



I agree

A. J. H. 8/12/23

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L. J. H.

8/12/23

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used by Dr Marshall

& Dr Casshane

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copy Report, above  
deeph - to { 2 B B }  
  { 1 B B } -7 JAN 1924

copy above deep (with encl) to H. H. S. A. H. O. 29. 14 Jan 1924

copy report to Dr. Macfie. 28 Jan. 1924  
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copy report to Gen. }  
S. H. 88 } 28 Jan '24  
S. H. 17 }  
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TRANSLATION.

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REPORT ON THE TRIAL OF BAYER 205 IN AFRICA. - II.

By F.K.Kleine and W. Fischer.

59150

CAN TRYPANOSOMES IN THE FLY BE AFFECTED BY BAYER 205?

47725

In our first report we showed that infected flies do not lose their infectivity by feeding on an animal that has been treated with Bayer 205. The parasites could not be killed in the salivary glands of the insect. To determine the question whether the trypanosomes could be affected in the gut of the flies during their development, we fed tsetse-flies, bred from pupae in the laboratory, for 3 days at first on a bullock with pagana and then from 29.4.22 for 8 days on a bullock (No.10 see below) previously treated with Bayer 205. After this they were put daily on a healthy dog. The dog became ill after 43 tsetsees had fed on him. Two of the tsetsees were infected. It is therefore evident that the development of the trypanosomes in the fly cannot be inhibited by Bayer 205, at least not with the doses so far used by us.

CATTLE EXPERIMENTS

Our fear, that cattle no.6 and 7, treated prophylactically with a subcutaneous dose of 10 gm. and then exposed to flies had acquired an infection, and that the multiplication of the parasites was only at first interfered with by the drug, has been confirmed. About 5 weeks after the last exposure to infection, the presence of trypanosomes in the cattle was proved by blood-inoculation into monkeys. To strengthen the deficient prophylactic protection we injected Bayer 205 again, after all danger of infection was over.

Bullock no.9 received, from 24.4. to 27.22, doses of 2.5 gm., in all 10 gm., of Bayer 205 subcutaneously. After a lapse of 15 days, 1014 flies were fed on it between 12.5. and 18.5.22. At the end of the feeding it received another 6 gm. on 22.5. and 23.5.22, that is another total of 12 gm., subcutaneously. A monkey inoculated on 21.6. with 10ccm. of defibrinated blood showed trypanosomes in the blood on 30.6.22.

Bullock no.10 received 2.5 gm. daily from the 24.4. to 27.4.22, a total of 10 gm. of Bayer 205, subcutaneously. After a lapse of 17 days 1004 flies were fed on it between 14.5 and 20.5.22. At the end of the feeding it was given 8 gm. on 22.5 and 23.5.22, another 12 gm. in all, subcutaneously. A monkey inoculated on 8.7. with 10ccm. of defibrinated blood showed trypanosomes in the blood on 17.7.22. Inoculations made on 22.6. remained negative.

Bullock no.11 received 6 gm. on 21.5. and 22.5.22, a total of 12 gm. Bayer 205, subcutaneously. From 23.5. to 9.6.22, 2003 flies were fed on it. On 10.6. it was given 5 gm. and on 12.6.22, 6 gm., making another 11 gm., intravenously. Two monkeys inoculated with 10ccm. of defibrinated blood on 30.6, that is 18 days after the last injection, had trypanosomes in their blood on 15.7.22.

Bullock no.12 received 5 gm. on 29.5. and 1.6.22, altogether 10 gm. of Bayer 205, intravenously. From 10.6. to 23.6.22, 1232 flies were fed on it. On 24.6. it was given 6 gm. and on 26.6.22 5 gm., making another 11 gm., intravenously. On 3.7. 10ccm. of defibrinated blood was inoculated into each of two monkeys. Both animals died from other causes. The inoculation was repeated on 17.7. with the result that both inoculated animals became ill on 27.7. and 31.7.22.

The experiment with bullock no.14 is particularly instructive. Whereas in the other cases several days were allowed to elapse between the treatment and the feeding of the flies in order to imitate normal conditions as closely as possible and trusting to a lengthy prophylactic action, in this case the treatment followed immediately after the feeding of the flies.

The objection could not reasonably be raised that the infection was too massive. Of about 250 flies caught here at the most one was infective. The bullock therefore would be bitten by about 8 infective flies in the course of 17 days, an occurrence that could certainly take place in nature. The number of flies used by us in each infection experiment was always regulated by the moment at which the control animal became infected, i.e. the untreated animal; as soon as trypanosomes were found and we were thus assured that among the flies utilised at least one was infective, the experiment was terminated.



