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RESEARCH INTO THE TRYPANOSOMIASIS PROBLEM: A CRITICAL CONSIDERATION OF SUGGESTED MEASURES.

BY PROFESSOR WARRINGTON YORKE, M.D.

Six years have elapsed since the subject of trypanosomiasis was last discussed by this Society. During this period comparatively little has been done on the subject, but since the war ended several very important papers have appeared, and further investigations are now contemplated by both the French and ourselves. I feel, therefore, that it is now opportune to review the present position, and consider briefly the direction which further research should take.

If we refer for a moment to the position shortly before the war, we remember that as a result of a considerable polemic which arose out of certain observations made by KINGHORN and myself in Northern Rhodesia, and by the Royal Society Commission in Nyasaland, the Secretary of State for the Colonies appointed an Inter-Departmental Committee, the terms of reference of which were as follows:—

To report—

(1) Upon the present knowledge available on the question of the parts played by wild animals and tsetse-flies in Africa in the maintenance and spread of trypanosome infections of man and stock.

(2) Whether it is necessary and feasible to carry out an experiment of game destruction in a localised area in order to gain further knowledge on these questions, and, if so, to decide the locality, probable cost, and other details of such an experiment, and to provide a scheme for its conduct.

(3) Whether it is advisable to attempt the extermination of wild animals, either generally or locally, with a view of checking the trypanosome diseases of man and stock.

(4) Whether any other measures should be taken in order to obtain means of controlling these diseases.

This Committee examined numerous witnesses, and considered written statements from various foreign experts and others who were unable to attend in person. In May, 1914, it issued a report, the general conclusions of which are as follows :—

Knowledge of the disease, its cause, and its remedies, is still in the making, and hasty and imperfectly considered action of a drastic character, such as the attempt to effect a general destruction of wild animals, is not justified by the evidence before your Committee. On the other hand, your Committee recommend that until direct means of checking the fly have been discovered, the food supply of the fly and the chances of infection should be lessened in the vicinity of centres of population and trade routes by the removal of wild animals, and that for this purpose freedom be granted both to settlers and natives to hunt and destory the animals within prescribed areas and subject to prescribed conditions.

So far as regards the disease in Uganda, the measures already taken have effectually checked the epidemic, and removed the mass of the population from the danger of further infection. While, no doubt, it is desirable that the land lying near Victoria Nyanza should be rendered again available for the use of that population. this is not a question of immediate urgency, and may well await the acquisition of further knowledge.

With regard to the Nyasaland and Rhodesian form of the disease, its incidence on the population is slight, and it is not increasing. The evidence points to its being an old disease, endemic and not extensive, and though it is unsafe to prophesy, there is no apparent reason to anticipate its appearance in an epidemic form. Having regard to the importance of the question whether man forms a reservoir of the human trypanosome, your Committee would lay emphasis on the desirability of further experiments, as suggested in paragraphs 41 and 42 above. (See also Appendix D.)

It must be recognised that the evidence all points to the conclusion that, if tsetse-fly could be eliminated or removed from contact with human settlement, sleeping sickness would practically disappear, infection conveyed by other biting flies being a negligible factor in the spread of the disease.

For this reason your Committee attach great importance to a proper and sufficient equipment of entomological research into the bionomics of the incriminated tsetse-flies. This form of research has, in their view, been insufficiently pursued up to the present time. The workers have been zealous, but few in numbers, and the work consequently limited to only a very small portion of the fly-belts and areas from which the danger arises.

Different views are taken as to the prospect of dealing with the fly, but it was, as your Committee think truly, said by more than one of the witnesses that in this form of research there is a large element of chance—that accident may at any time lay bare a secret which may lead to the solution of the problem—and that the multiplication of workers is the multiplication of those chances.

Your Committee think, therefore, that, within reason, there should be devoted to this form of inquiry a considerable portion of such funds as may be available in British Possessions, and that endeavours should be made to obtain the co-operation in this work of Foreign Powers in their African Possessions, the results of the work being from time to time tabulated and collected.

Research will, no doubt, be continued as to the nature of the different trypanosomes, and the part they play in the infection of man or of domestic stock.

