The fight against trypanosomiasis : the British contribution.

THE FIGHT AGAINST TRYPANOSOMIASIS: THE BRITISH CONTRIBUTION

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THE FIGHT AGAINST TRYPANOSOMIASIS: THE BRITISH CONTRIBUTION

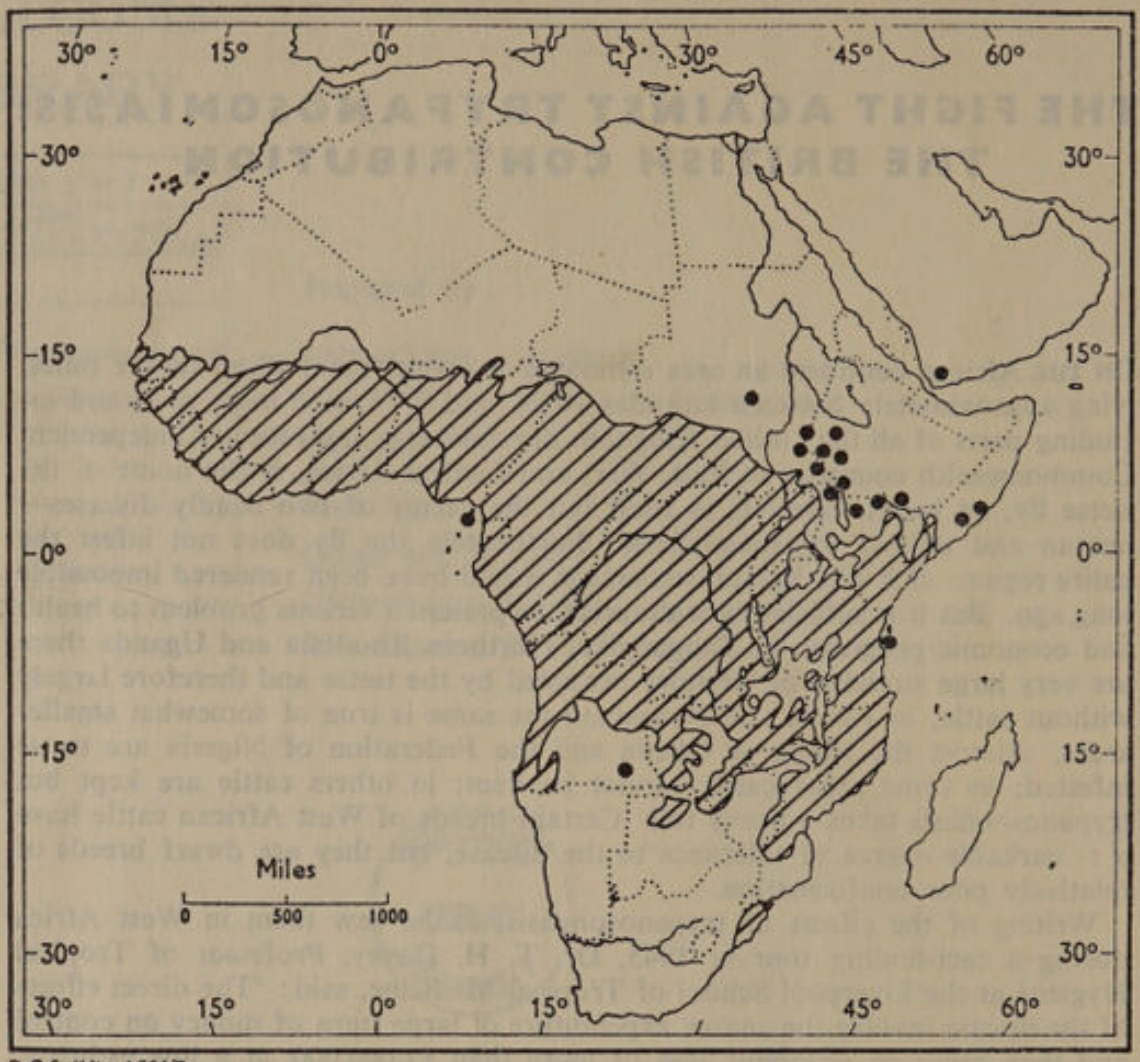
On the African continent an area estimated at about four million square miles, lying approximately between latitudes 10°N. and 25°S. (see map, p. 2) and including parts of all the United Kingdom dependencies and recently independent Commonwealth countries in East, West and Central Africa, is the home of the tsetse fly, an insect harmless in itself but the vector of two deadly diseases—human and animal trypanosomiasis. Fortunately the fly does not infest the entire region: if it did, human settlement would have been rendered impossible long ago. But it is sufficiently widespread to present a serious problem to health and economic progress. In Tanganyika, Northern Rhodesia and Uganda there are very large stretches of territory occupied by the tsetse and therefore largely without cattle; in Kenya and Nyasaland the same is true of somewhat smaller areas. Almost the whole of Ghana and the Federation of Nigeria are tsetse infested: in some areas cattle cannot be kept; in others cattle are kept but trypanosomiasis takes a heavy toll. Certain breeds of West African cattle have a remarkable degree of tolerance to the disease, but they are dwarf breeds of relatively poor conformation.

Writing of the effects of trypanosomiasis, as he saw them in West Africa during a fact-finding tour in 1945, Dr. T. H. Davey, Professor of Tropical Hygiene at the Liverpool School of Tropical Medicine, said: 'The direct effects of the disease involve the annual expenditure of large sums of money on control and they cause an economic loss of more than £1,000,000, at a low estimate, through the death of cattle. The losses through indirect effects of the presence of fly cannot be computed but must be estimated as serious. They are demonstrated in the diminished vitality of the people, the serious deficiency of their diet in high-grade protein, the steady loss of fertility of the soil and the absence of beasts for draught or work. These factors are causing a progressive impoverishment of the people, while medical and administrative policies are encouraging a steady growth of the population. No attempt at progress in West Africa will be satisfactorily based if it does not undertake, as a fundamental and preliminary step, the control of trypanosomiasis, which shows its effect in practically every field of human activity.'

Since the date of Dr. Davey's report a great deal of progress has been made. Modern developments in medical treatment, together with the extension of medical services, have brought human trypanosomiasis, or sleeping sickness, to the stage where it is no longer a major cause of sickness or death, although, according to a recent official report, 'it is a constant threat only to be met by vigilance and energetic preventive measures'. Animal trypanosomiasis has been more difficult to combat, but drugs now in use are proving effective in curing the disease, and the development of prophylactic drugs for animals has made possible the productive maintenance of cattle in areas which are lightly infested with tsetse.