Nevertheless the possibility of a too massive infection cannot be entirely excluded under the conditions of our experiments.

In bacterial infections the quantity is of great importance, and it must also be taken into consideration in infections with protozoa.

The possibility of prophylactic treatment against *T. brucei* is by no means negated by the foregoing experiments; for likewise in malaria we could not protect ourselves from infection by large isolated doses, but had to continue taking the drug for some time after the danger of infection was over. We therefore availed ourselves of an opportunity that offered for acquiring further experience and moved, at the invitation of the Governor-General of the Belgian Congo, to Elisabethville at the beginning of December '22. There we received every help thanks to the interest shown by the Acting Governor, Mr. Heenen, in our work.

At the end of December '22 a troop of 50 head of government cattle was being moved from Katentania to Kabinda through an area that was partly fly-infested though not very dangerous, half the animals were injected intravenously before departure with 10 gm. of Bayer 205 diluted in 20ccm. of rainwater. In view of the large doses that we considered it necessary to administer, subcutaneous injections were entirely abandoned, and two more injections were given at 10 day intervals. Further details will not be given of the experiment as no results were obtained; the treated animals remained healthy, but so also did the controls. They were seldom annoyed by tsetse on the road.

In March '23 the Government placed 20 additional small bullocks from their farm Katentania at our disposal. Of these 16 were given 8 gm. of Bayer 205 intravenously on 27.3., 4 were left as controls. In spite of difficulties of transport arising from African conditions, it was possible with the help of the Director of Agriculture, Mr. de Neuter, to get the cattle at the right time into a fly-infested area that had been located by the Government Medical Officer, Dr. Gensénius, in the vicinity of Bukama. The first, though very slight opportunity for the cattle to become infected occurred on 30.3. From the time of arrival at the chosen spot on 2.4. tsetse (*Glossina*

morsitans and G. fusca) were abundant.

We repeated the prophylactic intravenous injections on the 6th, 16th and 25th April. In the last (fourth) injection half the previously treated cattle were given only 4 gm. intravenously, the remaining 8 gm. as before. On the 17.4 the cattle returned from the fly-belt.

Already on the 12.4 blood examinations showed that all controls were infected. In the treated cattle trypanosomes were not present. On 7.5., that is 20 days after the end of the danger of infection, and 12 days after the last injection of Bayer 205, 9 of the 16 treated animals showed trypanosomes in their blood. On 18.5. two were still free, 6 however had again lost their parasites; in 5 we found isolated ones in thick smears, in 3 a few. Whereas the control animals succumbed or were destroyed after great emaciation, the treated animals appeared to be in good condition. This may prove of practical importance. We remember that in Kamerun animals from the north intended for slaughter arrived at the coast in the worst possible condition.

According to microscopical preparations we apparently have to deal in many cases with mixed infections (Trypanosoma vivax, brucei, congolense). Investigations into this matter are in progress. We also intend to undertake a prophylactic experiment in which the duration of the infection will be reduced, also the interval between the injections of Bayer 205, but their number will be augmented.

Curative experiments with trypanosome-infected cattle will be reported on later; the observations are not yet quite concluded. We would only mention that in the blood of treated animals isolated trypanosomes may frequently be found by microscopical examination in thick smears. As we said in our previous report the species in question is Tr. bovis (identical with Tr. vivax ?), that is, a parasite not transferable to monkeys. This trypanosome shows very little susceptibility to Bayer 205. Tr. brucei on the other hand is so much affected in its numbers and developmental capacity that its presence can only be ascertained by the inoculation of large amounts of blood.

Even after its transference to monkeys Tr. brucei shows evident signs of the influence of the drug. A normal uninjured Tr. brucei can be microscopically determined in a monkey without any trouble, but this is by no means the case with the parasites derived from cattle that have been heavily dosed; they only appear sparsely in the blood of the monkey, so that one may have to search for half an hour before finding - in a thick smear - a single trypanosome. Often they disappear entirely for several days; their virulence is weakened, and the spleen enlargement in the animals is slight. The reduction of the virulence in the treated animals allows of the possibility that naturally infected animals that have been treated with Bayer 205 may be clinically healthy even when actually carrying parasites. In cattle, trypanosomes easily become immune <sup>from</sup> to Bayer 205; in four out of five strains we noticed that after their injection into monkeys, in spite of their reduced virulence, they did not react to a dose of the drug that would normally be adequate. To prove this immunity it is essential that the dose that would normally affect the trypanosome must be ascertained for several species of animals. The susceptibility of the parasites to a drug is primarily dependent on the infected animal and changes with it. The proportion of dose to body-weight that is suitable for one species of animal is not applicable to another. According to Martin Mayer and H. Zeiss the curative dose for a mouse, for instance, is 0.00006 gm. According to body weight this would mean for a heavy man of 70 kilos 0.2 gm. and for a bullock of 7 cwt. 1.0 gm. It need hardly be explained that actually the doses would be very different.

