its own programme, the Tsetse Research Department in Tanganyika is quite rightly called upon to advise and help when acute tsetse troubles arise in other territories. Moreover, as a result of the Department's enterprise and success, adjoining territories have been encouraged to tackle some of their more urgent tsetse problems, and on their invitation Mr. Swynnerton and several members of his scientific staff have for the past two years visited Uganda and Kenya to advise and assist in the carrying out of various anti-tsetse measures.

38. There has thus been established a most friendly liaison between these three territories in regard to tsetse work, and this development is in the highest degree satisfactory and should be encouraged in every way. At the same time, work of this kind necessarily adds to the claims on Mr. Swynnerton and his technical staff, and thus tends to divert their attention from the work in progress at Shinyanga. If, therefore, this desirable co-operation is to be maintained and extended, it is highly probable that some expansion of the Department will be necessary in the future.

39. The work which the Department is doing is of vital importance not only to the economic life of Tanganyika, but also to that

of all parts of Africa where tsetse flies are found. It is, moreover, work the need for which, so far from being transitory in character, will remain imperative for many years to come. The problem of the control of tsetse flies is a highly intricate one, involving a considerable number of different species, each of which has different life habits and will require to be studied in relation to the various types of terrain. In a question of this kind it is impossible to draw any clear distinction between the work of research and the application of the results of research in practice, each depends so intimately on the other and presents so many problems in common. It is idle, therefore, to suppose whatever the progress made by research, that a point will shortly be reached where by the application of simple rules of thumb the tsetse fly can be rendered harmless or can be eradicated. We anticipate that for several decades at least a fully qualified scientific staff will be required in dealing with this problem.

40. In the light of these considerations we feel that the existing provision for tsetse research in Tanganyika is open to criticism not only in view of its limited scale, but also on the score of its temporary character. The European officers employed in the Tsetse Research Department have hitherto been serving some of them for considerable periods on temporary contracts and in a non-pensionable capacity. It cannot, however, be expected that the work of the department can be successfully maintained on this basis for an indefinite period. It would, in our opinion, be most unfortunate if for this reason the department were to lose the services of officers who by training and by past experience are exceptionally qualified for their work. The Administration of the Territory has on a previous occasion expressed its readiness to recognise that it has a moral obligation towards the officers of the Tsetse Research Department, and will be prepared to consider sympathetically the question of granting permanent status to individual officers of that staff if this should become necessary to maintain the existing trained personnel. We feel, however, very strongly that this is a question which should receive consideration at the earliest moment which financial circumstances will permit without regard to the question whether there is any immediate risk of the loss of some part of the existing personnel.

41. In the discussion contained in the preceding paragraphs of this section, we have so far been concerned with the general plan of the investigations on tsetse control included by the Entebbe Conference as item (1) in the programme of research, a summary of which was printed as appendix I to their report. It will, however, be convenient to consider also at this point two items of research which, while they are of a comparatively specialised character, have nevertheless a close connection with the development of methods of tsetse control.

42. The first of these is the biological study of tsetse flies in *rhodesiense*, *gambiense* and *brucei* areas, a subject discussed in

section A. VIII, of the report of the Conference and recommended for inclusion as item (f) in the programme of research. Investigations on this question are proceeding in Tanganyika, in Kenya, and in Uganda, the work in all three territories being carried out on a common plan following the lines adopted in Tanganyika by Mr. Swynnerton. The subject is a wide one and affords scope for much useful observation. It should, however, be emphasised that investigations of this kind can only be satisfactorily carried out by specialist entomologists. We are therefore in favour of the continuance of the work upon existing lines. In particular, we have noted with satisfaction this instance of fruitful co-operation between the entomological officers stationed in the various territories concerned.

43. The second of these two questions is the study of the food supply of tsetse as determined by biological study of the stomach contents of the fly. This subject was discussed in section A. X, of the report of the Conference, and was included in the programme of research as item (g). The investigation in question is concerned with a special aspect of the larger inquiry described by Mr. Swynnerton in appendix III of the report of the Entebbe Conference (page 36). Mr. Swynnerton is engaged in investigating the function of game animals in relation to tsetse flies, not only as a source of infection, but also as their principal food supply. For several years close observations have been carried out on the relation of fly and game, but these have hitherto been, generally speaking, conducted on the basis of leaving the game undisturbed. It remains to supplement these observations by the study of game that is not undisturbed. What, for example, will be the effect of harrying the game in such a way that the fly cannot form regular feeding habits? And what will be the effect of driving out various classes of game animals, leaving the fly to feed only upon those that remain? Mr. Swynnerton's belief is that wholesale extermination of game will not be necessary for fly control, or even possible. His experiment will, however, show the extent to which occasional and partial attacks upon game may be of value as one element in a scheme for controlling tsetse fly.

44. Mr. Swynnerton's experiments are of the nature of practical field trials. But their value will be much increased if they are reinforced by laboratory experiments having for their object the analysis of the stomach contents of tsetse flies. By the use of various exact tests, such as the precipitin test and serum reaction tests, it should be possible to throw light upon the nature of the food supply of the fly. By precipitin tests, for example, it can be shown whether the blood found in the stomach of a fly is human, mammalian, or bird blood. Similarly, by testing the blood with sera obtained from game animals, it should be possible to ascertain from what species of animal the blood was ingested by the fly.

45. We consider that the results of these experiments will be of definite value as a link in the chain of evidence regarding the important question of the relation of wild animals to the maintenance and spread of tsetse flies. We concur, therefore, in the recommendation of the Conference that such experiments should form part of the programme of tsetse research in East Africa. We note that they will be carried out by Mr. C. B. Symes, Medical Entomologist, Kenya, at the Medical Research Laboratory, Nairobi, and that Mr. Swynnerton will co-operate by supplying sera from game animals as opportunity offers.

(d) The control of trypanosomiasis by chemotherapy.

46. The third of the principal methods of control of trypanosomiasis is the treatment of the disease by drugs. Considerable progress has been made in the last fifteen years in developing this type of treatment both for human and for animal trypanosomiasis. The introduction of the drug known as germanin (Bayer 205) in 1920 and of tryparsamide in 1921, may be said to have marked a new stage in the treatment of sleeping sickness by chemotherapeutic methods. Similarly in the field of animal trypanosomiasis the preparation called antimosan appears to possess all the trypanocidal properties which are known to belong to the antimonial compounds without exercising the dangerous effects, particularly upon the liver, which are in many cases associated with other antimonials such as tartar emetic. With the exception of Bayer 205, which is a coal-tar derivative, the principal drugs employed in treating both the human and animal forms of the disease fall into two main classes, the arsenical compounds* such as atoxyl and tryparsamide, and the antimonials such as tartar emetic and antimosan. In the treatment of sleeping sickness, the general practice is to make use of these two types of drug, either alternately or in combination. Bayer 205 is also used in conjunction with tryparsamide. While the chances of effecting a cure are very much smaller once the disease has progressed beyond the stage at which the brain and spinal cord become affected, the early administration of drugs exercises a valuable effect in arresting the development of the symptoms. Germanin (Bayer 205) has proved to be of special value in the treatment of European cases, particularly of the Rhodesian form of sleeping sickness which is generally resistant to other forms of treatment. Tryparsamide is even more potent in its action, especially in cases where the central nervous system is involved. Remarkable cures have been recorded by the use of this drug in advanced cases where formerly there would have been little hope of recovery. Care is, however, required in its administration as it is apt to produce damaging effects upon vision.

* To this class belongs the drug known as orsanine or Fournau 270, which is much used in the treatment of human trypanosomiasis in the French and Belgian Congo.

47. In addition to the curative effects exercised by germanin (Bayer 205), this drug has been found to possess valuable prophylactic or preventive properties. When injected into cattle it affords protection against infection for considerable periods, thus enabling them to travel through fly-belts where this would otherwise have been impossible. In the case of sleeping sickness also it has been shown by a number of clinical trials that germanin exercises valuable prophylactic effects lasting for some months. There is, however, at present some lack of the data necessary to enable it to be employed to the fullest effect in this direction.

48. It was to this last point that the Entebbe Conference particularly directed their attention in discussing the control of sleeping sickness by chemotherapy (section A. XII, of their report, pp. 16 and 17). We agree with them in thinking that other aspects of the question of drug treatment have been very fully covered in the researches of the last few years. But we concur also in the view that further experimental work will be necessary before the preventive use of Bayer 205 can be recommended as a routine practice. We therefore favour the suggestion of the Conference that the investigation of the prophylactic value of Bayer 205 should be included as item (h) in the programme of East African trypanosomiasis research. The proposal of the Conference was that such investigations should be undertaken at the Human Trypanosomiasis Institute, Entebbe. Our support of this suggestion is, in consequence, subject to its modification in accordance with the recommendations which we submit below (paragraphs 71 to 75) in regard to the future of that Institute.

49. The Entebbe Conference made a further recommendation on this subject at a later stage of their report (section B. IV (i)) where they expressed the view " that it was important that the question of the rapidity of excretion of Bayer 205 from the body should be investigated, but that this work could not be carried out in East Africa owing to lack of staff." They recommended " that the Medical Research Council should be approached with a request to work on this problem " and they suggested that the subject might be of interest to Dr. A. Wormald of Leeds University, who is engaged on research work on cognate subjects, under the auspices of the Medical Research Council.

50. For the purpose of giving consideration to this suggestion, we decided to place ourselves in touch with the Medical Research Council, and accordingly at the invitation of our Chairman, the Secretary of the Council, Dr. Edward Mellanby, attended one of our meetings and discussed this subject with us.

51. The subject which the Entebbe Conference recommended for investigation is one which has an important bearing upon the use of germanin (Bayer 205) as a preventive of sleeping sickness.