Britain has taken a major share in the fight against the tsetse and trypanosomiasis. From the time of David Bruce, who at the end of the nineteenth century

THE DISTRIBUTION OF THE TSETSE FLY IN AFRICA



D.C.S. (Misc.) 226/7

Genus Glossina

Small areas or isolated records

Reproduced from Professor P.A. Buxton's The Natural History of Tsetse Flies, London School of Hygiene and Tropical Medicine, Memoir No. 10, 1955.

discovered the role of the fly in transmitting the disease, British scientists and field workers, in Britain and in Africa, have played a leading part in the development of curative and prophylactic drugs, in devising and executing methods of eliminating the tsetse, and in basic research on related problems. Since 1945 Britain has contributed over £1·8 million from Colonial Development and Welfare (CD and W) funds for trypanosomiasis and tsetse research for the benefit of its dependent territories. But it is not only the dependent territories which have benefited and will continue to benefit from British work in this field. Through the results of research at laboratories in Britain, through the service of Britons in veterinary, medical and tsetse control departments and in regional and territorial research organisations in Africa, and in other ways, Britain is continuing to provide scientific assistance to the newly independent African countries.

Meanwhile, the Governments of the African countries concerned have not been slow to recognise their responsibilities or to realise that the battle against the tsetse fly is a battle against poverty and under-development as well as

against disease. It is not enough to find a cure: means must also be found of re-populating and bringing back into efficient use the great tracts of potential farm and pasture land which in the past have been left in possession of the fly. Increasingly it is coming to be understood that tsetse and trypanosomiasis control must be a combined operation, in which scientific research, medical, veterinary and entomological work, land reclamation, agricultural development and education all play their part. With this in mind, Governments in Africa no longer treat tsetse control as an isolated problem, but as an integral part of the whole question of the economic use of land in the general development of their territories.

EARLY DEVELOPMENTS

Although few written records exist, it is probable that the trypanosomiasis diseases of man and domestic animals have had great historic importance for the African continent. The Arabs of the tenth century—the earliest known invaders of Africa—and the Portuguese in the fifteenth century found their conquests and explorations limited by the boundaries of the fly-country. Although Europeans have traded with West Africa for five centuries, they penetrated the continent only a very little way until the nineteenth century, because of the prevalence of disease, especially the 'negro lethargy' or sleeping sickness, and the complete absence of transport animals, which could not survive in fly-country.

The first known recorded account of sleeping sickness was given by the fourteenth century Arab writer Al Qualq-Washudi, who referred to a Malle chieftain, living in the bend of the River Niger, who developed chronic somnolence for some years before his death.

The first record by a European is by John Atkins, an English naval surgeon, who visited the coast of Guinea in 1721 and later wrote a graphic description in his book, *The Navy Surgeon*. Sufferers seldom recovered from the lethargy induced by the disease, he said, and even if they did, 'they lose the little reason they have and turn idiot'.

The Africans tried to treat sleeping sickness, but having no idea of the cause, they treated only the symptoms and could find no effective cure. They did not know that there was any connection between human sleeping sickness and the killing disease which attacked their cattle and horses in fly-country: but for that, too, there was no cure.

The situation remained without hope until nearly the end of the nineteenth century. But in 1894 David Bruce, a young British surgeon who had already done valuable work in isolating the cause of Malta fever, was sent to Zululand to investigate a disease, known as nagana, which was ravaging the native cattle. Bruce identified nagana as tsetse fly disease, and within the next two years proved that it was caused not by poison injected by the fly, but by the introduction into the victim's blood of minute organisms known as trypanosomes.

In 1901 an outbreak of sleeping sickness on a tremendous scale flared up in Uganda, decimating the African population. A commission, sent out from Britain at the request of the Foreign and Colonial Offices, could not trace the cause of the disease, and once again Bruce was sent for. Working in conjunction with members of the commission, he proved, within a few months of his arrival in 1903, that sleeping sickness in man, like nagana in cattle, was produced by trypanosomes transmitted by the tsetse fly.

Bruce's discoveries formed the foundation for all the subsequent work which, in little more than half a century, has made it possible to control sleeping sickness and has gone some way towards achieving control over trypanosomiasis of domestic animals.

In the years immediately following the completion of Bruce's work, although some progress was made in developing curative drugs, the real problem was realised to be the vastness of the area infested by tsetse and the inadequacy of scientific knowledge about the fly itself. In 1919, Charles Swynnerton, who was appointed the first Game Warden in Tanganyika and was later made Director of Tsetse Research in the territory, began an investigation into the life history and habits of the tsetse fly. Like Bruce, Swynnerton ranks as a pioneer in the fight against the tsetse fly, for he was the first to develop the method of attack against the fly itself and to suggest the means of reclaiming tsetse infested land.

When Swynnerton began his work, four-fifths of Tanganyika was under fly and unusable for cattle, and large areas were equally dangerous to human

inhabitants. By a careful study of the habits and habitats of different types of tsetse, Swynnerton discovered that three out of the five deadly types were to be found in dry woodland of medium density, but that they could not live permanently either in dense thicket or in the open. Since the clearing of vast tracts of bush was impossible, he devised methods of clearing corridors to form a barrier to the fly's advance, and of establishing in the fly-free corridors human settlements to drive away the wild game which form a reservoir of trypanosome infection. Swynnerton was the first to realise and act upon the knowledge, that once an area is cleared of tsetse, the best safeguard against reinfestation is human settlement. He enlisted the co-operation of Africans in his work of bush clearing and resettlement, and taught them much about modern methods of mixed farming and crop rotation. By 1938, when Swynnerton died, large areas had been reclaimed from the fly and put to agricultural use and the foundations of modern methods of control had been laid.

The work pioneered by Bruce and Swynnerton has gone ahead rapidly. Methods of combating the fly and the disease have advanced far beyond the stage at which the only practical solution was to move both people and cattle from infested areas—a solution which brought its own problems of overgrazing, soil erosion, poverty and malnutrition in the limited fly-free country, while it left valuable farming land in possession of the tsetse.

THE TSETSE AS A VECTOR OF DISEASE

Human trypanosomiasis is found only in areas where tsetse are known to exist, and it is at present considered improbable that the disease can be transmitted by any other means. Researches have, however, established that in certain areas —for example, in Northern Rhodesia and Nyasaland—animal trypanosomiasis can be transmitted, though never originated, by other biting flies. If a biting fly, feeding on an infected animal, is interrupted in its feed by, say, the swish of the beast's tail, it may alight on an adjacent healthy animal and plunge its still wet proboscis into it, thus transmitting the parasite directly, or mechanically, without the latter having undergone any change or development. The tsetse is nevertheless by far the most dangerous vector, since it is the only insect which is capable of cyclical, as opposed to direct, transmission of trypanosomes.