The proposed experiment of removal of wild animals from a selected area may produce valuable results, both as regards knowledge of the habits of the fly, and as to the extent to which the infectivity of the fly, and subsequently the infection of man or stock, is derived from the wild animals.

As has been pointed out, the result of this experiment cannot be confidently anticipated. There are possible fallacies and uncertainties involved from the very nature of the problem, and in dealing with natural conditions there is always the possibility of unknown factors vitiating or defeating action based on the apparent results of any such experiment.

Nevertheless, your Committee think that there is sufficient to justify an expectation of useful results, and they recommend that if a suitable locality can be found, where an experiment can be carried out at a reasonable cost, it should be undertaken. They are, however, of the opinion that the carrying out of the other measures recommended should not be delayed pending the results of the experiment, which cannot be expected to emerge for two or three years.

It is perhaps needless for your Committee to say that they hope that medical research as to treatment of the disease and the production of immunity will be continued.

The above recommendations relate mainly to the acquisition of knowledge on which further action may be based. As regards immediate action, your Committee strongly recommend that measures of clearing should be undertaken where they are practicable and would tend to check the spread of the disease, and render life in settlements and travel by road safe for men and stock.

This question has been fully dealt with already, and it is only necessary to say here that your Committee attach much importance to this matter.

> Your Committee would point out that the action in various directions which they have suggested is for the general benefit of every part of Africa in which tsetse-fly exists, and is or may be the cause of sleeping sickness, so that so far as the cost would fall on local funds they should not fall only on that Possession which may be selected for any particular experiment, as being that in which the knowledge sought is most likely to be attained. It is even possible that Foreign Governments might be willing to share in the cost, but this is hardly a matter on which it is fitting that your Committee should make any substantive recommendation. Nor is the question of a contribution from public funds one for them to deal with, though it is, they think, doubtful whether local funds would be sufficient to bear the costs of the various inquiries and experiments which they think desirable.

Action on this report was necessarily deferred owing to the outbreak of war; other work and other diseases monopolised attention, and research into trypanosomiasis practically ceased. It has now become apparent that the ravages of sleeping sickness have increased during the war in certain of the French equatorial colonies, and also in portions of the Belgian Congo. This knowledge caused the Société de Pathologie Exotique to appoint a committee, under the presidency of M. LAVERAN, to consider what means should be taken to deal with the situation. This Committee reported in July to the Société, and its report was accepted and forwarded to the Colonial Minister, and also to the Governors-General of the French Colonies in Africa. About the same time our Secretary of State for the Colonies took action on the report of the Earl of Desart's Inter-Departmental Committee, and asked the Imperial Bureau of Entomology for recommendations. The matter was referred by the Bureau to its Glossina Sub-Committee, which subsequently issued a report containing certain recommendations for future action.

Now, the different procedures adopted in France and in this country seem to me to be a matter not without interest to this Society. In France the Société de Pathologie Exotique took action and advised their Government; in this country the Government has to seek for advice, and does so, not from this Society but from the Imperial Bureau of Entomology. One cannot help feeling that herein lies a moral which this Society should take to heart. Surely on matters relating to tropical medicine, in all its various aspects, a Society like ours, which contains amongst its hundreds of members, medical men, veterinarians, entomologists and zoologists from all quarters of the earth, should be able to crystallise its ideas, and advise the Government accordingly. If this Royal Society is to be a living force, and not a mere agglomeration of academic pedants, it should be able to function in this manner on questions of great medical and economic importance.

In this paper I propose to refer briefly to the report of the Société de Pathologie Exotique, and then to discuss in more detail the report and recommendations of the Glossina Sub-Committee of the Imperial Bureau of Entomology. It is important to realise at once that the problems which confront us are, in many respects, different from those with which the French have to deal.