Those who have used the drug prophylactically suggest that protection against sleeping sickness persists for as much as six to ten months after two injections. There is little doubt that Bayer 205 remains in the blood and tissues for a considerable time, probably for several months, and that it is eliminated in the urine very slowly. Quantitative data as to the rate of elimination are, however, scanty. Since the appearance of Bayer 205 in 1920 very little research has been done on the rapidity or manner of excretion of the drug from the animal body. Experiments were made on small laboratory animals in the years following its introduction, but these were incomplete and we are not aware of any investigations on the question of excretion in man.

52. In view of these considerations, and in the light of our discussion with Dr. Mellanby, we are satisfied that this is a subject which calls for investigation, which in the earlier stages at least could well be carried out in England. We understand from Dr. Mellanby that Dr. Wormall has expressed his willingness, in conjunction with Mr. W. E. Gaunt and with the support of Professor B. A. McSwiney, to undertake preliminary investigations, the aim of which would be to establish a suitable method and furnish some indication of the extent of the experiments which would be necessary to provide a satisfactory solution of this question. Dr. Wormall proposes to undertake in the first place a study of the methods of Steppuhn and Utkina-Lyubowzewa (1924)* and of Lang (1931)† for the chemical determination of Bayer 205; and secondly quantitative studies on small animals (rabbits and dogs) in order to examine completely the excretion of Bayer 205 after one or more injections of the drug. On the completion of these investigations it will be possible to decide whether further investigations on man could be undertaken with advantage.

53. As a result of our consideration of this question we are of opinion that the investigations which Dr. Wormall has suggested might be of great value. We therefore recommend that the Secretary of State for the Colonies should invite the Medical Research Council to arrange for preliminary investigations into the question of the rapidity of excretion of Bayer 205 to be carried out by Dr. Wormall on the lines which he has suggested.

54. At the same meeting we discussed also with Dr. Mellanby the recommendation put forward by the Entebbe Conference (Section A. XII, p. 17, of their report) that the Medical Research Council should be approached with a view to interesting prominent British research workers in the synthesis of therapeutic compounds for the treatment of trypanosomiasis. The suggestion of the Conference was that such drugs could then be tested in East Africa. From

* Steppuhn and Utkina-Lyubowzewa (Utkin-Ljubowzow), 1924, *Klin. Wschr.* 3: 154.

† Lang, 1931, *Arch. exp. Path. Pharmac.* 160: 560.

the discussion which we had with Dr. Duke and Dr. Kauntze at our second meeting, we understand that it is the feeling of those engaged in work on trypanosomiasis in British Territories in Africa that the drugs at present employed, which are mainly foreign in origin, are susceptible of improvement. The Conference was therefore anxious to secure the co-operation of scientific workers in this country in the production for subsequent trial in Africa of new forms of drug for use against trypanosomiasis.

55. In the course of his discussion with us, we were assured by Dr. Mellanby that there is no lack of such new compounds awaiting experimental use in Africa. In 1927 the Medical Research Council, with the co-operation of the Department of Scientific and Industrial Research, appointed a Chemotherapy Committee with the main object of investigating drugs having specific actions in trypanosomiasis and malaria. For some years before this, the Medical Research Council had already been supporting two groups of workers engaged in a search for new trypanocidal drugs. These were, on the one hand, Professor J. B. Cohen at Leeds with Professor C. H. Browning at Glasgow, and, on the other, Dr. H. King and Miss F. M. Durham at the National Institute for Medical Research, Hampstead.

56. The Chemotherapy Committee began by inviting a number of well known chemists to prepare series of new compounds for test on experimental trypanosomiasis along lines which had been carefully discussed beforehand. To deal with the new compounds, another biological station, under Professor Warrington Yorke at the Liverpool School of Tropical Medicine, was established by the Medical Research Council, in addition to the two already so engaged. Compounds received from the chemists have been distributed, after card-indexing, to the appropriate biological stations.

57. During the past six years about a thousand potentially trypanocidal drugs have in this way been tested on trypanosomiasis in mice. They have comprised a very wide variety of types, and have included substances built on the pattern of Bayer 205, of tryparsamide, and of certain azo-dyes. The more promising of these drugs have also been prepared on a larger scale and tested on generalised trypanosomiasis in rabbits.

58. In 1931-32 a promising styryl-dye prepared by Professor J. B. Cohen and tested experimentally by Professor C. H. Browning on mice was sent out to several stations in Africa, *e.g.*, to Dr. Maclean, Sleeping Sickness Officer, Tanganyika Territory, for trial on man; to Dr. D. Riding, at the Wellcome Tropical Research Laboratories, Khartoum, for testing on trypanosomiasis in camels; and to Dr. P. J. du Toit, Onderstepoort, South Africa, for trial on cattle and horses. Unfortunately, development of local reactions precluded its practical use.

59. Within the last two years Professor G. T. Morgan, Director, Chemical Research Laboratory, Teddington, has prepared a series of compounds distantly related to tryparsamide, and these have been shown by Professor Warrington Yorke to possess high trypanocidal activity. By exhaustive chemical investigation in this field Professor Morgan has arrived at five drugs which appear to have maximal activity. So far, three of these have been tested on rabbits infected with *T. rhodesiense* S. & F., and have been found to be relatively non-toxic and as active as tryparsamide. The study of these drugs is now in a position where clinical trial on man or domestic animals is necessary. In fact, 250 grams of one compound have already been sent to Dr. H. M. O. Lester of the Nigerian Sleeping Sickness Commission for test on human trypanosomiasis.

60. Dr. H. King of the National Institute for Medical Research, has also arrived at two arsenical drugs of novel type having extreme efficacy on trypanosomiasis in mice in very low doses. These also are curative for infections of *T. rhodesiense* S. & F., in rabbits, and are ripe for testing in the field.

61. Dr. Mellanby further informed us that having regard to the fact that there were now seven drugs which had been synthesised by workers under the Chemotherapy Committee, and which were known by animal experiments to have a specific destructive action on *T. rhodesiense* S. & F., the Medical Research Council believed that the time had come when the best opportunities for the clinical trial of these drugs should be made available. The desirability of arranging for practical veterinary trials should also be kept in view. The Council would be glad to give every assistance in their power by supplying sufficient quantities of these substances, and in any other way that might be suggested to ensure the success of this work.

62. In the light of this information, we proceeded to consider the best means of securing a full investigation under clinical conditions of the possibilities of the new drugs described by Dr. Mellanby. Past experience of field trials of drugs for use against other diseases has convinced us that there are many difficulties associated with clinical tests of this kind. Many examples might be quoted of the difficulty of arriving at any definite and agreed conclusion as a result of a number of scattered observations. We consider that the importance of securing the most precise information possible in regard to the use of these new drugs is such that the appointment of a special investigator to undertake this work would be fully justified. We believe that this is a course which would have substantial advantages. We have been informed, moreover, by the Colonial Office representatives on our Sub-Committee, that if the Medical Research Council could arrange for such an investigator to proceed to Africa, the Colonial Office would, they anticipated, have no difficulty in arranging for the provision of facilities for this work. In particular, it would be necessary to secure the concentration in one hospital of a

large number of sleeping sickness cases under conditions which would enable them to be kept under continuous observation. We recommend, therefore, that the Secretary of State for the Colonies should invite the Medical Research Council to arrange for an investigator to proceed to Africa for the purpose of conducting clinical tests of trypanocidal drugs, and should arrange for him to be afforded all necessary facilities for his work, including the concentration at some suitable centre of a sufficient number of sleeping sickness cases who could be kept under observation.

63. It is equally of great importance that the veterinary effects of the drugs referred to above should be tested in a similar manner. We have given careful consideration to the method by which such tests might best be carried out, and in this case also, for reasons generally similar to those which we have outlined above, we consider that such work is most likely to be successful if it is entrusted to a single investigator. For this purpose we think that valuable assistance might be obtained from Mr. Ll. E. W. Bevan, who is engaged upon work on trypanosomiasis in Southern Rhodesia with the assistance of a grant from the Beit Trustees. Mr. Bevan is in charge of an organisation, entitled the Trypanosomiasis Bureau, equipped with facilities for research on a considerable scale. He is specially concerned with the investigation of the veterinary aspects of trypanosomiasis, and we therefore feel that his co-operation in testing drugs for use against animal trypanosomiasis would be of special value. We recommend, therefore, that the Secretary of State for Dominion Affairs should ascertain from the Government of Southern Rhodesia whether it would be possible for Mr. Bevan's organisation to undertake an investigation on these lines. From many points of view also the Veterinary Research Institution, Onderstepoort, offers admirable facilities for testing the veterinary effects of drugs. We recommend, therefore, that the Secretary of State for Dominion Affairs should ascertain from His Majesty's Government in the Union of South Africa whether it would be possible for that Institution to arrange for a member of its staff to collaborate with Mr. Bevan in this work.

III.—PROTOZOOLOGICAL RESEARCH.

(a) The work of the Human Trypanosomiasis Institute, Entebbe.

64. In the preceding section of our report we have described in outline the principal methods of treatment employed against human and animal trypanosomiasis, and have indicated our views in regard to certain items of research proposed by the Entebbe Conference which have a specific bearing upon the development of those methods. From the short account, however, given at the beginning of the section (paragraphs 5 to 11 above), describing the basic causal factors responsible for the disease, it will have been evident that in the long run an important element in the control of trypanosomiasis will be the progress of protozoological research, the investigation, that is to say, of the behaviour and relationships of the protozoal germs or trypanosomes from which the disease takes its name.

65. The outbreak of serious epidemics of sleeping sickness at the beginning of the century gave renewed impetus to research on these subjects, and the years before the War were fruitful in important discoveries. The discovery by Bruce in 1895 of the transmission of trypanosomes by tsetse flies,* the discovery by Castellani in 1903 of a trypanosome in the cerebro-spinal fluid of a human subject in Uganda,† the discovery by Stephens in 1909 of *T. rhodesiense* S. & F., and the demonstration by Kleine in 1909 of the biological nature of the process of transmission may be considered as having laid the foundations of our knowledge of the disease. In general, it may be said that the outstanding and fundamental observations on trypanosomiasis had been completed by 1912. The possibilities of advance at the present time are necessarily more limited. In the early stages the problem was comparatively straightforward and clear-cut, and important additions to knowledge could be achieved by a single series of experiments and confirmed in a few weeks. To-day any substantial progress may require as many years, and numerous experiments in different areas are needed before results can be obtained which will be generally accepted. Nevertheless, there are still questions of great importance which remain to be answered, and we expect to see valuable light thrown on these problems in the future by the steady pursuit of scientific investigation.