In order to infect man or a domestic animal, the tsetse must first become infected itself. One of the main reservoirs of infective trypanosomes, especially of those which infect domestic animals, exists in wild animals, which form the first choice of food for some of the most prevalent species of tsetse and which harbour trypanosomes, frequently without themselves being affected.

Inside the fly a trypanosome undergoes a cycle of development lasting about three weeks, after which the fly becomes infective to other hosts upon which it feeds, and remains infective for the rest of its life, which may last as long as six months, but is generally very much shorter, commonly three to six weeks.

The exact relationship of the infected tsetse to disease is determined by a number of factors, the principal being the habits of the particular species of tsetse and the characteristics of the particular species of trypanosome with which it is infected. While, so far as is known, most species of tsetse are prepared to feed on cattle, either from choice or in the absence of other suitable food, in fact, only a small number of species, whose habits are such as to bring them into contact with man and his domestic animals, are important as vectors of disease. They fall into two main groups: the riverine tsetse (typified by *Glossina palpalis* and *Glossina tachinoides*), which live and breed in the vegetation fringes of streams, rivers and lakes; and the woodland, or game, tsetse (typified by *Glossina morsitans*), which inhabit savannah woodland through which they range widely in search of food. Wild animals frequenting the habitat provide hosts for tsetse of this group. A third group, the forest tsetse (typified by *Glossina fusca*), inhabit deep forest and have little contact with man, but it has recently been proved that they can carry the trypanosomes which infect cattle. In general the woodland tsetse inhabit country where human population is sparse, and the likelihood of sleeping sickness being derived from the bite of infected woodland tsetse is therefore relatively small, although in East Africa the woodland tsetse is responsible for a fair number of cases. Riverine tsetse, on the other hand, infest sources of water used by people going about their ordinary lives, and sleeping sickness is a very real danger in areas where contact exists between the two.

Tsetse are sometimes infected with two or more species of trypanosomes, one of which may be transmissible to man, while the other may be transmissible only to stock. Some kinds of tsetse appear to be infected only with trypanosomes which affect animals, while others may, in circumstances not yet clearly understood, occasionally become infected with trypanosomes dangerous to man.

The trypanosomes which cause disease are injected by the tsetse into the bloodstream of the host while the insect is feeding. The species which infect man eventually find their way into the nervous system if the infection is of sufficiently long duration, and it is at that stage that they produce the symptoms of wasting and intense lethargy which are characteristic of sleeping sickness; death may, however, occur before these classical symptoms develop. Many of

the species which infect domestic animals kill them without involving the nervous system.

There are two main types of human sleeping sickness, known as Gambian and Rhodesian, named after the territories in which they were first diagnosed. Gambian sleeping sickness, which extends throughout West Africa and eastwards as far as Lake Victoria, is carried by riverine tsetse. The disease is usually slow to evolve and may endure for many months in a mild form. This favours transmission, so that extensive epidemics of this form of sleeping sickness are relatively common. Evidence strongly suggests that *T. gambiense* is transmitted from man to man and that animals are unimportant as a reservoir of the parasite.

Rhodesian sleeping sickness, the vector of which is normally one of the woodland tsetse—principally *G. morsitans*—is the form of the disease usually found in East and Central Africa. It is a serious and rapidly developing disease which, unless the sufferer receives early treatment, may well put him beyond the reach of curative drugs. Unlike the widespread distribution of the Gambian disease, the Rhodesian form tends to be distributed in small foci, with a tendency to occur in outbreaks. Although the total number of cases found in a year is usually low, when this disease does occur it is a serious problem because of the rapid course of infection.

Trypanosomiasis in cattle may be caused by any of a number of trypanosomes, the most important of which are *T. vivax, T. congolense* and *T. brucei.* So far as is known most species of tsetse may transmit animal trypanosomiasis, although it is probable that some species may do so more effectively than others. Since animals in general have far more contact with tsetse than man, the incidence of the disease among cattle is many times higher than it is in man, and control measures are correspondingly more difficult. Both riverine and woodland tsetse are carriers in West Africa; in East and Central Africa the woodland tsetse predominates. In East Africa trypanosomiasis of cattle is an immense and pressing problem; it is also a severe problem in West Africa, though in some areas certain dwarf breeds of West African cattle have developed partial immunity.

METHODS OF CONTROLLING TRYPANOSOMIASIS

Since trypanosomiasis is caused by a specific parasitic organism, the trypanosome, which is transmitted by a specific vector, the tsetse fly, any means of controlling *either* the parasite *or* the vector will achieve control of the disease. The prevention of contact between the vector and its animal or human host will also achieve control. Normally all these approaches are now used. Until comparatively recent times, however, the only effective means of control was through control of the tsetse. This remains, particularly since the development of modern insecticides, a most effective means of control.

Control of the Tsetse

Methods of tsetse control are for the most part an attempt to exploit the existing knowledge of the biology of the fly, and as that knowledge has increased, new methods have been adopted. Total extermination over even a limited area is very costly and extremely difficult by any known method, and in practice the choice of method must often be determined by cost and the availability of suitable labour. Moreover, the control of tsetse is not an end in itself. It is but one step in the reclamation of land for man and his domestic animals. The potential value of the land and the costs of other necessary measures such as pasture improvement, water conservation, road building, and even medical and educational facilities for an incoming population, must be taken into account.

Apart from cost, practical considerations influence the choice of control measures. Relevant factors are the species of tsetse, the nature of the surroundings and of the climate, the size of the infested area, and whether the infection is mainly medical or mainly veterinary.

Methods of tsetse control at present in use include the direct attack on the fly, principally with insecticides, and indirect methods which seek to make the environment unsuitable for the fly, for example, by clearing the bush which forms its habitat, by controlling the game which forms its food, or by human settlement, which changes the ecology of the environment. In practice most countries employ a combination of two or more methods.

Methods Directed Against Vegetation

Among the first scientific facts to be established about the tsetse were its need of shade and its preference for certain types of vegetation. These facts were the basis of the earliest form of attack on the tsetse fly—that of bush clearing. This method has been used in almost all tsetse-infected countries. With increasing knowledge of the tsetse's habits, methods of clearing have developed from the ruthless clearing of all vegetation in a given area to the discriminative or selective clearance of only those parts of the vegetation known to be essential to the flies.