In the French equatorial colonies the most urgent need of the moment is the control of the epidemics of *gambiense* sleeping sickness, which are ravaging certain parts of them. The primary prophylactic measure recommended by the French is the atoxylisation of the sick, with the object of destroying the flagellates in the blood of all infected cases. Marvellous results are to be anticipated from this procedure, provided a sufficient personnel be available for some years in all infested districts, so that all the infected could be recognised and treated. With reference to measures directed against the tsetse, the report states that one can hardly dream of causing the complete disappearance of the Glossina, which swarm on the banks of most of the streams of equatorial Africa, but measures can be taken to remove the natives and to protect them against bites. Clearing has been declared by all observers one of the most useful measures which can be practised. There is room for research to ascertain whether we cannot destroy Glossina by opposing them with other insects or animals which are their natural enemies. It is recalled that pigs are particularly attractive to Glossina, and it is suggested that possibly herds of these animals, and of other resistant beasts, could be grouped at certain places in the vicinity of the villages in such a manner as to form a sort of protecting screen. As the spread of sleeping sickness is due to the incessant movement of porters and travellers, and as the disease is aggravated by want, excessive porterage, and fatigue, strict administrative control is necessary. The manner in which the above recommendations should be applied, and the organisation necessary, are discussed in detail at the end of the report.

Although in none of the British colonies is there at the present time any very serious epidemic of *gambiense* sleeping sickness, we have in Central and South-Eastern Africa to deal with a situation, which in its way is just as serious, and at least as difficult of solution, as that which confronts the French in their equatorial colonies. Fortunately, the amount of *rhodesiense* sleeping sickness occurring in Central and South-Eastern Africa is at the present time small, but the question of trypanosomiasis of domestic stock is one of the greatest economic importance. This fact is clearly indicated in the opening paragraphs of the report of the Glossina Sub-Committee, which reads as follows :—

> Some idea of the importance of the tsetse-flies of the *Glossina morsitans* group as an obstacle to the development of Tropical Africa may be gathered from a consideration of the wide areas over which they range. In Southern Rhodesia, in which the fly-belts are comparatively small and have been more carefully surveyed than elsewhere, their extent has recently been estimated at 9,000 square miles. With reference to North-Eastern Rhodesia, Messrs. KINGHORN and MONTGOMERY have expressed the opinion that it would be difficult to find a continuous area of fifty square miles free from *G. morsitans* anywhere except on the Serenje plateau, around Fort Jameson, and on the high plateau between Lakes Nyasa and Tanganyika. In Nyasaland probably more than a fifth of the area is infested by tsetse-flies ; while in Tanganyika Territory the fly-belts must cover nearly half the country.

The Report of the Glossina Sub-Committee consists of three portions : the first summarises very briefly the present position as regards the various tsetse-flies ; the second gives a list of suggestions for observations and experiments ; and the third makes detailed recommendations concerning the organisation necessary for the elucidation of the foregoing problems. It is to the second and third portions of this report that I desire to draw your attention.

It is impossible here to give a list of all the suggestions for observations and experiments, but they deal with the following points : (1) the distribution of the fly, (2) the effects of clearing, (3) breeding-grounds, (4) food of the fly, (5) destruction of adults, (6) parasites, (7) enemies of the fly, and (8) influence of odours. It will be observed that the subject which was the main one before the Earl of Desart's Inter-Departmental Committee in 1913-14, and which was really the cause of the appointment of that Committee, viz., the inter-relationship of game, tsetse, and the pathogenic trypanosomes of man and domestic stock is completely ignored. This is the more remarkable as the report of the Glossina Sub-Committee was called for directly as the result of the report of the 1913-14 Inter-Departmental Committee. However, I will not go further into this matter at the moment, but proceed to discuss the methods by which the Glossina Sub-Committee propose to investigate the problems which they themselves have decided it is desirable should be solved. The following are the recommendations :—

> For the elucidation of the foregoing problems it seems desirable that there should be at least six different experimental stations, widely distributed over Tropical Africa, and the countries that suggest themselves as being most suitable for the purpose are Zululand, Southern Rhodesia, Nyasaland, Tanganyika Territory, the Sudan and Northern Nigeria.
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> The selection of the precise areas in these countries that would afford the best facilities for these investigations would require a more intimate knowledge of local conditions than the Sub-Committee at present possesses. But it may be laid down generally that the various areas should be representative of different types of environment, and that they should, as far as possible, be situated in localities in which the presence of tsetse-flies is actually obstructing settlement, or is likely to do so in the near future.
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> Each of these stations should be under the control of a competent entomologist, and he should have at least one assistant who would be able to carry on the work in the event of the senior man falling sick or going on leave. Unfortunately, at the present time there are very few men who combine the requisite qualifications and experience for this class of work. This difficulty could be met by starting, in the first instance, say, two stations only. In these the new men could be concentrated for training purposes. After a time, the most promising pupil could be left in charge, and the others would proceed to open up a new station elsewhere.
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> While the observers in each station would be expected to keep an alert watch on all aspects of this complex problem, it would probably be advisable for some of the stations to give special attention to certain lines of work, such as control by clearing, artificial breeding-places, rearing of parasites, etc.
>
> Each station ought to send in a monthly progress report to the Imperial Bureau of Entomology, so that the Glossina Sub-Committee may be kept advised of all the latest developments. They