* Bruce's discovery in 1895, which was made in Zululand, related to animal trypanosomiasis (*T. brucei* infection). It was not until 1903 that he concluded that tsetses played a similar rôle in sleeping sickness.

† Further investigation by Bruce and Nabarro confirmed this observation, and as a result they definitely established that *T. ugandense* Castellani, 1903, was identical with the trypanosome discovered in the Gambia by Forde in 1901, and subsequently named *T. gambiense* Dutton, 1902; and in consequence that the disease then known as sleeping sickness was merely the final stage of human trypanosomiasis.

66. Intensive research upon the problems of sleeping sickness has been carried out since the War at the Human Trypanosomiasis Institute at Entebbe. This organisation originated in the work of the International Commission appointed by the International Conference on Sleeping Sickness held in London in 1925. On the termination of the work of the Commission the Institute was continued, at first as an East African research station, the cost of which was met from loan funds, and subsequently as a purely Uganda service maintained by the Government of Uganda from year to year. In the course of its existence the Institute, under the direction of Dr. H. Lyndhurst Duke, has carried out much valuable research, particularly on the questions of immunity, both natural and acquired, and on the part played by wild and domestic animals as a reservoir of infection.

67. Unfortunately, however, the progressive deterioration of the financial conditions during the period in which the Institute has been at work has necessitated successive reductions in the scope of its investigations and in the size of its staff. To-day the work of the laboratory is being carried on by Dr. Duke almost single-handed. Furthermore, the financial provision approved for the Institute terminated at the end of the year 1934. We understand that for the present temporary arrangements have been made for the continuance of the Institute on its existing basis. We have to consider, therefore, what is to be the future of this organisation, whether it is desirable that its work or any part of it should be continued and, if so, under what conditions.

68. This question was amongst those discussed at the Entebbe Conference, whose conclusion on this subject is recorded on page 23 of their report. The Conference felt that the present time was inopportune for the formulation of any opinion on this subject. They recommended that if the Governor of Uganda agreed, the Institute should be maintained on its present footing for another year, i.e., to the end of 1935. From a letter which we received from the Colonial Office dated the 1st June, 1934, we learned that as a result of the discussions which took place at the Governors' Conference held at Nairobi in May 1934, the Governor of Uganda had agreed to this course subject to a definite decision having been reached in the meantime in regard to the future of the Institute.

69. In considering this question we were naturally anxious to obtain the fullest information in regard to the work of the Institute and the experience gained by those who have been most closely concerned with it. We were fortunate, therefore, in having an opportunity, through the presence, on leave in this country, of Dr. Duke and Dr. Kauntze, of discussing with them the various issues involved. In the course of the discussion, Dr. Duke described to us the work upon which he is at present engaged at the Institute and which he would hope to complete during a further year of

research. We understand that this will include the investigation of such questions as: (i) spontaneous cure and natural and acquired immunity in man, and (ii) experiments on relatively resistant ruminants with strains of *T. rhodesiense* S. & F., and *T. gambiense* Dutton. These are all fundamental questions relating to conditions tending to bring about the spread of the disease. Two examples may be mentioned of the work dealing with these questions, upon which Dr. Duke has been engaged. In the first place, Dr. Duke has recently published a paper* in which he describes the results of investigations in regard to some of the problems concerned with the use of germanin (Bayer 205) as a preventive against sleeping sickness, a subject some aspects of which were discussed in the preceding section of our report (paragraphs 47 to 53 above). This work is being continued by him and was recommended by the Entebbe Conference for inclusion as item (h) in the programme of research.

70. Secondly, in the course of his discussion with us, Dr. Duke described in outline the results of a series of experiments, the object of which has been to study the development of trypanosomiasis infection in the blood of game animals, such as antelopes, after they have been subjected to the bites of tsetse flies which have first been infected with the parasite from human sources. Dr. Duke's experiments have so far been mainly concerned with one species of parasite, *T. rhodesiense* S. & F. He has obtained definite indications suggesting that human strains of this germ tend to lose their power to produce infection in man after a period of sojourn in the blood of hosts other than man or other primates, particularly in ungulate hosts such as antelope. On the other hand, the passage of the infection by means of fly through primates such as monkeys, which belong to the same natural order as human beings and, therefore, resemble them more nearly in their biological characteristics, appeared to exercise no effect on the infectivity of the parasite to man. The inference, therefore, towards which these experiments point, is that the part played by game as a reservoir of infection is, at least in the case of the Rhodesian form of sleeping sickness, very much less important than has sometimes been supposed. Dr. Duke is anxious to follow up these experiments by a series of similar investigations in regard to *T. gambiense* Dutton, the other main species of germ producing sleeping sickness. He expects, within the course of a further year's work, to be able to carry his researches to a point at which additional results of definite value will be obtainable.

71. The Entebbe Conference referred to these experiments on page 8 (section A. I) of their report. They expressed the view that this work should be included as items (a), (b) and (c) in the

* "On the protective action of 'Bayer 205' against the trypanosomes of man." Duke (H. L.), 1934, *Lancet*, 1: 1336-1338.

programme of research together with inquiries on similar lines which were in progress at Tinde and Mpwapwa. We ourselves, after careful consideration, are satisfied that it is highly desirable that Dr. Duke should be enabled to continue his work for another year since we understand that within that period it will be possible for him to bring his inquiry in regard to most of these questions to a satisfactory conclusion. We welcome the statement of the Governor of Uganda that he will be willing to continue the necessary financial provision for the Institute until December 1935, subject to a decision having been reached in regard to the question of its continuance after that date. We therefore recommend that the Secretary of State for the Colonies should concur in the action which the Governor has proposed.

72. We may refer here in passing to a small matter which was brought to our attention in the course of our discussion with Dr. Duke. For the purpose of the experiments which we have mentioned, Dr. Duke requires large numbers of the pupae of the principal species of tsetse fly, *G. morsitans* Westw. The flies which emerge from these pupae are used by Dr. Duke in various experiments involving the transmission of trypanosomiasis from flies to animals. In view of the fact that as we have mentioned elsewhere (see paragraph 6 above), only a small percentage of the flies which ingest trypanosomes become capable of transmitting infection, a very large number of pupae are required. For this purpose it is not necessary to arrange for the artificial breeding of tsetse flies. All that is required is that arrangements should be made for the collection of pupae during the period of pupation in some suitable fly-belt, as, for example, at Kikori in Tanganyika. It should, we think, be easy for the Government of Uganda to arrange with the Government of Tanganyika for the despatch of pupae collected by natives under the supervision of a European government servant, on the understanding that the expenses involved would be met by the Uganda Government.

73. We turn next to the consideration of the future of the Institute at Entebbe, after the termination of the year ending December 1935, during which we have recommended that the work of the Institute should be continued. During the period of its existence, the Institute has done work of great value on some of the central problems of trypanosomiasis, and if this were the only factor to be considered we should be glad to see the Institute continued. There are, however, other circumstances which must be taken into account. It must in the first place be recognised that the conditions under which the Institute has recently been working are very different from those in which its work was begun. Financial circumstances have necessitated successive reductions of staff and at the present time the scale of the laboratory accommodation at Entebbe is quite inappropriate to the scope of the work being done. In view of the many urgent calls upon public funds in Uganda we do not

feel that a return to the original plan of organisation at Entebbe would be practicable. In spite of the dangers, actual and potential, of trypanosomiasis in East Africa as a whole, the maintenance in Uganda of a permanent research institute devoted to its problems would be disproportionate to the importance of the disease as compared with the other medical needs of the Protectorate.

74. On this question, therefore, our conclusion is that at the close of the year ending December 1935, the existing provision for research at the Human Trypanosomiasis Institute, Entebbe, should be discontinued.

75. At the same time, the closing down of the Institute by no means implies that all research in Uganda on the question of trypanosomiasis should be abandoned. Before the establishment of the Institute, such research was carried out on a very considerable scale by the laboratories division of the Medical Department. In the event of the Institute being discontinued, it would, in our view, be highly desirable that the Medical Department should keep in close touch with the progress of scientific knowledge of the disease, and should endeavour as opportunity offered to make its own contribution to such knowledge. In doing so, it should bear in mind as possible subjects for inquiry, not only any outstanding problems which may remain after the conclusion of Dr. Duke's work at Entebbe, but also those questions which were suggested by the Entebbe Conference as subjects for future inquiry by the Human Trypanosomiasis Institute. Under this heading we include such questions as the retention of acquired characteristics by trypanosomes during cyclic evolution in the body of the tsetse, the evolution of different trypanosomes in the body of tsetse and other biting flies, discussed in section A. VI, pp. 10-12, of the Conference's report, the development of new methods of diagnosis in trypanosomiasis, and the possible existence of other reservoirs of *T. gambiense* Dutton, than man. These subjects were dealt with in sections A. III and B. V, pp. 9 and 22, of the Conference's report.

76. Of these questions the subject of diagnosis seems to us in particular to call for more attention than it has hitherto received. The present methods of diagnosis of human trypanosomiasis have long been in use and given time and laboratory assistance are fairly efficient. In dealing with natives, however, the employment of more prompt and certain methods, such as serological tests, is desirable. Reliable and rapid methods of diagnosis are necessary to the success of many measures for the control of trypanosomiasis. In Nigeria, for example, attempts are being made to control the disease by treatment and for this early and efficient diagnosis is the first essential. If infected natives, some of whom may be apparently well, are examined and passed as free from trypanosomes they may continue to infect tsetse which feed upon them. Again on the southern border of the Uganda Protectorate an effort is being made to prevent natives

infected with a virulent strain entering Uganda from the south in search of work and they are subjected to examination as they pass through. The success of these measures clearly requires that the diagnostic methods employed should be such as will not allow leakage. Finally, early diagnosis is of importance on more general grounds since it leads to early treatment and the saving of life. For all these reasons the development of new methods of diagnosis seems to us important, and we hope, therefore, that an opportunity will be found for investigation of this subject either by the Medical Department in Uganda or by workers engaged on research elsewhere in Africa. Further information on the question will be found in a note prepared for us by Sir Arthur Bagshawe, one of our members, which we print as appendix 2 to this report.