In West Africa the riverine tsetse have been the main object of attack. A close study of these tsetse enabled entomologists to define within narrow limits their climatic requirements during certain seasons, and to alter the environment adversely by partial clearing of the vegetation along the banks of rivers, and particularly at fords, crossings, village approaches and wherever people are likely to congregate. In Northern Nigeria this method has been used on a large scale since 1938. For example, in 1950–58 more than 3,000 miles of riverine vegetation were cleared in the provinces of Zaria, Katsina and Kano, and in Benue Province the rivers were treated in an area of 600 square miles. But bush clearing, in Nigeria, is now giving way to other, less costly, methods or is being used in association with insecticides to prepare the way for the latter. Elsewhere in West Africa, owing to the high cost of labour, this method has

been largely abandoned, having been replaced by other methods (see below).

In East and Central Africa the elusive and widely ranging woodland tsetse has presented a different and more intractable problem, though it is in this region, for example in Tanganyika, where discriminative clearing is used on a large scale throughout the country, that some of the best results have been obtained. Clearings are often made to isolate the permanent breeding grounds of tsetse from the much larger areas over which they will range at certain seasons, and sometimes with the intention of stopping an advance of tsetse. Areas a mile or more wide and several miles long may have to be cleared. The task is immense, costly and fraught with difficulties even if clearance is confined to key types of vegetation. Unless cleared land is occupied and 'worked' by a community, regeneration takes place fairly rapidly and the area may go back to tsetse. Tropical soils, deprived of their forest cover, become infertile. It has therefore come to be recognised that clearance schemes should be initiated only as part of a general land development policy.

Tsetse Clearance by Human Settlement

Human settlement as a method of planned tsetse control has until recently been considered chiefly as a means of consolidating the position after tsetse have been expelled by other methods. It has been proved that if cleared land is occupied at a sufficient density of population, human activities such as woodcutting and the planting of crops will drive away wild game and so change the ecological conditions that tsetse fly will no longer be able to exist. In many parts of Africa human settlement has in the past been used unwittingly to this effect, the various activities of the African settlers having effectively driven back the flies.

The idea that settlement might be used as a positive method of tsetse eradication, with all the safeguards of modern drugs and the help of modern technical and scientific knowledge, has gained favour in recent years, and a considerable body of expert opinion is now in favour of a broad ecological approach, which seeks to modify the whole environment of an area so that it becomes inimical to the continuance of trypanosomiasis.

Experience has shown that careful planning and well calculated inducements such as wells, schools, dispensaries and other facilities are necessary to persuade people from over-populated areas to settle deliberately in fly-belts. Cases of sleeping sickness are likely to occur in the early years and strict medical supervision is necessary. It was thought until recently that cattle—so important for agricultural purposes—would have to be excluded from the settlements until fly had been completely expelled, but this difficulty now seems to have been overcome, for recent research in Kenya has shown that cattle can be maintained by the use of modern trypanocidal drugs in areas where the challenge of infection is not too great pending human settlement in sufficient density to exclude the fly altogether. People protected by modern drugs can penetrate into fly-bush and settle there without prior clearing.

All the East African countries provide examples of human settlement as a planned measure of tsetse control. In Tanganyika, for example, where fly-infested country includes some of the best land for stockraising and arable farming, human settlement combined with bush clearing is the principal anti-tsetse measure. Sixty settlement zones, with a total population of about 500,000, have been established, mainly in the Western Province. In Kenya there are nine settlement schemes, and in Uganda human settlement is one of the measures used to establish 'consolidation lines' to prevent reinfestation of cleared areas. A project recommended by a recent World Bank mission for implementation in Uganda involves the settlement of cattle-owners on economic holdings in an area cleared of tsetse. The settlement would be in the nature of a pilot

project to test and demonstrate the feasibility of 'settled' ranching in a relatively good cattle-grazing area normally grazed in a nomadic fashion.

Game Control

Since certain species of tsetse commonly feed on game, the fly may be attacked indirectly by attacking or driving away these host animals. Fencing may be erected, as has been done, for example, in Northern Rhodesia, to maintain a game-free zone between the fly-belt and the farming area. Large-scale successes have been achieved by game control in Southern Rhodesia and Uganda. For example, in Uganda, where there were extensive advances by two species of woodland tsetse in the 1930s and early 1940s, the Department of Tsetse Control had by the end of 1957 freed more than 7,000 square miles of country as a result of a major programme to halt the advances, to reclaim the newly invaded country—mainly by game elimination—and to prevent its reinfestation. Game control is not always easy to apply, however, and in general is not willingly resorted to unless there appears to be clear evidence, not only that it will be practicable, but that there is no practical alternative. In any case it is generally recognised that it should be used only within the framework of an over-all land-use policy.

Control by Insecticides

One of the major developments of recent years has been the synthesis and use of modern insecticides, principally DDT (dichloro-diphenyl-trichlorethane) and Dieldrin, which are either applied to objects on which tsetse will rest or broadcast over an area. The use of insecticides, already far cheaper in most conditions than clearing vegetation, is likely to become cheaper still as experience is gained and the scale of operations expanded.

Where the fly has a restricted habitat, either seasonally or continuously, success has already been achieved on a fairly large scale. In Northern Nigeria, for example, a number of schemes have been carried out with success against the riverine tsetse *G. palpalis* and *G. tachinoides*. Under one of these schemes, in South Zaria, 400 miles of rivers and streams have been reclaimed from *G. palpalis*. Elsewhere in Northern Nigeria use has been made of the fact that towards the northern end of its range, the normally far-ranging woodland tsetse, *G. morsitans*, is seasonally restricted by dryness of conditions to evergreen vegetation. One scheme, started in 1956, has provided 350 square miles of tsetse-free grazing along the flood plains and adjoining uplands of the Komadugu Gana river. In Kenya, Uganda and Tanganyika the principal carrier of human sleeping sickness *G. palpalis* is being successfully combated by a method of insecticidal control developed by the East African Trypanosomiasis Control Organisation (see p. 16). In Kenya, by 1960, more than 2,000 square miles had been freed of this fly.

Immense problems remain to be solved before the far-ranging woodland species of East and Central Africa can be exterminated over large areas, though large-scale trials with insecticides are being carried out. In this region the use of aircraft for the application of insecticides has obvious advantages, but is expensive.

One potential drawback to the use of insecticides is that once the effect of the insecticide has worn off, the treated area is again one in which tsetse can survive and multiply and it may be reinvaded from the periphery or from a small area accidentally left untreated.