would thus be in a position to co-ordinate the work, to prevent overlapping, and to arrange promptly for the testing under divers conditions of any new hypothesis that may be put forward.

As the work progresses, it is probable that special lines of inquiry will become necessary, for which the aid of a protozoologist or veterinarian may be required, and provision should be made for such eventualities.

It will be observed that what, in brief, the report recommends is (1) that there shall be set up at least six different experimental stations in widely-separated places in Tropical Africa; (2) that each of these stations should be under the control of a competent entomologist, who should have at least one assistant who would be able to carry on the work in the event of the senior man falling sick or going on leave; and (3) that each station should send in a monthly report to the Imperial Bureau, which would then be in a position to co-ordinate the work

Now the sum of £50,000 (if such a sum can be raised) has been mentioned as the cost of this organisation over a period of five years. A brief calculation will, however, shew that such a sum, which allows for an annual expenditure by each experimental station of £1,700, is totally inadequate for the purpose. Such an amount is hopelessly insufficient to provide for salaries, transport, camps, labour, equipment and leave of the personnel of the Commission; there will be no balance for the purpose of experiment and investigation, to say nothing of the many other incidental expenses inseparable from such undertakings, and the possibility of any experimental work requiring the employment of labour is completely excluded.

The first criticism I have to make, therefore, is that if the above recommendations are adopted, a much greater sum than £50,000 must be provided.

Let us, however, assume for the moment that money is a matter of no consequence, and proceed to consider whether such an organisation as this is likely to succeed in obtaining the information which will enable the Imperial Bureau to answer the questions which it enumerates within a period of five years.

It is admitted that "unfortunately at the present time there are a very few men who combine the requisite qualifications and experience for this class of work." In order to get over this difficulty it is proposed to start with only two stations and concentrate the "new men" in these for training purposes. Now the task of training these "new men" would obviously be a lengthy one; ill trained men who were ignorant of the literature of the subject, which is already rather extensive, and who know neither Africa nor the native or his language, could hardly be expected to advance knowledge of this most complex subject very much. If four of the proposed stations, therefore, require to be staffed by "new men," nothing very valuable in the way of information is to be anticipated from them for a number of years.

Again, if we assume that this difficulty can be surmounted and sufficient well-trained entomologists can be found within, say, a year, to provide each of the six experimental stations with its full staff of one competent entomologist and at least one assistant, would such an organisation prove adequate to the task which is required of it? If allowances be made for such contingencies as sickness and furlough, it is clear that during a considerable proportion of the five years there would be in each station only one entomologist—a condition of affairs not far removed from that which has obtained during the past ten years.

Realising these facts, we must ask ourselves whether it is probable that the solution of the problems enumerated in the report would be obtained within any reasonable space of time by such an organisation. Let us for a moment consider several of the more important problems which it is proposed that the one or two men in each of these widely scattered stations are expected to investigate:—

1. What are the precise factors that determine the limits of a fly area?
2. In the open "orchard bush" so much frequented by *G. morsitans* is it sufficient to clear away shrubs and branches of trees to a height of twelve or fifteen feet, or must trees of twenty to thirty feet be felled?
3. What is the minimum width of cleared belt that would effectively check the spread of the fly?

4. Can the number of fly be materially reduced by judicious burning of grass at times when food is scarce and shelter limited?
5. Compare the results obtained by indiscriminate clearing and by the clearing of breeding places after these have been defined.
6. Test the possibility of introducing additional parasites of different kinds from remote parts of Africa.