(b) Investigations in other parts of Africa.

77. In addition to the investigations on sleeping sickness conducted at Entebbe by Dr. Duke, in regard to which we have stated our recommendations in preceding paragraphs, there is a considerable body of work of a fundamental character on both animal and human trypanosomiasis, which is being carried on by veterinary and medical officers in the various territories in East Africa. These inquiries, with those of Dr. Duke and the research work in regard to tsetse-fly control discussed in previous sections, together make up the programme of tsetse and trypanosomiasis research in East Africa put forward by the Entebbe Conference. We shall complete our examination of that programme, therefore, by considering in this section the various items of research which it was proposed should be undertaken by individual workers in the different territories.

78. Of these the first which calls for comment is the work being carried out by Dr. J. F. Corson at the Research laboratory for the study of *T. rhodesiense* S. & F. at Tinde in Tanganyika. This work is closely allied to that of Dr. Duke discussed in the previous section (items (a) and (b)). Like Dr. Duke, Dr. Corson is engaged upon experiments concerned with various aspects of the question referred to in the report of the Entebbe Conference under the general heading "natural immunity, spontaneous cure and acquired immunity in man." The particular angle from which Dr. Corson has approached this problem is the study of the relationship between the three polymorphic species of trypanosome *T. gambiense* Dutton, *T. rhodesiense* S. & F., and *T. brucei* P. & B. We referred briefly in an earlier section (see paragraph 9 above) to the important bearing which this problem has upon the understanding of trypanosomiasis and the measures taken to control it. From a practical standpoint the issue it raises is the relation of human trypanosomiasis to the disease in wild and domestic animals and the part which may be played by such animals as reservoirs of sleeping sickness infection. Expressed scientifically the question asked is what are the relation-

ships of *T. gambiense* Dutton, *T. rhodesiense* S. & F., and *T. brucei* P. & B., and more especially what are the conditions, if any, under which one of these parasites may lose its character and assume that of one of the other two. It is well-known that morphologically the three species are indistinguishable. Microscopic examination of *T. gambiense* Dutton and *T. rhodesiense* S. & F. in the blood of man reveals no differences of form. When, however, they are inoculated into the blood of laboratory animals, certain differences develop between the two species, which may be described by saying that *T. rhodesiense* S. & F. produces numerous posterior-nuclear forms amongst the short and broad individuals, while *T. gambiense* Dutton produces none or very few. Of these two parasites which infect man, *T. rhodesiense* S. & F. is only distinguishable from the third parasite *T. brucei* P. & B. by the fact that at the present time *T. brucei* is not known to be able to give rise to infection in human beings. In all other respects they are indistinguishable and as we have seen above (see paragraph 9) it is maintained by British workers that they are in fact the same.

79. For the purposes of experimental work on this question, however, it is a common practice to refer to trypanosomes originating in game-tsetse areas where human trypanosomiasis is unknown as belonging to the species of *T. brucei* P. & B., while trypanosomes having the same morphological characteristics but which are already known to have infected human beings are taken as being examples of *T. rhodesiense* S. & F. In this sense the question which Dr. Corson is investigating may be described as being, not whether *T. rhodesiense* S. & F. and *T. brucei* P. & B. are the same, but under what conditions *T. brucei* P. & B. can become *T. rhodesiense* S. & F., and similarly, under what conditions *T. rhodesiense* S. & F. can become *T. brucei* P. & B. In theory the difference between these two methods of formulating the question is of course considerable. In practice, however, the effect is broadly similar since they amount in each case to the question whether or not wild and domestic animals play an important causative role in the spread of sleeping sickness.

80. Some recent experiments by Dr. Corson on this subject have given interesting results. The object of the first experiment was to ascertain whether *T. brucei* P. & B. maintained in the blood of animals for a certain period would become capable of infecting man. A strain of *T. brucei* P. & B. was isolated from a cow and maintained by direct inoculation in a series of laboratory animals such as rats, goats, guinea pigs, &c. This process was continued for four and a half years, and at the conclusion of that period tsetse flies were infected by feeding them upon the guinea pigs. Dr. Corson and Mr. H. C. Smith, of the Veterinary Department, then exposed themselves to the bites of these flies. It was afterwards shown by feeding the flies on uninfected guinea pigs that, of the flies by which Dr. Corson and Mr. Smith were bitten, at least three in the case

of the former, and probably one at least, in the case of the latter, were infective. Neither Dr. Corson, however, nor Mr. Smith became infected. No evidence, therefore, has been obtained from this experiment which would conflict with the view that *T. brucei* P. & B. is incapable of infecting man. It is, however, interesting to note that a strain of this trypanosome which had been maintained by inoculation in animals for four and a half years was found to be readily transmissible by tsetse flies.

81. Dr. Corson has also carried out a somewhat similar experiment in regard to the transmission of *T. rhodesiense* S. & F. to man. In this case his object was to discover whether a human strain maintained by inoculation in a series of animals would lose its power to infect man, would acquire, that is to say, the distinguishing characteristic of *T. brucei* P. & B. At the time of the experiment the trypanosome had been maintained in a series of goats, rats and sheep for nineteen months. A number of tsetse flies were put to feed upon these animals, and subsequently Dr. Corson was bitten by them. Experiments with guinea pigs showed, however, that only a small number of the flies were capable of transmitting infection, and Dr. Corson therefore decided to inoculate himself from one of the infected guinea pigs. This he did, and as a result he became infected with sleeping sickness, the incubation period being six or seven days. After the infection had been transmitted from his blood to rats by inoculation, he was treated with Bayer 205 and recovered. As a result of this experiment, therefore, it may be said that a strain of *T. rhodesiense* S. & F. had not lost its power to infect man, *i.e.*, had not become converted into *T. brucei* P. & B. by a stay of nineteen months in the bodies of goats and sheep.

82. In a third experiment* similar to the second, an African volunteer developed sleeping sickness after being bitten by a tsetse fly infected with a human strain which had been transmitted by flies from a guinea pig through a series of dik-diks for a period of a year.

83. In concluding this brief account of Dr. Corson's experiments, we should like to congratulate him on his work and to express our appreciation of his action as also of that of Mr. Smith and of the African assistant, in exposing themselves to infection with sleeping sickness. We feel that no praise is too high for services such as these rendered at considerable risk to the cause of science. We have heard with satisfaction that under existing arrangements Dr. Corson's work is to be continued for a further period of two years, and we look forward to the achievement of valuable results by him during that time.

84. Experiments on somewhat similar lines are being carried out by Mr. Hornby in the Veterinary Laboratory at Mpwapwa (items (a) and (b) in the programme of research), and these investigations

* Corson, J. F., 1935, *J. trop. Med. Hyg.* 38 (1): 9-11.

will play an important part in confirming and supplementing the results obtained at Entebbe and Tinde. It is always possible, as the Research Conference observed, that different strains of trypanosomes may display considerable variations in pathogenicity, and we agree, therefore, with the view of the Conference that it is desirable that the experimental work on this question should be carried out on as wide a basis as possible. We understand that for financial reasons it has lately been found necessary to restrict the scope of Mr. Hornby's work. For the reasons, however, which we have given, we hope that it will be possible for Mr. Hornby to continue to co-operate in this important inquiry as suggested in the programme of research prepared by the Entebbe Conference.

85. The next question of importance discussed by the Conference was the retention by trypanosomes during their cyclic evolution in the body of the tsetse of acquired characteristics, such as resistance to therapeutic remedies, exalted virulence, &c. (item (d)). This is a question which will, we think, become increasingly important. One of the most positive achievements in the control of animal and human trypanosomiasis has been the development of successful methods of treatment by drugs. It now appears, as a result of observations in areas where treatment has been systematically carried out over a considerable period, that there is a tendency for trypanosomes to acquire powers of resistance to the trypanocidal properties of drugs to the action of which they have been subjected for some time. If, therefore, these methods of treatment are to retain their efficacy, it is important that more light should be thrown upon such phenomena. We therefore concur in the suggestion of the Conference that research on this subject should form part of the East African programme and should be carried out, as regards *T. congolense* Broden, and *T. vivax* Ziemann, at Mpwapwa, and as regards *T. rhodesiense* S. & F. at Tinde. We note that as regards *T. gambiense* Dutton, it was understood that the work would be undertaken by the Human Trypanosomiasis Institute at Entebbe. If this should prove impossible owing to the closing of the Institute in a year's time, we hope that the Medical Department in Uganda will consider the possibility of undertaking an investigation on this subject.

86. In addition to the work which is to be done on this subject in East Africa, we wish to suggest that steps should also be taken to enlist the co-operation for this inquiry of Mr. Bevan, who is engaged in work on trypanosomiasis in Southern Rhodesia with the assistance of a grant from the Beit Trustees. We have already referred to Mr. Bevan's work in an earlier paragraph (see paragraph 63 above). As we have there stated, he is specially concerned with the problems of animal trypanosomiasis. The question of resistance to treatment is one of particular importance from the veterinary point of view and we therefore recommend that Mr. Bevan should be approached with the suggestion that he should undertake

the investigation of this question in co-operation with the veterinary workers in other territories.