Much work is at present directed towards refinement of techniques of insecticidal control. The careful study of the resting sites of the fly may, for example, reveal these to be limited in extent. An immense economy in effort

and material can then be achieved. But the difficulty often arises that what applies to one species and one habitat will not apply to another species and other habitats. Further, in dealing with different habitats, there is the complication of variation in rainfall and hence in the persistence of the insecticide. To be effective an insecticide must remain lethal (or be renewed) for more than a pupal period (say for two months). In a dry area DDT wettable powder will last long enough; in a more humid area DDT emulsion may be required, and in a still more humid area only Dieldrin emulsion can be expected to persist long enough. Thus there are problems of how and where to apply insecticides most economically for each species and of determining the optimum choice and concentration of insecticide in each type of habitat.

Examples of refinements in technique are provided by the control schemes in Northern Nigeria referred to on p. 10. In South Zaria the strength of the insecticide, Dieldrin, has gradually been reduced and the spraying made more selective until eradication has now been achieved with one spraying of 2 per cent Dieldrin emulsion concentrate, and restricting spraying to one bank only of the narrow rivers and in some cases only spraying on each side of the river crossings. Similarly, in the Komadugu Gana river scheme, the strength of the insecticide, in this case DDT wettable powder, and the area and extent of tree trunks sprayed, have gradually been reduced, until complete eradication can now be obtained after a single spraying of tree trunks with a diameter of over nine inches to a height of five feet from the ground, with a suspension of 2½ per cent DDT wettable powder.

Other Direct Methods of Control

A form of control against woodland tsetse, mainly used in East and Central Africa, is the 'de-flying house' or 'chamber'. Tsetse flies often travel with moving objects: a post is therefore set up on the edge of fly-belts, for the examination of pedestrians and vehicles before they enter fly-free country. In this way the flies are caught and prevented from entering uninfected country as they would otherwise do.

The technique of catching flies by hand is a method of sampling rather than of fly control. It is particularly useful for the woodland tsetse of East Africa, where 'fly boys' are regularly employed on this work. They use themselves or some domestic animal, such as an ox, as bait, and their catches supply the data on the distribution, density and habits of the fly, which are essential for the entomologists who devise and check methods of control.

Other methods of direct attack on the fly, including trapping, the use of natural parasites or predators, and sterilisation by irradiation or hybridisation, have been carefully studied, but none has shown much promise.

Control of the Parasite

The great developments of recent years, apart from the use of insecticides, have been in the control of the infecting organism itself, the trypanosome. Recent developments in the production of curative and prophylactic drugs have revolutionised the treatment of human sleeping sickness and have enabled great advances to be made in the treatment of animal trypanosomiasis, although the latter problem still presents formidable difficulties. Experimental work with new drugs and combinations of drugs goes on continuously both in Africa and in laboratories in Britain.

Drugs for Human Trypanosomiasis

Among the earliest trypanocidal drugs to be used with success was the German Bayer 205 (suramin). The formula for this drug was kept secret, but was discovered by French workers and, shortly before the outbreak of war

in 1939 an identical compound, named Antrypol, was synthesised by British scientists in the laboratories of Imperial Chemical Industries. It is still used to a considerable extent, alone or in conjunction with other drugs, in the treatment of human trypanosomiasis, particularly in its early stages.

Tryparsamide, developed by American scientists at the Rockefeller Institute in New York in the 1930s, was found to be effective against the Gambian infections, especially late cases; it is often used in conjunction with Antrypol.

Shortly before the war a new series of drugs, the diamidines, was produced in the United Kingdom, and one of the series, Pentamidine, synthesised by May and Baker, is now the most widely used drug for treatment in the early stages of the disease and for prophylaxis.

Among newer drugs which are being used with some success are Melarsen and its related compound Mel B (Arsobal or melarsoprol), both produced by Dr. Friedheim of New York. Mel B has become the drug of choice for late cases of Rhodesian infection, where the central nervous system is involved. A high proportion of cures has been achieved among these late cases, which were hitherto considered incurable. Mel B has also been used for the treatment of Gambian infections and has produced a significant percentage of cures in cases which were resistant to Tryparsamide. A single dose has been used successfully for the cure of early cases, but because of its toxicity it is generally administered only in hospital and under medical supervision.

Mass Diagnosis and Treatment

In most of the countries where sleeping sickness is a problem, the disease has been controlled for a number of years by a system of mass surveys and treatment first developed by a Frenchman, Dr. Jamot. Mobile teams of Africans, trained in precise methods of diagnosis, aim at a regular examination of the whole population in the affected zones. These surveys permit infected persons to be treated, either by the teams or in local hospitals or dispensaries, and also furnish valuable epidemiological information on which other control measures can be based.

Throughout the area affected by the Gambian form of sleeping sickness, mass surveys and treatment have helped to bring about a spectacular decrease in the incidence of the disease over the last 15 years, though its reduction below its present level remains a problem, and precautions cannot safely be relaxed.

In Northern Nigeria, for example, as a result of the activities of the mobile teams of the Sleeping Sickness Service and clearances directed against the riverine tsetse, the total number of new cases of sleeping sickness found has fallen from 85,000 in 1935 (from among 400,000 examined) to under 4,000 in 1960 (from among 1,600,000 people examined). Over one million people are examined each year by the mobile teams alone, and patients are also treated at sleeping sickness dispensaries, Native Administration dispensaries, and general hospitals. The drugs normally used are Antrypol in conjunction with Tryparsamide or Pentamidine in conjunction with Tryparsamide. In Ghana, where the disease is kept under control by Medical Field Units, large-scale surveys and mass treatment with Pentamidine supplemented by anti-tsetse measures have helped to reduce the incidence from 6,800 new cases in 1939, at the height of a serious epidemic, to around 2,000 in 1948 and to only 830 in 1958. In Sierra Leone an energetic campaign by mass diagnosis and treatment brought to an end a serious epidemic that occurred in 1939 in the eastern part of the country. The incidence of the disease has since decreased to such an extent that mobile survey teams have been disbanded. Only 26 new cases were reported in 1958. In Uganda sleeping sickness has been greatly reduced by a combination of mass surveys and treatment and an insecticidal attack on the vector, *G. palpalis*.

Rhodesian sleeping sickness has proved more difficult to control, the number of new cases fluctuating irregularly from year to year, rather than showing a downward trend, though the new drugs now available result in a high proportion of cures and the overall incidence is low.