These are doubtless important questions, and their solution and that of the others enumerated in the report might enable us to formulate some scheme for dealing with the problem, but what I wish us to consider is whether it is reasonable to expect that one or two entomologists, unable by lack of sufficient funds to dispose of more than a very limited amount of native labour, are likely to succeed in providing answers to them.

My general criticism of this portion of the report is, then, that the organisation which is recommended is entirely inadequate for the work which it is expected to perform. The solutions of the very questions which the report states require elucidation can be obtained only by intense and concentrated effort and not by the adoption of such a scheme as the one we have just considered, which involves dissipation of energy and precludes possibility of experimental investigation on a large scale. The adoption of the measures recommended in this report will result in failure not only to elucidate any practical solution of the problem, but to advance knowledge in any considerable degree; the report is, in fact, a proposal to perpetuate as regards research the state of affairs which existed before the war.

These remarks, however, do not complete my criticism of the report of the Glossina Sub-Committee; as I have already stated, the main question which was before the Earl of Desart's Committee, viz., the relation of game, fly, and trypanosomiasis of man and domestic stock is completely ignored. The work which immediately preceded, and which was the direct cause of, the appointment of Lord Desart's Committee demonstrated that the main, and for practical purposes the only, reservoir of the pathogenic trypanosomes of man and domestic stock is the big game. So far as I am aware, nobody has criticised the results obtained by KINGHORN and myself in the Luangwa Valley, and by the Royal Society Commission in Nyasaland, in so far as they relate to the pathogenic trypanosomes of domestic stock. Now it is important to recognise that, judged from the economic point of view, trypanosomiasis of domestic stock is at present in Central and South-Eastern Africa immeasurably more important than is trypanosomiasis of man. On this account alone it seems to me that the effect of game elimination in a definite zone should be decided once and for all by a carefully designed and controlled experiment.

The observations by KINGHORN and myself that 16 per cent. of the game in the Luangwa Valley were infected with *T. rhodesiense*, the trypanosome pathogenic to man, although quickly confirmed by the Royal Society Commission in Nyasaland, met with the most hostile criticism on all hands. While most of this criticism was based on hypotheses and speculation, and was therefore of no value, some of it was founded on scientific observations, and requires careful consideration; I shall refer to it later.

The question whether game really forms the main reservoir of the trypanosome pathogenic to man is not of mere academic importance, as a glance at the report of the Conference on Sleeping Sickness, held at Pretoria on 9th March, 1920, will shew. This Conference was called by the Minister of Public Health in connection with an application to the Union Government by the Natal Coast Labour Recruiting Corporation, Ltd., for the removal of the prohibition in respect of recruitment of native labourers for the sugar estates from the country between the Limpopo and Zambesi Rivers—also with the recently reported extension southward of tsetse-fly and the infection of sleeping sickness. Unfortunately, time does not allow one to record in detail the findings of this Conference. The following are, however, among the most important.

It was unanimously agreed that it would be dangerous to allow recruiting for the Natal Sugar Estates in the belt of country between the Limpopo and the Zambesi Rivers, or in any area where there is any risk of an infected native being recruited.

In regard to the question, "What are our present southern limits of sleeping

sickness infection, and what are the risks of the introduction of the disease into the Union?" it was decided by the Conference that under the present conditions the risks of introduction of infection were undoubtedly very great, and that both as regards the Zululand-Mozambique border and infected areas in Rhodesia, the existing arrangements for safeguarding against introduction of sleeping sickness are totally inadequate.

After discussion, it was agreed :—

> That the Zululand-Mozambique border should be closed for all native movement inwards, except at two ports of entry, namely, Nduma and Maputa—this not to interfere with the existing system of visiting passes for local natives. Medical examination at the border would be very difficult to enforce, and would be unreliable even if supplemented by a microscopic examination of the blood. A prolonged period of medical observation, with blood examinations and animal inoculations, is necessary in order to exclude the disease.

This resolution is followed by others relating to the strengthening of police patrols on the border the provision of penalties for infringement of regulations, and the issuing of certain additional regulations.

I have ventured to refer to this report at such length because it bears most directly upon the subject under discussion. It will be seen that the resolutions are of a rather drastic character, and interfere m a greater or less degree with the economic life of the community.