87. In section A. VI, of their report (pp. 10-12), the Entebbe Conference discussed the question of the evolution of different trypanosomes in the body of tsetse and other biting flies and the relationship to environment (climate, &c.) of cyclic transmissibility and pathogenicity (item (e) of the programme of research). These matters were also mentioned in later portions of the report, section A. IX, and section B. VI. The subject in question is a large one and the topics raised in the discussion included the possibility of the hereditary transmission of infectibility in tsetses, the question of the mechanical transmission of trypanosomiasis infection by flies of the family TABANIDAE, and the cyclic transmission of trypanosomes in the bodies of biting flies other than tsetse. The discussion of this last question was the occasion of an interesting account by Dr. W. A. Lamborn of the work which he has been doing in Nyasaland with the assistance of Professor J. G. Thomson, in regard to transmission by biting flies other than tsetses. His researches have covered various species of the family TABANIDAE, and of the genera *Haemotopota* Meigen, *Stomoxys* Geoffr., *Haematobia* Rob.-Desv., and *Lyperosia* Rondani, as well as species of other genera. The possibility of transmission by *Lyperosia* is of particular importance in view of its presence in large numbers amongst game and cattle.

88. The subjects discussed by the Conference under this heading are all of considerable importance and we welcome the proposal that work on these lines should be included in the programme of East African research. We note that in addition to Dr. Lamborn's work in Nyasaland, investigations are in progress in the Veterinary Laboratory at Entebbe, at Mpwapwa and at the Human Trypanosomiasis Institute. As regards the work at Entebbe, we have already expressed the hope (see paragraph 75 above) that this question may be borne in mind as a subject for inquiry by the Uganda Medical Department, should it be decided to discontinue the Institute after a further year's work.

89. In section A. XI, of their report, the Entebbe Conference discussed the inclusion in their programme of morphological studies of trypanosomes, to be extended to all members of the polymorphic group. We agree with them in thinking that this subject had already been discussed under previous headings (e.g., section A, IV) and the necessary items included in the programme of research. Moreover we would add that important work on this question is being carried on by Dr. Cecil Hoare at the Wellcome Bureau of Scientific Research, London. We feel satisfied, therefore, that adequate provision has been made for the investigation of this subject at the present time.

90. A subject which has some bearing upon the questions considered in the previous paragraph was discussed by the Conference in

section B. III, of their report. Under this heading the Conference considered the question of the cultivation of trypanosomes on artificial media (item (k) of the programme of research). Many attempts have been made in the last thirty years to cultivate the trypanosomes pathogenic to man, but until recently with no very great success. The results, however, of recent work carried out by Dr. E. Reichenow at Hamburg have been more favourable.* He attributed the frequent failures to cultivate pathogenic trypanosomes to the use of old laboratory strains which had lost the power to develop either in the insect host or in the culture tube. He therefore used strains of trypanosomes immediately after their isolation from man and found that they were readily cultivated for some time although eventually—after say three years—they lost their cultural capacity completely. The cultures showed, however, trypanosomes only of forms similar to those found in the gut of the tsetse fly; salivary gland forms, such as are alone capable of causing infection in man, were never found.

91. The work being carried out on this subject in Africa is at present confined to the attempted cultivation of animal trypanosomes. Mr. R. W. M. Mettam, Veterinary Pathologist, Uganda, described to the Conference the efforts which he had made at the Veterinary Laboratory, Entebbe, to obtain a culture of *T. congolense* Broden, and *T. vivax* Ziemann. The importance of these attempts lies in two directions. On the one hand the production of a successful culture might make it possible to obtain a suitable antigen which could be utilised in the artificial production of immunity of trypanosomiasis. On the other hand, the study of trypanosomes in culture would facilitate the work of identifying them by means of their morphological appearances. The Conference recommended that this work should be included as item (k) in the programme of East African research. We feel, however, that in view of the highly elaborate technique required for the cultivation of trypanosomes, such work as this could more conveniently be undertaken in one of the laboratories in Europe possessing the necessary specialised equipment for biochemical investigations of this kind.

92. In addition to his work on the cultivation of trypanosomes, Mr. Mettam is engaged at the present time upon other protozoological investigations in regard to animal trypanosomiasis in the Veterinary Laboratory, Entebbe. Two of these were discussed in sections B. I, and B. II, of the report of the Entebbe Conference. The first concerns the work which Mr. Mettam has been doing as a result of which he is of the opinion that a certain species of animal trypanosome, hitherto known as *T. uniforme* Bruce, Hamerton,

* Reichenow, Eduard, September 1932, "Das Verhalten von *Trypanosoma gambiense* in der Kultur." *Z. Parasitenk.* 4. (4.): 784-793.

Reichenow, Eduard, July 1934, "Die Züchtung der pathogenen Trypanosomen." *Arch. Schiffs- u. Tropenhyg.* 38. (7.): 292-302, 6 figs.

Bateman, and Mackie, 1911, is not a distinct species, but is in reality identical with *T. vivax* Ziemann. Mr. Mettam has not as yet succeeded in definitely establishing his thesis which is questioned by Dr. Duke. The second of these investigations concerns the bionomics of an important species of animal trypanosome, *T. brucei* P. & B. Mr. Mettam has had under investigation the pathogenicity for stock of various strains of this trypanosome isolated from different fly-belts in Uganda. The Conference recommended that these inquiries should be included as items (i) and (j) of the programme of research. We ourselves consider that both these subjects will repay further investigation and that Mr. Mettam's work on the second of the two will form a valuable supplement to the investigations in progress elsewhere, notably at Tinde, regarding the relationship of *T. brucei* to human trypanosomes.

93. The possibility that the acute trypanosomiasis occurring in pigs might be due to a hitherto unrecorded species of trypanosome was discussed by the Conference in section B. XI, of their report and appears as item (m) in the programme of research. We agree with their conclusion that further inquiry on this point would be of value, and we note that any material which becomes available will be transmitted to the Veterinary Laboratory at Entebbe or to Mpwapwa.

94. Finally it seems desirable to record our agreement with the view expressed by the Conference in section A. II, of their report, that the investigation of the question of natural immunity to sleeping sickness in baboons of the genus *Papio* Erxleb., 1777,* and mangabeys (*Cercocebus* Geoffr., 1812), is not of immediate importance.

* These baboons were referred to the genus *Cynocephalus* Cuvier, 1818, in the report of the Entebbe Conference.

IV.—CONTACTS WITH RESEARCH WORKERS IN OTHER COUNTRIES.

95. The main purpose of the Entebbe Conference was to co-ordinate the tsetse and trypanosomiasis research being done at the present time in East Africa, to secure, that is to say, within the limits of the resources available, the best possible distribution of time and money over the various parts of the field of inquiry. From our examination of the programme of research drawn up by the Conference, we are convinced that that result has been in large measure attained. We consider that the results of this the first of the conferences on tsetse and trypanosomiasis research which it is proposed to hold at regular intervals, under the ægis of the Governors' Conference, have amply demonstrated the value of a permanent machinery for securing co-operation in the field of research and we look forward to the attainment of further valuable results by this means in the future. In order, however, to succeed fully in such a task it is essential that research workers in Africa should take into account not only the work on parallel lines being done in neighbouring territories, but also the many different investigations having a bearing on the same field which are being carried out in other parts of the world. In some cases there may be subjects the investigation of which can definitely be undertaken more advantageously in Europe. Even where a question is obviously more suitable for investigation in the tropics, workers in Africa may obtain valuable assistance from the results of work on some cognate subject which have been obtained elsewhere.

96. That the Conference was fully conscious of the need for close contact with the progress of research is shown by the discussion recorded in section C of their report, which was concerned, amongst other matters, with the facilities existing for the communication of the results of research on trypanosomiasis which is being carried on in various laboratories in the Colonial Empire. The Conference on that occasion recorded its opinion that further facilities for the distribution of published and unpublished reports should be given and recommended that some central body in England should be approached with a view to its undertaking the distribution of reprints of scientific papers to workers who might be interested. They further recommended that the cost of providing the increased number of reprints which would be needed should be borne by the Government concerned. The difficulty of obtaining full and early knowledge in regard to the results of current research is one which confronts the scientific worker in almost every field. The great increase in the number of scientific journals, the growing number of workers and the much greater variety of languages in which scientific papers are now published are all contributing factors in the problem. In modern conditions no worker, even in a comparatively specialised field, can hope to keep abreast of developments

in his science without the help of some organisation which will undertake the task of reviewing current periodical literature and publishing in summary form the results recorded in every paper which appears. In the case of trypanosomiasis, these functions are discharged by the Bureau of Hygiene and Tropical Diseases, an organisation originally established in 1908 under the title of the Sleeping Sickness Bureau, the scope of which has since then been enlarged. As it is now constituted, its duties cover the dissemination of information on all subjects coming under the heading of hygiene and tropical diseases. It fulfils these functions in two ways, in the first place, by supplying information free of charge in response to any individual inquiries it may receive, secondly, by the regular publication of two journals, the *Bulletin of Hygiene* and the *Tropical Diseases Bulletin*. The latter journal contains reviews of all papers published on tropical disease. Both publications appear monthly.

97. The publication of the *Tropical Diseases Bulletin* goes far towards filling the need for information felt by research workers in trypanosomiasis, and tributes were paid at the Conference to the assistance received from the Bureau in this and other ways. In the light, however, of the recommendation of the Conference and of the discussion which we had upon this subject with Dr. Duke and Dr. Kauntze, we have reached the conclusion that in one direction there is room for a small improvement. It has been represented to us that, whereas the information supplied by the *Bulletin* is fully adequate in regard to the general mass of published work, difficulties may sometimes arise in regard to work, the results of which have not as yet been published or have been published too recently to enable a review of them to appear in the *Bulletin*.

98. In so far as unpublished work is concerned, this is not in our view a matter upon which it is proper to look for assistance to an organisation such as the Bureau. It is quite true that inconvenience may sometimes be caused to research workers through ignorance of the results already obtained, but not yet published, by others working in the same field. This is, however, a difficulty which can only be met by workers themselves. Almost everyone engaged in scientific work recognises the necessity of forming as wide a system as possible of liaison through personal contact and correspondence with his fellow workers. By this means he will often be able to learn, in advance of actual publication, what work is being pursued and what results have been obtained from it. We do not consider that it is possible to add to the information which may be obtained in this informal manner by any form of intervention on the part of a central organisation.