Prophylaxis

Prophylaxis is applied, on a selective basis, in many countries affected by Gambian sleeping sickness, though less widely in the English-speaking countries than elsewhere. In Northern Nigeria, for example, it is used on a very limited scale, to clear an epidemic focus or to protect labourers whose work brings them into contact with tsetse. In general it is considered as a temporary control measure, which in some circumstances can supplement mass surveys and treatment and measures directed against the tsetse. The British drug, Pentamidine, is the drug normally used. Against Rhodesian sleeping sickness, prophylaxis is not in general use, though it has been used in some areas to deal with epidemics.

Treatment of Animal Trypanosomiasis

Unfortunately the new drugs which were developed before and during the war for the treatment of human trypanosomiasis had little or no effect on most of the animal trypanosomes. Scientists were experimenting, however, in this field too, and a number of new drugs have been synthesised, in many cases by British scientists, which have made it possible to keep cattle in the presence of relatively low concentrations of fly; either, in light fly, by treatment of such cases of trypanosomiasis as occur, or, in rather heavier concentrations, by giving prophylactic injections. In Kenya, for example, the area of formal ranching schemes in tsetse-infested country—where cattle are brought in, fattened, and sold—now totals many hundred square miles, and the total number of cattle now annually protected by drugs exceeds half a million. In Northern Nigeria, where the future success of the important cattle industry will depend upon the heavily tsetse-infested but well-watered areas in the south of the region becoming available during the long dry season as grazing grounds for the Fulani herds from the north, the situation has already been much improved by the introduction of modern trypanocidal drugs, though the number of cattle presented for treatment—600,000 a year—places a heavy strain on the resources of the region's veterinary staff.

The major obstacle to the widespread employment of chemotherapy is the liability of trypanosomes to acquire resistance to the drugs at present available. Some drugs generate resistance not only to themselves but to other drugs as well. Resistance may not prove to be such a serious problem, however, if 'sanative pairs' of drugs can be found (that is, pairs of drugs between which no cross-resistance occurs and which will cure resistance to each other). In the case of curative drugs, a procedure involving the alternate use of one such pair is currently undergoing long-term field tests in Kenya, so far with success. When resistance to the principal drug, Homidium (ethidium), occurs, a change is made to the other drug, Berenil, for one year. In the case of prophylactic drugs no 'sanatives' seem to be available at present, but here, too, methods of overcoming cross-resistance are being tested in the field.

Drugs for Animal Trypanosomiasis

Notes on some of the more important drugs used against animal trypanosomiasis, the majority developed in British laboratories, are given below. They provide an effective battery for the curative treatment of trypanosomiasis in cattle, but there is still a very real need for a reliable prophylactic capable of protecting cattle for several months.

The British drug, Antrycide, synthesised in the laboratories of Imperial Chemical Industries, was the first drug to have, in greater measure than any existing drug, the principal properties for which research workers were looking. It was tried out with success in 1948—the readily soluble Antrycide methylsulphate as a curative drug and the less readily absorbed Antrycide prosalt for prophylaxis. Antrycide methylsulphate has since been used in the treatment of several million cattle with excellent results, though with slightly less success in *T. vivax* cases than with *T. congolense*, and its value as a curative drug is well recognised. It is used, for example, to treat 250,000 cattle annually in Uganda and some 70,000 in Southern Rhodesia. In Nyasaland it is being used to limit the effects of trypanosomiasis transmission by biting flies. Antrycide prosalt, injected at two-monthly intervals, has been extensively used to protect cattle in the presence of fly, not only as a practical measure of control but also as the standard of comparison in the trial of newer prophylactics. In Uganda 16,000 head of cattle are living inside the tsetse belt under protection with this drug. Special uses have been to protect cattle passing through fly-infested country and to protect cattle moved into a tsetse area to resettle it. Neither form is toxic if used in the right dosage. There is, however, a tendency in some areas for trypanosomes to emerge which are resistant to Antrycide, and there is as yet no 'sanative' on the market which can be used to cure this resistance.

Studies of the phenanthridines, a series of drugs which British scientists had discovered before the war to be active against *T. congolense*, led to the testing of a very considerable number of compounds in the laboratories of British pharmaceutical firms and to the further testing of a number in the field. One, Homidium (Boots Pure Drug Company), has proved to be a curative drug of great value; in Northern Nigeria cattle are treated with this drug and Antrycide equally, and it is the principal drug being used in Kenya in the current research into the control of drug-resistance (see p. 13), a change being made to the German drug, Berenil, when resistance occurs. Another, Prothidium (Boots Pure Drug Company), shows considerable promise as a prophylactic particularly in East African conditions; a prophylactic procedure being tested in Kenya is to inject Prothidium at four- or five-monthly intervals, with the curative drug Berenil interposed whenever resistance is suspected. Metamidium (May and Baker), a phenanthridinium compound not yet on the market, shows considerable promise as a curative drug, and it seems that it may be useful as a 'sanative' where resistance to Antrycide or Prothidium has developed.

Berenil, which has been tried out in the last few years, has been found to have many attractive features as a curative drug. One is that it appears to be the drug least prone to cross-resistance. It has thus come to be regarded as an invaluable drug to be kept in reserve for the elimination of strains which have become resistant to other drugs, though it appears that it may be less effective in West Africa than elsewhere.

The relatively insoluble complexes of suramin with various trypanocidal drugs, developed at the West African Institute for Trypanosomiasis Research (see p. 17), have given long periods of protection in field trials, but severe swellings and other reactions at the site of the injection are a problem which has yet to be overcome. These complexes are among the newer drugs which are being tried out as prophylactics.

Immunisation

The prevention of any disease by the use of drugs becomes a second-best if it is possible to stimulate natural resistance by an inoculation which produces active immunity. This goal has not yet been achieved for trypanosomiasis in man and his domestic animals, but much fundamental research in the science

of immunology, supported by experiments in the field, is now being carried out both in Africa and in Britain (see p. 16) and some recent important discoveries, in addition to the known natural resistance of some animals to trypanosomiasis, at least give hope for the future. The role immunity might play in chemoprophylaxis is also being studied, for it may be that if immunisation alone will not provide protection against the disease, induced immunity and chemoprophylaxis acting together will be more effective than either on its own.

Active measures to combat tsetse diseases and to eradicate the fly are the responsibility of individual African Governments. The research and experimental work upon which active measures are based are, however, in the Commonwealth countries of Africa, largely the concern of inter-territorial organisations or special research units at various centres in Africa and in Britain.

For some time before the second world war, research stations had been established in East and West Africa to carry on research into fundamental problems such as the ecology of the fly, to organise and carry out bush clearance schemes, and to re-settle populations on reclaimed land, in accordance with the system first adopted by Swynnerton (see p. 4). At the same time, research into human sleeping sickness had made considerable progress and the first effective drugs had been developed to cure it.