Now the deliberations of this Conference and the resolutions it passed are based on the assumption that man constitutes the main reservoir of the trypanosome which affects man in these localities, viz., *T. rhodesiense.* If this be not so, and the game be the main reservoir of the virus pathogenic to man, then the above recommendations, with the resulting economic disturbance and the expenditure involved in putting them into force, are futile.

I will now review briefly the evidence on which those who deny the identity of the human parasite with that of the same appearance found in game base their contention.

(1) *Epidemiological.* It has been asserted that these two parasites are undoubtedly different; because in certain *morsitans* areas, the animal trypanosome (*T. brucei* vel *T. ugandae* vel *T. pecaudi*) is found in game and stock and in tsetse-fly without cases of human trypanosomiasis occurring.

(2) *Experimental inoculation of the human subject with the game trypanosome.* As it is upon these observations that most faith is placed, it is necessary to refer to them in detail. In 1913 TAUTE fed upon himself, with negative result, laboratory-bred *G. morsitans* which had been rendered infective with the *rhodesiense*-like game trypanosome; he also subsequently inoculated himself with 2 cc. of the blood of a dog naturally infected with the same trypanosome, and here again the result was negative; these experiments were carried out at Lubimbinu, in Portuguese East Africa. Much more impressive, however, is a later series of experiments performed in 1919 by TAUTE and HUBER. They inoculated themselves and 129 natives, many of whom were in poor condition from malaria and other causes, with the *rhodesiense*-like trypanosome from four naturally infected horses and two mules. In no instance was an infection obtained in man, although the animals (rats, dogs and a goat) used as controls all became infected and died. Naturally, the greatest importance has been attached to these experiments, which by many are regarded as conclusive in shewing the human and game parasites are not the same.

While I am quite prepared to admit that at first sight this conclusion may seem correct, I think, if we consider the facts more closely, it will become clear that KLEINE and TAUTE have not proved their point, and that their observations are quite in harmony with the view that the two trypansomes are identical. To my mind the various facts which have been elicited regarding human trypanosomiasis in South Central Africa can best be explained on the view that the game is the great reservoir from which man (as well as his domestic animals) becomes infected. To develop my argument, I find it necessary to commence with the postulate that man is extremely resistent to infection with any member of the genus Trypanosoma under natural conditions, or, in other words, that he possesses great natural immunity to infection. This postulate is, however, no

mere baseless hypothesis, but is supported by considerable evidence. In view of the fact that man has never been found infected with *T. congolense*, and only on a single occasion with *T. vivax*—pathogenic trypanosomes which are exceedingly common and of universal distribution in Tropical Africa—it is evident that man must possess a considerable degree of natural immunity to them. Again, certain facts regarding *T. gambiense* are in harmony with this postulate. If man be readily susceptible to infection with *T. gambiense*, it is difficult to account for the absence of sleeping sickness in an epidemic form in the West Coast Colonies and in certain other parts of Tropical Africa. The cause of the epidemic in Uganda has recently been discussed by DUKE, in a most able paper, and explained by him on the ground of a mechanical transmission by *G. palpalis* from man to man of a strain of *T. gambiense* of increased virulence. It is a well recognised fact that passage of *T. gambiense*, or of any other African trypanosome, in the laboratory, from animal to animal greatly increases its virulence for that species of animal; for example, the strain of *T. gambiense* maintained by us in Runcorn was at the time of its isolation from the human being of very slight virulence for rats, these animals living, on an average, over a hundred days, but after the strain had been passed through these animals for a number of years its virulence for them had so increased that they died in about fourteen days. This increase of virulence is, of course, artificial and does not take place when the parasite is passed alternately through the vertebrate and invertebrate hosts; but, as DUKE has pointed out, an analogous increase in virulence probably also takes place in nature when conditions are favourable—that is, when there is a broad and intimate contact between man and fly. Such conditions were found in the densely-packed canoes on the fly-infested shores of Victoria Nyanza, the fly acting the part of the syringe in the laboratory and conveying infected blood mechanically from one native to another.