99. The case, however, is somewhat different as regards published results which have not yet been reviewed in the *Tropical Diseases Bulletin*. Even here the friendly co-operation of scientists in exchanging with one another reprints of their papers should go

a long way towards meeting the need for early knowledge of results of current work. The primary responsibility rests, therefore, in our view, upon research workers themselves. It is possible, however, that in some cases the necessary contacts may not have been established, and in consequence the publication of an important paper, the results of which have a direct bearing upon the research upon which a worker is engaged, may pass unnoticed by him. It is here, we think, that organisation can be of some assistance. The plan suggested by the Entebbe Conference was that reprints of all papers published by scientific workers in Government employment throughout the Colonial Empire should be circulated at Government expense to all their colleagues. We think, however, that such an arrangement would go further than would be necessary to secure the object in view. We consider that it would be sufficient for the central organisation to ensure that workers are given full and early notice of the existence of all new papers, leaving it to the worker himself to take steps to secure copies of any which concern his work.

100. We suggest that the end which we have in view could be most easily achieved in the following manner. It is, we understand, the practice of the editor of the *Tropical Diseases Bulletin* to compile each week a list of titles of papers awaiting review. Sir Arthur Bagshawe, the Director of the Bureau and one of our members, has assured us that he is willing to arrange for this list to be reproduced in cyclostyle and distributed to the Directors of Medical Services at a small charge. We believe that this small addition to the work already undertaken by the Bureau in disseminating information will be of real service to those engaged upon trypanosomiasis research in Africa.

101. We would, however, repeat our observation in regard to the primary responsibility of scientific workers for maintaining the necessary contacts with their colleagues elsewhere, in connection with a discussion which took place at the Entebbe Conference and which is recorded in section A. VII, of their report. Under that heading the Conference discussed a suggestion that further work was required on the pathological anatomy of trypanosomiasis in man and animals. As a result of their discussion, the Conference recommended that arrangements should be made whereby workers could be put in touch with experienced pathologists in Europe who would be prepared to undertake the investigation of post-mortem material. It is true that comparatively little work has been done on the pathological anatomy of trypanosomiasis since the researches of Peruzzi (1928) referred to in the report, which concerned the lesions of the myocardium, of the brain, and of the serous membranes produced by trypanosomiasis in monkeys. We can, moreover, well understand the difficulty of arranging for elaborate histological investigation in Africa of post-mortem material. We do not consider, however, that any formal machinery is required for the purpose of placing trypano-

somiasis investigators in Africa in touch with pathologists of the necessary experience in Europe. We feel that it should in practice be a simple matter for trypanosomiasis workers to write to well-known pathologists with many of whom, particularly in this country, they are already acquainted, and to enlist their help and advice in investigating these questions. We feel no doubt at all that such help would be given without hesitation. Indeed, we know that such is already the case in regard to many other subjects in which co-operation between medical and veterinary workers in Europe and in Africa has been found to be of advantage.

V.—SUMMARY OF PRINCIPAL CONCLUSIONS AND RECOMMENDATIONS.

(a) PRINCIPAL CONCLUSIONS.

102. We summarise our conclusions as follows:—

THE CONTROL OF TRYPANOSOMIASIS IN MAN AND ANIMALS.

The general character of the problem.

(1) In the present state of our knowledge there are three principal methods for the control of trypanosomiasis* in man and animals:—

- (a) administrative methods, such as the evacuation of population from an infected area, the control of movements of population (when in search of work, &c.), the clearing of water places, and the concentration of settlement;
- (b) the control of tsetse flies;
- (c) control by chemotherapy, *i.e.*, treatment by means of various drugs (paragraphs 5–11).

Control by administrative measures.

(2) Administrative methods represent an attempt to prevent or eradicate infection by controlling the movements of population (paragraphs 12–16).

(3) Apart from direct attacks upon fly, experience has shown that the most effective means of holding up the advance of fly is by the concentration of scattered native populations into closer settlements, thus destroying the environment which the fly requires for its existence (paragraphs 17–21).

The control of tsetse flies.

(4) The concentration of population must, if it is to succeed in its purpose, be coupled with active measures for reclaiming areas already infested and for holding up the advance of the fly over a wide front (paragraph 22).

(5) The main part of the research work directed to the discovery of methods of tsetse fly control has been concentrated in the Tanganyika Territory in the Tsetse Research Department under the direction of Mr. C. F. M. Swynnerton (paragraph 23).

(6) In Tanganyika the biggest fly-belt is 500 miles at its longest by 300 miles at its widest point. A problem of this magnitude can only be dealt with if means are found whereby these great tracts of

* In discussing trypanosomiasis in this report we deal only with the diseases known as sleeping sickness in man and as nagana or tsetse fly disease amongst animals.

territory can be split up into areas of a more manageable size. With this object various methods of creating artificial fly barriers have been devised in recent years, *e.g.*, by the cutting down of bush, the planting of deciduous thickets, or the production of natural thickets by protecting selected strips of land from grass fires (paragraphs 24 and 25).

(7) Flies can be eradicated within a given area by the wholesale clearing of bush, but such clearings are expensive to make and also to maintain. Moreover, in areas of comparatively low rainfall, there is a great danger that clearing on a large scale may lead to widespread erosion of the soil, with disastrous results to agriculture and forestry (paragraphs 26-28).

(8) The following methods for eradicating tsetse flies are giving promising results:—

- (i) organised grass fires;
- (ii) differential, as opposed to wholesale, clearing;
- (iii) fly and game barriers formed by dense strips of thicket;
- (iv) fly traps; and
- (v) eradication of the fly by protecting blocks of bush from grass fires (paragraphs 29-31).

(9) The most recent advance has been the discovery of the practical value of the fifth of these methods, *viz.*, the densification of the vegetation. It has been found that if a patch of tsetse-infested bush is protected from grass fires for several seasons, the growth becomes so dense as to be highly unfavourable to certain species of tsetse. Further investigations on these lines, but on a considerably larger scale, would be of great value (paragraph 32).

(10) The Tsetse Research Department of the Tanganyika Territory is to be congratulated on the substantial progress it has achieved in recent years in devising methods of tsetse control (paragraphs 33-45).

(11) In addition to carrying out its own programme, however, the Tsetse Research Department in Tanganyika has in recent years been called upon to advise when acute problems of tsetse fly control have arisen in other territories. Mr. Swynnerton and several members of his scientific staff have in the past two years visited Uganda and Kenya to assist in the carrying out of various anti-tsetse measures. There has thus been established a most friendly liaison between these three territories in regard to tsetse work. If, however, this desirable co-operation is to be maintained and extended, it is highly probable that some expansion of the Tsetse Research Department in Tanganyika will be necessary in the future (paragraphs 37-45).

The control of trypanosomiasis by chemotherapy.

(12) Considerable progress has been made in the last fifteen years in developing methods for the treatment by drugs both of human and of animal trypanosomiasis. The introduction of the drug known as

germanin (Bayer 205)* in 1920 and of tryparsamide in 1921 marked a new stage in the treatment of sleeping sickness by chemotherapeutic methods. Similarly, important progress in the field of animal trypanosomiasis has been made by the discovery of the drug antimosan (paragraph 46).

(13) In addition to the curative effects exercised by germanin (Bayer 205), this drug has been found to possess valuable prophylactic properties. Further experimental work will, however, be necessary before the preventive use of this drug can be recommended as a routine practice. In particular, further work is required on the rate of elimination of the drug from the body (paragraphs 47 to 53).

(14) In general, the drugs at present in use in Africa for the treatment of trypanosomiasis leave room for improvement, and it is desirable that clinical trials of newer drugs should be carried out (paragraphs 54-64).

PROTOZOOLOGICAL RESEARCH.

(15) In the long run an important element in the control of trypanosomiasis will be the progress of protozoological research, that is to say, the investigation of the behaviour and relationships of the protozoal germs or trypanosomes from which the disease takes its name (paragraphs 64 and 65).

The work of the Human Trypanosomiasis Institute, Entebbe.

(16) The Human Trypanosomiasis Institute, Entebbe, under the direction of Dr. H. Lyndhurst Duke, has in the course of its existence carried out much valuable research, particularly on the questions of immunity, both natural and acquired, and on the part played by wild and domestic animals as a reservoir of infection (paragraphs 66-72).

(17) Financial circumstances have, however, necessitated successive reduction of staff of the Institute, and at the present time the scale of the laboratory accommodation at Entebbe is inappropriate to the scope of the work being done. In view of the many urgent calls upon public funds in Uganda, we do not feel that a return to the original plan of organisation at Entebbe would be practicable. In spite of the dangers, actual and potential, of trypanosomiasis in East Africa as a whole, the maintenance by the Government of Uganda of a permanent research institute devoted to the problems of this disease would be disproportionate to its importance as compared with the other medical needs of the Protectorate (paragraphs 73 and 74).

(18) In the event of the Institute being discontinued, it would be highly desirable that the Medical Department in Uganda should keep in close touch with the progress of scientific knowledge in regard to sleeping sickness, and should itself undertake research on this disease. It might investigate not only any problems remaining over from

* A French preparation of the same composition is designated Fourneau 309 or moranyl.

Dr. Duke's present work, but also those questions which were suggested by the Entebbe Conference as subjects for future inquiry by the Human Trypanosomiasis Institute. Of these questions, the subject of diagnostic methods in human trypanosomiasis calls for special attention (paragraphs 75 and 76).

Investigations in other parts of Africa.

(19) We desire to congratulate Dr. J. F. Corson on his work at Tinde on the relationship of the trypanosomes *T. gambiense* Dutton, *T. rhodesiense* S. & F., and *T. brucei* P. & B. We have learnt with satisfaction that his work is to be continued for a further period of two years (paragraphs 78-83).