In 1944 the British Secretary of State for the Colonies appointed a Tsetse Fly and Trypanosomiasis Committee to consider and advise on the co-ordination of action, including research, directed against human and animal trypanosomiasis. It has also had responsibility for advising on the best ways in which to apply funds made available under the British Colonial Development and Welfare (CD and W) Acts. The committee has published annual reports, concerned chiefly with the work of the East African Trypanosomiasis Research Organisation and the West African Institute for Trypanosomiasis Research, but it also keeps in touch with individual departments in British dependencies engaged in trypanosomiasis control and tsetse clearance and with research workers in Britain, and sends representatives to inter-national conferences. Since 1961 the committee has been advisory to the new Department of Technical Co-operation, instead of to the Colonial Office, and its services made available not only to colonial territories but also to those which have evolved to independent status.

The East African Trypanosomiasis Research Organisation

The East African Trypanosomiasis Research Organisation (EATRO) serves principally Kenya, Tanganyika and Uganda, but it also provides advice on trypanosomiasis problems to other countries. It combines the former East African Tsetse Reclamation Department, the Tsetse Research Institute at Shinyanga, Tanganyika (of which Swynnerton was the first director), and the Trypanosomiasis Research Station at Tinde, Tanganyika. In order that the various aspects of research could be better co-ordinated, all work has recently been concentrated on one new organisation at Sukulu, near Tororo, in Uganda. The buildings were erected at a cost of some £200,000 provided by the British Government from CD and W funds. The same funds provided half the recurrent expenses of the organisation up to mid-1956 and currently contribute towards these expenses at the rate of 27½ per cent.

The coming into use in the last few years of more efficient drugs and other recent advances in knowledge have led to the reorganisation of research at EATRO. The emphasis has shifted from pure tsetse research to a broad approach to trypanosomiasis from several angles. Advance in immunology has recently been considered the subject most likely to affect almost all other aspects of trypanosomiasis research, and methods of testing immune reactions are under study. An important epidemiological development has been the incrimination of *Glossina palpalis* in the transmission of Rhodesian sleeping sickness in the Busoga area of Uganda, suggesting that it may be the species responsible for long-term persistence of the disease in lake coast environments. In the field of chemotherapy, attention has been directed to the improvement

of the treatment of late cases of human sleeping sickness refractory to the usual drugs; two new drugs, nitrofurozone and Mel W, have been examined in this connection. Biochemical studies have included an investigation of the changes undergone by nitrofurozone in the human body. EATRO has also evolved a method by which trypanosomes can be preserved alive in a deep frozen state and is now well known as a source of newly isolated trypanosomes for laboratory experiments in other countries.

The West African Institute for Trypanosomiasis Research

The West African Institute for Trypanosomiasis Research serves the four Commonwealth countries in West Africa—Nigeria, Ghana, Sierra Leone and the Gambia. Located partly in Kaduna and partly in Vom, Northern Nigeria, it cost some £234,000 to build and equip, two-thirds of which was provided by the British Government from CD and W funds and the rest jointly by the four West African Governments. Britain also put up, from CD and W funds, one half of each dependency's contribution to the Institute's recurrent expenses. (Britain still contributes one-half of the Gambia's contribution. The other three countries, having attained independence, are no longer eligible for assistance from CD and W funds.)

Work on human sleeping sickness has included investigations into new methods of diagnosis, and trials of the curative effect of Berenil for early cases and of Mel W for intermediate and advance cases. Work on animal sleeping sickness has included the development of a technique for the detection and measurement of antibody against trypanosomes, investigations to find a reliable prophylactic drug capable of protecting cattle for several months, and the demonstration that trypanosomiasis in pigs can be controlled by prophylaxis with Antrycide-suramin complex or Antrycide chloride. Recent protozoological experiments have shown that under conditions in Nigeria the semi-domesticated black pig can act as a carrier of *T. gambiense*, just as game animals in East Africa carry the trypanosome of Rhodesian sleeping sickness, and further that it may do so without symptoms of the infection and without the parasite being demonstrable in blood films. Other experiments are being undertaken to study the modifications which may occur in strains of trypanosomes when they become drug-resistant. Entomological work has included the identification of the origins of blood meals from tsetse flies, which may be of great potential value in formulating proposals for control measures, and the identification of the nocturnal resting sites of *G. palpalis* by using ultra-violet light to find flies previously marked with luminescent paint. In a field trial this has resulted in great economy in the use of insecticide.

Other Research in Africa

The Kenya Veterinary Department has carried out investigations into the tsetse's natural resting sites and food-hosts and the use of traps and attractants. It has conducted experiments on induced immunity, mechanised bush clearing, arboricides and insecticides. It has studied the combined effects of several methods of tsetse reclamation, to find out how land usage can be made finally to eradicate the fly once settlement has obtained a foothold. Many of these experiments have yielded useful results. For example, laboratory studies have evolved methods of overcoming drug-resistance, by the use of 'sanative pairs' of drugs, which are now undergoing extensive tests in the field (see p. 13). As a result, chemotherapy is likely to be increasingly used in Kenya to facilitate penetration of the people into fly-bush without clearing. Field experiments on induced immunity have suggested that by breeding cattle in fly-bush it may be possible to select lines that are relatively insusceptible to trypanosomiasis. In the course of investigations on the problems of adapting insecticidal methods

to the far-ranging woodland tsetse, a substance which attracts the fly to deposits of insecticide has been discovered and developed.

Research by the Uganda Department of Tsetse Control has included investigations into the use of insecticides and new formulations of drugs, and trials to see if Dieldrin can safely be sprayed on cattle in order to mop up residual pockets of tsetse not eliminated by game control measures.

In Tanganyika large-scale trials of insecticides have recently been carried out and research has also included the investigation of tsetse breeding sites, the use of traps scented with animal extracts and trials of new drugs.

The Tropical (formerly Colonial) Pesticides Research Unit, Tanganyika, which is under the aegis of the Colonial Pesticides Research Committee in Britain, carries out research with insecticides against many kinds of insect pests, including much valuable work on tsetse. For example, the unit developed the method now used in Kenya, Tanganyika and Uganda to control the riverine tsetse, *G. palpalis*. More recently, experimental spraying from the air on an 11 square mile block of savannah woodland in Tanganyika, using one pint of 2½ per cent Dieldrin per acre, has reduced catches of *G. morsitans* and *G. pallidipes* by 99·5 per cent, though the cost is still about £300 per square mile. The unit also experiments with arboricides which might be of use in making tsetse clearings or in suppressing regeneration.