To return now to *rhodesiense* sleeping sickness, how can we explain its distribution otherwise than on the assumption that man possesses great natural immunity? The more its distribution is investigated, the more does it become apparent that the infection is distributed more or less uniformly over an enormous stretch of country in Central and South-Eastern Africa. Now, if infected man were the reservoir from which other men become infected, one would naturally expect to find a more or less considerable focus of the disease in every locality where an infected case is found. This, I think, is not so; the total number of cases of *rhodesiense* infection which have as yet been discovered is still rather small, but the figures, such as exist, suggest that the disease is widely and uniformly distributed, allowances, of course, being made for differences in the density of *G. morsitans*. I hold, therefore, in direct contradistinction to KLEINE, that what epidemiological facts we have at our disposal suggest that man becomes infected from the widely diffused game reservoir rather than from other infected men.

Turning now to TAUTE'S remarkable experiments on the human subject, let us consider what exactly he has proved. In my judgment, all that TAUTE has proved is that man is very resistant to infection. I believe that if, in his first experiment, TAUTE had fed his laboratory-bred flies on an infected man, instead of on monkeys and antelopes, he would have obtained a similar result; whereas if, in the second experiment, his inoculations had been made from the blood of an infected man, instead of from infected horses and mules, the result might well have been different, because of the exaltation in virulence of the strain for the human being, which might manifest itself as the result of passage through two human hosts consecutively without an intermediate passage through the invertebrate host. TAUTE'S results, far from militating against the hypothesis that the game is the reservoir from which man is infected, are only what would be expected if the hypothesis is correct. KINGHORN and I shewed that in the Luangwa Valley one in five hundred flies was infected (in an infective condition) with the *rhodesiense*-like trypanosome, and similar figures were afterwards obtained by the Royal Society Commission in Nyasaland. Under these circumstances large numbers of human beings must be bitten every day by an infective fly, and yet cases of human infection are very few. The only conclusion we can draw from this is that man is remarkably resistant to the trypanosome in question; consequently, on the assumption that the game trypanosome is the same as that found in man, many more than 130 persons would have to be used in experiments

such as that conducted by TAUTE and HUBER before one could expect to obtain a positive result.

Before leaving the subject, I should like to draw attention to another aspect which has apparently been entirely overlooked by those who, like KLEINE and TAUTE, deny the identity of *T. rhodesiense* with the trypanosome of the same appearance found by KINGHORN and myself in game. It is clear that a large proportion of the game must be infected with *T. rhodesiense*. The Royal Society Commission in Uganda, in 1910, succeeded in infecting all of eleven antelopes by feeding upon them laboratory-bred *G. palpalis*, experimentally infected with *T. gambiense* from a case of sleeping sickness. FRASER and DUKE (1912) found that the antelopes so infected remained in perfect health for over a year, and DUKE later recorded that he was able to infect *G. palpalis* from an antelope infected experimentally with *T. gambiense* twenty-two months previously. WECK (1914) records that in German East Africa he inoculated successfully an antelope with blood from a human being infected with *T. rhodesiense*; the antelope shewed no signs of disease, but its blood was infective for monkeys and dogs five weeks later, and there appears no reason for doubting that the blood of this antelope would also have infected *G. morsitans*; nor is there any ground for doubting that if antelope can be infected directly from the human being, they could also be infected from one another. This being the case, it follows that antelope must become infected with *T. rhodesiense* one from the other by *G. morsitans* precisely in the same way as they are infected with the common pathogenic trypanosomes of domestic stock.

I maintain, therefore, that the game constitute the main reservoir from which *G. morsitans* draws the trypanosomes pathogenic to man and his domestic stock. For practical purposes the game constitute the only reservoir, because man, domestic stock, monkeys and the small vermin rapidly die of the infection, whereas the antelope are tolerant, and harbour the parasites in their blood presumably for long periods without exhibiting signs of disease.

There seems to me, therefore, to be a clear indication that any investigation which is contemplated with a view to enable us to deal with the problem of trypanosomiasis in South and Central East Africa should have as its primary objective the obtaining of precise information concerning the inter-relationship of game, fly, and the trypanosomes pathogenic to man and stock.