(20) We anticipate that the investigations on immunity and on the relationship of the trypanosomes named in the preceding conclusion now being carried out by Mr. H. E. Hornby at the Veterinary Laboratory, Mpwapwa, will be of great value in supplementing the investigations of Dr. Duke and Dr. Corson referred to in conclusions (16) and (19) above (paragraph 84).

(21) Observations have suggested that trypanosomes tend to acquire powers of resistance to the trypanocidal properties of drugs to the action of which they have been subjected for some time. We think that this question will become increasingly important (paragraphs 85 and 86).

(22) The question of the cultivation of trypanosomes on artificial media is one of definite importance both for the development of methods for the artificial production of immunity to trypanosomiasis, and in the study of the morphology of trypanosomes. In view, however, of the highly elaborate technique required for the cultivation of trypanosomes, such work as this could more conveniently be undertaken in one of the laboratories in Europe possessing the necessary specialised equipment for biochemical investigations of this kind (paragraphs 87-93).

(23) The identity of *T. uniforme* Bruce, Hamerton, Bateman, and Mackie, 1911 (item (i) in the programme of research), and the bionomics of *T. brucei* P. & B. (item (j) in the programme of research) are subjects which will repay further investigation (paragraph 92).

(24) Further inquiry would be of value regarding the identity of the trypanosome responsible for acute trypanosomiasis in pigs (paragraph 93).

CONTACTS WITH RESEARCH WORKERS IN OTHER COUNTRIES.

(25) It is desirable that for the purpose of securing a permanent machinery for co-operation in East Africa in the field of research, there should be periodical conferences of specialist workers in human and animal trypanosomiasis similar to that held at Entebbe in November 1933 (paragraph 94).

(26) We fully share the view of the Entebbe Conference regarding the need for close contact between workers in Africa and those engaged in research on the disease in other parts of the world (paragraph 95).

(27) In modern conditions, no worker even in a comparatively specialised field can hope to keep abreast of developments in his science without the help of some organisation which will undertake the task of reviewing current periodical literature and publishing in summary form the results recorded in every paper which appears. In the case of trypanosomiasis these functions are discharged by the Bureau of Hygiene and Tropical Diseases, which renders invaluable assistance in this field (paragraph 95).

(28) It was suggested by the Entebbe Conference that reprints of all papers on trypanosomiasis published by scientific workers in Government employment throughout the Colonial Empire should be circulated at Government expense to all their colleagues as soon as possible after publication. We think, however, that such an arrangement would go further than would be necessary to secure the object in view. We consider that it would be sufficient for the central organisation to ensure that workers are given full and early notice of the existence of all new papers, leaving it to the worker himself to take steps to secure copies of any which concern his work (paragraph 98).

(29) Comparatively little work has been done on the pathological anatomy of trypanosomiasis since the researches of Peruzzi. It is, no doubt, difficult to arrange for elaborate histological investigation in Africa of post-mortem material. We do not consider, however, that any formal machinery is required to place trypanosomiasis investigators in Africa in touch with pathologists of the necessary experience in Europe (paragraph 100).

(b) RECOMMENDATIONS.

103. We summarise our recommendations as follows:—

THE CONTROL OF TRYPANOSOMIASIS IN MAN AND ANIMALS.

Control by administrative measures.

(1) The control of trypanosomiasis by administrative measures calls for constant co-operation between the large number of departments concerned. We consider, therefore, that small *ad hoc* bodies might with advantage be set up in the larger territories to secure an adequate machinery for consultation and discussion of problems as they arise. We should not favour a proposal that a central body should be set up either in Africa or in the United Kingdom to conduct a general investigation into the principles to be adopted in applying administrative methods of control (paragraphs 20 and 21).

The control of tsetse flies.

(2) We strongly recommend that the fullest financial support should be given to the Tsetse Research Department in the Tanganyika Territory, the investigations of which should be included as item (1) in the programme of East African research. The work of this department is of vital importance not only to that territory, but to all parts of Africa in which tsetse flies occur (paragraphs 33 and 39).

(3) In existing conditions there is a grave danger that the department may lose the services of officers who, by training and by past experience, are exceptionally qualified for their work. We recommend, therefore, that the question of granting permanent pensionable status to the officers now working in the department should receive consideration at the earliest possible moment (paragraph 40).

(4) We recommend that the biological study of tsetse flies in *rhodesiense*, *gambiense*, and *brucei* areas should be included in the programme of research as item (f), and should be continued on existing lines by specialist entomologists (paragraph 42).

(5) We recommend that the biological study of the stomach contents of the tsetse fly should be undertaken by Mr. C. B. Symes at the Medical Laboratory, Nairobi, and be included in the programme of research as item (g) (paragraphs 43–45).

The control of trypanosomiasis by chemotherapy.

(6) We recommend that in order to give effect to conclusion (13) above:—

- (a) the investigation of the prophylactic value of Bayer 205 should be included as item (h) in the programme of research (paragraph 48); and

(b) that the Secretary of State for the Colonies should invite the Medical Research Council to arrange for preliminary investigations into the question of the rapidity of excretion of Bayer 205 to be carried out by Dr. A. Wormall on the lines suggested by him, in which we concur (paragraph 53).

(7) In order to give effect to conclusion (14) above, we recommend:—

(a) that the Secretary of State for the Colonies should invite the Medical Research Council to arrange for an investigator to proceed to Africa for the purpose of conducting clinical tests of trypanocidal drugs, and should arrange for him to be afforded all necessary facilities for his work, including the concentration at some suitable centre of a sufficient number of sleeping sickness cases who could be kept under observation (paragraph 62);

(b) that the Secretary of State for Dominion Affairs should ascertain:—

(i) from the Government of Southern Rhodesia whether it would be possible for the Trypanosomiasis Bureau now under the direction of Mr. Ll. E. W. Bevan to test the veterinary effects of some of the new drugs referred to in (a) above (paragraph 63);

(ii) from His Majesty's Government in the Union of South Africa whether it would be possible for the Veterinary Research Institute, Onderstepoort, also to test the veterinary effects of some of the new drugs referred to in (a) above (paragraph 63).

PROTOZOOLOGICAL RESEARCH.

The work of the Human Trypanosomiasis Institute, Entebbe.

(8) As regards the future of the Human Trypanosomiasis Institute, Entebbe, we recommend:—

(a) that arrangements should be made to maintain the Human Trypanosomiasis Institute, Entebbe, on its present basis for a final period of one year from the 31st December, 1934, in order to enable Dr. Duke to complete his present experiments on the question of immunity, and on the relationship of the trypanosomes *T. gambiense* Dutton, *T. rhodesiense* S. & F., and *T. brucei* P. & B., and the reservoirs of the first-named trypanosome (items (a), (b), (c) in the programme of research (paragraph 71);

(b) that as from the 1st January, 1936, the Institute as such should be closed (paragraph 74); and

(c) that thereafter the Medical Department in Uganda should, so far as its resources permit, undertake research on the problems of trypanosomiasis on the lines indicated in conclusion (18) above (paragraph 75).

(9) In order to assist Dr. Duke in carrying out the remaining stages of his investigations, we recommend that the Government of Uganda should arrange with the Government of the Tanganyika Territory for the despatch of pupæ of tsetse fly collected by natives in some suitable fly belt, *e.g.*, at Kikori, under the supervision of a European Government servant, the expenses involved being met by the Uganda Government (paragraph 72).

Investigations in other parts of Africa.

(10) We recommend that the fullest support should be given to the work of Dr. J. F. Corson at Tinde on trypanosomes, referred to in conclusion (19) above; and that these investigations should form part of items (a) and (b) in the programme of research (paragraph 83).

(11) We recommend that the investigations on immunity and the relationship of trypanosomes now being carried out by Mr. H. E. Hornby at the Veterinary Laboratory, Mpwapwa, should also form part of items (a) and (b) of the programme of research (paragraph 84).

(12) We recommend—

- (a) that research on the retention of acquired characteristics by trypanosomes during their cyclic evolution in the body of the tsetse should be included as item (d) in the programme of research (paragraph 85);
- (b) that as regards *T. congolense* Broden, and *T. vivax* Ziemann, this research should be carried out at the Veterinary Laboratory, Mpwapwa, and as regards *T. rhodesiense* S. & F., at the *T. rhodesiense* Laboratory, Tinde (paragraph 85);
- (c) that as regards *T. gambiense* Dutton, the Medical Department, Uganda, should consider the possibility of undertaking an investigation on this subject (paragraph 85);
- (d) that in the communication referred to in recommendation 7 (b) (i) the Government of Southern Rhodesia should also be asked whether it would be possible for the Trypanosomiasis Bureau to investigate the veterinary aspects of the question of the retention of acquired characteristics by trypanosomes during their cyclic evolution (paragraph 86).

(13) We recommend—

- (a) that the question of the evolution of different trypanosomes in the body of tsetse and other biting flies and the relationship to environment (climate, &c.) of cyclic transmissibility

- and pathogenicity should be included as item (e) of the programme of research;
- (b) that various aspects of this question should be investigated at the Veterinary Laboratories at Entebbe and Mpwapwa, and at the Medical Laboratory, Nyasaland;
- (c) that the Medical Department, Uganda, should consider whether they could co-operate in this work (paragraph 88).

CONTACTS WITH RESEARCH WORKERS IN OTHER COUNTRIES.

(14) We recommend that in order to give effect to conclusions (26) to (28) above, arrangements should be made by the Director of the Bureau of Hygiene and Tropical Diseases to distribute to the Directors of Medical Services in Africa copies of lists compiled each week, giving the titles of papers awaiting review in the *Tropical Diseases Bulletin* (paragraph 99).

(Signed) FRANCIS HEMMING, *Chairman.*
 W. HORNER ANDREWS.
 ARTHUR G. BAGSHAWE.
 GUY A. K. MARSHALL.
 F. G. LEE.
 A. T. STANTON.
 C. M. WENYON.

(Signed) D. H. F. RICKETT,
Secretary to the sub-committee.

Offices of the Economic Advisory Council,
 2 Whitehall Gardens, S.W. 1,
 February 4, 1935.