Research in Britain

British Colonial Development and Welfare grants for trypanosomiasis research were until recently disbursed mainly in support of the trypanosomiasis research organisations in the British territories in Africa. While this policy is being continued as far as political changes in Africa permit, the Tsetse Fly and Trypanosomiasis Committee, in its report for 1958–59, said it had noted many instances where it would seem that the advances in knowledge in some aspects of the trypanosomiasis problem had reached the stage where resources available in Britain to tackle such problems could usefully be exploited to a greater extent. With the development of rapid communications, collaborative studies could be undertaken between workers in Britain and in Africa. In particular, a great deal could be done, and indeed has been done, along these lines in the development and testing of curative and prophylactic drugs. It was suggested that the encouragement of research into the fundamental problems at a chain of research centres in Britain would be a useful means of rendering continued scientific assistance in this field to the emergent territories. With this in view a working party was set up towards the end of 1959 to encourage research of this kind and to keep it under review.

An example of current research is the work at Liverpool University under Professor R. M. Gordon on the development of the infection in the mammalian host from the time of biting of the tsetse fly and the maintenance of the different forms of trypanosomes in culture. At the National Institute for Medical Research work is being carried out on the resistance of trypanosomes to drugs —how it develops and how it can be detected and measured in the field. Another example of current research is the study of immunology, to which an invaluable contribution has already been made by Dr. B. Weitz at the Lister Institute of Preventive Medicine. Earlier research at this Institute by Dr. Weitz led to the development of a technique through which the institute has been able to assist the research organisations in Africa by identifying the blood meals in tsetse flies, and thus the animals on which they have fed.

International Co-operation

Since the tsetse fly menace is common to all countries of tropical Africa, international co-operation in research and in the exchange of information has a role to play in combating it.

The international bodies primarily concerned with tsetse and trypanosomasis problems are the International Scientific Committee for Trypanosomiasis Research and the Permanent Inter-African Bureau for Tsetse and Trypanosomiasis (known by its French initials, BPITT), which were established on the recommendation of a conference held in Brazzaville in 1948. Both are now under the aegis of the Commission for Technical Co-operation in Africa (generally known by its French initials, CCTA), of which the United Kingdom was a founder member.

Meetings of the Scientific Committee, which are attended by scientists from member States of the CCTA, have been held annually or biennially since 1949, sometimes in Africa and sometimes in Europe. At the meetings papers are read and views exchanged on all matters concerned with human and animal trypanosomiasis and with the tsetse. After discussion, certain courses of action are recommended by the committee for the attention of territorial authorities. For example, the Committee has encouraged the preparation of maps showing areas of sleeping sickness, of animal trypanosomiasis and of tsetse infestation and has advised the CCTA on the planning of joint campaigns for the control of trypanosomiasis in areas affecting several adjoining countries; it records its considered views on new drug developments; and it suggests further lines of research which might be undertaken. From the beginning, British scientists have made important contributions to the work of the committee.

BPITT's functions are mainly concerned with the publication and dissemination of information on tsetse and trypanosomiasis and with facilitating the interchange of views between experts of different nationalities.

THE FUTURE

The great increase in knowledge of the tsetse fly and of the diseases it carries which has taken place in the past sixty years, and the many medical and scientific advances in combating tsetse problems have led both to a lessening in the gravity of the tsetse fly menace and to a gradual reassessment of its nature.

While sleeping sickness is still endemic in East and West Africa, control measures are keeping the disease well in hand, and, according to recent reports, in some areas the incidence is so low that it is not easy to give medical staff practical training in the treatment and handling of actual cases.

Disease control measures are more difficult to apply to cattle, since they range over wide areas and are a great deal more vulnerable to trypanosomiasis than man. Yet here, too, advances in treatment and prophylaxis have substantially reduced the incidence of disease, while the use of insecticides and clearance schemes have increased the safe areas for grazing cattle.

Increasing ascendancy over the disease and increasing knowledge of the biology and habits of the tsetse fly have led to the emergence of a new attitude in which the problem is seen as part of the whole subject of economic development in Africa. The new knowledge is beginning to be used not only as a defence against tsetse and disease but as a weapon in a policy of advance into tsetse-infested country to open up new areas for agricultural development. Most Commonwealth countries in Africa now permit tsetse clearance schemes to be undertaken only as part of their general land policy, and the idea of actually encouraging settlement in tsetse areas, while providing adequate safeguards, is gaining ground.

Not all authorities are agreed on the best methods of attack on the trypanosomiasis problem. Indeed, there are no two areas in which the problem itself is identical. But it seems probable that the solution will ultimately be brought about by the utilisation of all existing knowledge to combine tsetse control with the establishment of progressive and efficient land utilisation schemes over ever-increasing areas. In the meantime it is expected that British scientists will continue to play an important part in the research and experimental work upon which active control measures are based.

SHORT READING LIST

BUXTON, *Professor* P. A. The Natural History of Tsetse Flies.	*H. K. Lewis*	1955	84s. 0d.
DAVEY, T. H. *and* LIGHTBODY, W. P. H. The Control of Disease in the Tropics.	*H. K. Lewis*	1961	47s. 6d.

Biennial Reports

Meetings of the International Scientific Committee for Trypanosomiasis Research: Eighth Meeting, Jos, 1960.	*Commission for Technical Co-operation in Africa (CCTA)*	1961	15s. 0d.

Official Documents

Annual Reports

Colonial Research (containing Tsetse Fly and Trypanosomiasis Committee Report). For 1960–61.	Cmnd. 1584. *HMSO*	1962	18s. 0d.
East African Trypanosomiasis Research Organisation. For 1960.	*Government Printer, Kenya*	1961	4s. 0d.
West African Institute for Trypanosomiasis Research. For 1960.	*Baraka Press, Kaduna*	1961	

Special Reports

Animal Trypanosomiasis in Eastern Africa, 1949, by H. E. Hornby.	*HMSO*	1952	7s. 6d.
Improvement of Cattle in British Colonial Territories in Africa.	*HMSO*	1953	10s. 6d. (o.p.)
Observations on Trypanosomiasis in Eastern Africa, by Professor P. A. Buxton.	*HMSO*	1948	3s. 0d. (o.p.)
Trypanosomiasis in British West Africa, by Professor T. H. Davey.	*HMSO*	1948	2s. 0d. (o.p.)
Tsetse Flies in British West Africa, by T. A. M. Nash.	*HMSO*	1948	2s. 0d. (o.p.)

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