Information on two questions, both of great importance, might be expected to emerge from a carefully conducted and controlled experimental elimination of game from a prescribed district. These are :—

1. The effect on the tsetse-fly.
2. The effect on the trypanosomiasis of man and domestic stock.

May I at this point refer for a moment to the great game drive which took place in Zululand in August, 1920, wherein 500 hunters are said to have taken part, and to have been aided by an army of 5,000 natives acting as beaters. The area comprised in this drive is stated to be the size of Cornwall and Devon. Unfortunately, I have no information regarding the organisation of this great drive, beyond the brief reference which has appeared in the daily press, but I should like to point out that, unless it was prece ded by a thorough and scientific investigation of the conditions, both in respect of fly and of the trypanosomes of game, man and domestic stock which existed before the drive, and unless it is followed by an equally careful investigation extended over a sufficient length of time, we shall have no precise information regarding the results of what must have been an unparalleled slaughter of game. I sincerely trust, therefore, that those who organised this drive had this fact in mind, otherwise the failure to take advantage of an unrivalled opportunity would be deplorable.

To sum up, I am of opinion that the report of the Imperial Bureau of Entomology is open to serious criticism, and that the recommendations contained in it should not be put into operation. I hold this view, firstly, because the report evades what I regard to be one of the main problems requiring immediate investigation, namely, the dependence of fly and trypanosomiasis on the game; and, secondly, because its recommendations concerning the method by which the problems, which the report itself considers to be of

primary importance, should be investigated are wholly inadequate for the purpose, are little if anything in advance on the methods adopted in the past, and are calculated to result in failure at the cost of much money and time; in short, these recommendations appear to me to indicate a lack of appreciation of the gravity and difficulty of the problem demanding investigation.

In contradistinction to the recommendation of the Imperial Bureau of Entomology, I would suggest (1) that in future investigation effort should be concentrated instead of dissipated; (2) that the work of entomological and medical and veterinary research into the trypanosomiasis problem be combined under one central organisation in Africa, and that such organisation be supported by the pooled contributions of all African States interested; (3) that the personnel of the investigating commission be large enough to ensure continuity of work in all directions, thus obviating interruptions due to such exigencies as illness or leave, and preventing the staleness and inertia which are so likely to result from isolation; (4) that sufficient funds be placed at the disposal of the investigating commission to allow of the employment of adequate native labour, so that experimental work can be undertaken on a sufficiently large scale, thus enabling the investigation of the dependence of fly and trypanosomiasis on game, and of the various problems enumerated in the report of the Imperial Bureau of Entomology to be carried out in a satisfactory manner, and with some reasonable prospect of success.

Discussion.

The President: Professor Warrington Yorke has raised some very important issues in this valuable paper, and as there are a number of Fellows here who have had a great experience in regard to trypanosomes and sleeping sickness, I shall expect the contribution to give rise to considerable discussion.

Professor Yorke has shewn the serious situation of sleeping sickness from the epidemiological as well as from the economic standpoint, and he has strongly emphasised the important fact that, in any investigation which may be undertaken to discover the best methods of combating or preventing sleeping sickness, the inter-relationship of game, the tsetse-fly and pathogenic trypanosomes in man and in domestic stock must not be ignored. He complains—very rightly, I think—that this aspect of the question has not been considered sufficiently in the recommendations of the Bureau of Entomology. And he further points out that the organisation which is proposed is totally inadequate for the problems to be solved. I agree with Dr. Yorke's point of view; I do regard it as a most important thing that the inter-relationship I have mentioned should be thoroughly investigated; and I agree, too, that the organisation proposed could not possibly advance the question further than its present stage. I remember that when, in 1913, I went to Uganda, I was amazed to find that there were only two scientists working at the subject there; or perhaps I should say one scientist, for one was a lady, Miss Robertson, who had been working on the subject for some considerable time, while the other was an American, Mr. Fiske, who had just arrived, and this in a region where 200,000 deaths had taken place within a few years, and when, even at the date of my visit, there was a certain amount of anxiety with regard to this disease. On my return home I availed myself of the opportunity of submitting, in my general report, an expression of my astonishment at the inadequate means being taken to deal with the subject. I do not blame the Colonial Office, because they do not hold the pursestrings; they are held by the Treasury, and the Treasury are not interested in tropical diseases or in the health of the inhabitants of the tropics. Colonies which are rich have to take take care of themselves—and rightly so, as they are quite able financially to look after their own health Colonies that are poor have to do the same, and they suffer accordingly. It is in this uneconomical attitude that the difficulty lies in securing proper research and efficient health conditions.