Programme of tsetse and trypanosomiasis

Summary similar to that prepared by the Conference on Tsetse and Entebbe, November 1933, with references to the section and page in respectively dealing with the various

Item of research.	Station recommended by Entebbe Conference
(a) Question of natural immunity, spontaneous cure and acquired immunity in man	Human Trypanosomiasis Institute, Entebbe Veterinary Laboratory, Mpwapwa ... Trypanosoma Rhodesiense Laboratory, Tinde
(b) Experiments on relatively resistant ruminants with strains of <i>T. rhodesiense</i> S. & F., and <i>T. gambiense</i> Dutton, obtained over as wide an area as possible	Human Trypanosomiasis Institute, Entebbe Veterinary Laboratory, Mpwapwa ... Trypanosoma Rhodesiense Laboratory, Tinde
(c) Existence of other reservoirs of <i>T. gambiense</i> Dutton, than man	Human Trypanosomiasis Institute, Entebbe*
(d) Retention of acquired characteristics by trypanosomes during cyclic evolution in the body of the tsetse	Human Trypanosomiasis Institute, Entebbe* (for <i>T. gambiense</i> Dutton) Veterinary Laboratory, Mpwapwa (for <i>T. congolense</i> Broden, and <i>T. vivax</i> Ziemann) Trypanosoma Rhodesiense Laboratory, Tinde (for <i>T. rhodesiense</i> S. & F.)
(e) Evolution of different trypanosomes in body of tsetse and other biting flies and relationship to environment (climate, &c.) of cyclic transmissibility and pathogenicity	Human Trypanosomiasis Institute, Entebbe* Veterinary Laboratory, Entebbe ... Veterinary Laboratory, Mpwapwa ... Medical Laboratory, Nyasaland ...
(f) Biological studies of tsetse flies in <i>T. rhodesiense</i> S. & F., <i>T. gambiense</i> Dutton, and <i>T. brucei</i> P. & B., areas	Work now being carried on in various territories to be continued
(g) Study of food supply of tsetse as determined by biological study of stomach contents of fly	Medical Laboratory, Nairobi† ...
(h) Investigation of the prophylactic value of Bayer 205	Human Trypanosomiasis Institute, Entebbe‡
(i) Further investigation of identity of <i>T. uniforme</i> Bruce, Hamerton, Bateman, and Mackie	Human Trypanosomiasis Institute, Entebbe Veterinary Laboratory, Entebbe§
(j) Investigation of bionomics of <i>T. brucei</i> P. & B.	Veterinary Laboratory, Entebbe ...
(k) Cultivation of <i>T. congolense</i> Broden, and <i>T. vivax</i> Ziemann, on artificial media	Veterinary Laboratory, Entebbe ...
(l) Control of tsetse fly ...	Work now in hand or projected in all territories to be continued or put in hand
(m) Trypanosomiasis of pigs ...	Veterinary Laboratory, Entebbe ... Veterinary Laboratory, Mpwapwa ...

* The present report recommends that work on these items should be carried out by the Medical Department, Uganda, as opportunity offers.

† Mr. Swynnerton informed the Entebbe Conference that he was prepared to assist in supply of sera from game animals when opportunity offered.

‡ The Conference contemplated that a large-scale field experiment should be conducted in Tanganyika if the laboratory experiments indicated that this was desirable.

1.

research in East Africa.

Trypanosomiasis (Animal and Human) Research, held at the report of that Conference and of the present report subjects included in the programme.

Reference to section and page in report of Entebbe Conference.	Reference to paragraphs in present report.		
	Discussion.	Conclusions in summary given in paragraph 102.	Recommendations in summary given in paragraph 103.
A. I, pp. 7-9	69-71 84	(16)-(18) (20)	(8) and (9) (11)
... ..	77-83	(19)	(10)
A. I, p. 8	69-71 84	(16)-(18) (20)	(8) and (9) (11)
... ..	77-83	(19)	(10)
A. III, p. 9	75	(16)-(18)	(8) and (9)
A. V, p. 10	75	(21)	12 (a) and 12 (c)
... ..	85		12 (a) and 12 (b)
... ..	85		12 (a) and 12 (b)
A. VI, pp. 10-12	75	...	13 (a) and 13 (c)
... ..	87, 88	...	13 (a) and 13 (b)
...	13 (a) and 13 (b)
A. VIII, p. 13	42	...	(4)
A. X, pp. 14-15	43-45	...	(5)
A. XII, pp. 15-17	69	(13) and (16)	(6)
B. I, p. 17	92	(23)	...
B. II, p. 17	92	(23)	...
B. III, p. 18	90, 91	(22)	...
B. IV (iii), pp. 20-22	22-40	(4)-(11)	(2)
B. XI, pp. 22-23	93	(24)	...
... ..			

§ The Conference recommended that every endeavour should be made to furnish a strain of *T. uniforme* Bruce, Hamerton, Bateman, and Mackie, to Mr. Hornby.

|| The Conference agreed that material acquired in any territory should be transmitted to either of these laboratories.

APPENDIX 2.

Diagnostic methods in human trypanosomiasis.

Note by Sir Arthur Bagshawe, C.M.G., M.B., Director, Bureau of Hygiene and Tropical Diseases.

THE present methods of diagnosis have in view the discovery of trypanosomes. They may be conveniently classed as (a) simple field methods, and (b) skilled laboratory methods; class (a) being such methods as an intelligent native can be trained to apply, and class (b) such as can usually be carried out only by a European doctor and in which laboratory apparatus is required.

Class (a) includes blood examination in thin or thick film and gland puncture,

Class (b) includes centrifugation, spinal puncture and animal inoculation.

Opinions vary as to what percentage of infected persons the (a) methods will detect, but there is general agreement that at least one case in ten may escape detection. In the hands of unskilled persons the proportion may be much greater. The (b) methods are not employable on a large scale in the field.

Owing to the difficulty of detecting trypanosomes in infected persons, efforts have for many years been made to find a reliable serological test. The methods described are:—

- (1) the serum formalin reaction;
- (2) the complement fixation reaction;
- (3) the adhesion phenomenon (of which Duke's red cell adhesion seems to be a variant).

SICÉ (1929) has described a flocculation reaction, but since nothing more has been published in regard to it, it has presumably disappointed expectations.

(1) The serum formalin or formol-gel reaction has been well tested over a series of years. The general conclusion is that since it is positive in syphilis, yaws, and leprosy, it has little diagnostic value. It is evidence of chronic infection, and trypanosomiasis is only one of its indications.

(2) The complement fixation reaction has been worked out by WATSON (1913) in Canada for dourine. It has been in use there for many years as well as in South Africa, apparently with complete success. In dourine the parasites are often undiscoverable, and a better method of diagnosis was therefore essential if trypanosome carriers were to be eliminated. In other animal trypanosomiasis, this method has been less successful (ROBINSON, 1926), though animals infected with *T. brucei* reacted to the test when *equiperdum* (dourine) antigen was used. Two authors have stated that the test

is specific in Chagas' disease, but it is not clear whether in all their positive cases the presence of trypanosomes was proved. ZOTTNER (1934) has recently described a method of obtaining a stable alcoholic antigen for this reaction in the diagnosis of animal trypanosomiasis, and he states that it is as specific as WATSON's, but more stable. This should lead to further trials of this method.

(3) The "adhesion phenomenon" was brought into prominence by DAVIS and BROWN (1927), who showed it to be strictly specific in trypanosomiasis, and its application to human trypanosomiasis was studied by JOHNSON and LESTER (1929). In this phenomenon the blood platelets stick to the trypanosomes. The latter authors applied it in Nigeria to 200 cases diagnosed as sleeping sickness, and found it to be positive in 90 per cent. of untreated cases, 86.5 per cent. of cases under treatment, 84.6 per cent. of cases "within one year after treatment," 57.8 per cent. of cases "1-3 years after treatment." They say that the test cannot be trusted in early infections, but such are rarely seen. In the 2nd and 3rd stage, before treatment has been given, it is positive in a high percentage of cases. They suggest that it is an indication of acquired immunity.

DUKE and WALLACE (1930) in Uganda studied what seems to be the same or at least a similar phenomenon, but in the material studied by them it is not the blood platelets which adhere to the trypanosomes, but the red blood cells. They suggest that the two manifestations are merely different expressions of the same physiological state. They conclude that the adhesion phenomenon is irregular and uncertain in its appearance. Even where several observations have given negative results, the possibility of trypanosomiasis is not excluded. The test was applied to 200 human cases of human trypanosomiasis.

WALLACE and WORMALL (1931), working in Uganda, continued the study of what is designated red cell adhesion, and have also given their view of the mechanism of this reaction. For this test the red cells must be those of a primate.

SAUNDERS (1931) employed the adhesion test in the Volta river region on the Gold Coast. He observed adhesions of platelets as a rule, but in some instances also he found red cell adhesion. The numbers of cases tested is not clearly given (he mentions 77), but it is stated that 91 per cent. of cases of proved trypanosomiasis gave some degree of adhesion; feeble relapsing strains of trypanosomes were not reliable.

WORMALL (1933) carried the inquiry a stage further. He found that if the test was carried out with several different strains of trypanosomes, the number of negative observations in cases of trypanosomiasis decreased considerably; that in doubtful cases treatment with trypanocidal drugs improved the power of the patient's serum or plasma to give red cell adhesion; and that with the addition of phenol serum could be kept for 3 weeks or more before

being tested. Specimens, therefore, could be sent to a central laboratory. The test is, in his view, essentially one for the laboratory.

DUKE (1933) has tested 62 sera sent to the laboratory at Entebbe from various parts of the Protectorate. Of 12 sera obtained from cases clinically suspected of trypanosomiasis, 6 were positive to *T. gambiense* or *T. rhodesiense*. Of 47 sera obtained from suspects whose blood and glands were negative, all were negative. Of 3 sera obtained from cases in whose glands trypanosomes had been found, all were positive. Dried sera also gave positive results, and dried samples have been sent to England for testing. The investigation continues and the method seems a promising one.

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