#### SLEEPING SICKNESS IN RHODESIA.

Though we cannot give a definite opinion as to the limitations of the action of Bayer 205 in cattle affected with nagana, we are more and more assured of its efficacy in sleeping sickness of man, apart from certain cases exhibiting severe mental and nervous symptoms.

Of the six patients that we mentioned in our previous report, no. 1 has had a relapse in London and died. The intravenous treatment

(two injections) was apparently not sufficient. In the publication of Low and Hansen-Bahr this case is mentioned. The bad case no. 6 recovered so surprisingly after two subcutaneous injections that we thought we might omit the third injection, particularly as in this case the excretion of albumen was greatly increased; 56 days after the second injection trypanosomes appeared in the blood with a sudden onset of fever, and we then renewed the injections without any consequent increase in the albumen. On the contrary, the urine showed continually diminishing albumen reaction, the epithelia of the kidneys apparently becoming used to the drug. The four other patients, including two bad cases, were flourishing and healthy, and when discharged on August 22nd the urine was free from albumen.

In the middle of June 1922 we admitted another 30 cases to treatment, 16 being so ill that they could hardly stand, and some of them slept continuously. The diagnosis was made through finding parasites in the blood. All patients received for various reasons an injection of Bayer 205 on the spot where we found them. After that they were taken to our camp about 10 days journey away. To retard the elimination of the drug from the body as much as possible we preferred subcutaneous injections, using 1.2 gm. of Bayer 205 in 3 ccm. of warm saline solution in the back near the spine just between the shoulder-blades. After 10 days the second injection followed and after 18 days the last injection.

Patients with trypanosomes in the lumbar fluid or cases of relapse with trypanosomes in the blood received additional 4th and 5th injections. The pain accompanying the injection was described in various ways; some people apparently felt very little.

An old woman died of catarrhal pneumonia immediately after her arrival at the camp. A middle-aged man (medium case) died suddenly and unexpectedly 7 days after the 4th injection. A post mortem was unfortunately impossible, so that it is doubtful whether his death had any connection with our treatment.

The other patients showed improvement after a few weeks that reminded one of biblical healing. The blood of all, with two exceptions, was permanently free from trypanosomes. On the other hand, in October, on examining 21 patients (10 formerly bad cases, 6 formerly medium and 5 slight) by lumbar puncture, 8 contained isolated trypanosomes in the cerebro-spinal fluid. It cannot yet be decided whether these parasites would eventually succumb or whether there would be a gradual deterioration in the condition of the patient. The cases in which these trypanosomes were found had all shown serious nervous symptoms at the beginning of the treatment. These had almost entirely disappeared; 6 of the patients in whom trypanosomes were found by lumbar puncture appeared to be outwardly very fit and were carrying on heavy work.

As an explanation of these results we must conclude that Bayer 205 has also some effect on the parasites in the brain and that the trypanosomes that are not at once quite killed by the drug in the blood of man are greatly weakened in virulence.

At the beginning of November 1922 we discharged our patients to Rhodesia, although some of them were not quite cured. It is very difficult in Africa to keep the natives, who are used to freedom, in one place for months at a time far from their villages. And this is particularly difficult when using a drug like Bayer 205; for even after the first injection so many cases improve so much that owing to the deceptive feeling of well-being they want to return at once to their homes. Where at all possible, however, we recommend ambulant treatment. On the 3rd April 1923 the Native Commissioner of Lundazi district reported, in reply to our enquiries, that of the patients originating from his district 3 had died. Two had been recorded on our lists as serious cases, the third one was an old woman who had a large abdominal tumour that already caused great trouble in 1922; her death, therefore, cannot be ascribed to sleeping sickness. All the other 30 cases "are reported alive and in good health! If we consider that half of them at the beginning of the treatment were serious cases and that 6 of those

still living had shortly before discharge had trypanosomes in the cerebro-spinal fluid we must regard the results<sup>as</sup> very satisfactory.

#### SLEEPING SICKNESS IN THE CONGO.

In the Belgian Colony a small post, Kiambi, on the Luvua River, a tributary of the Congo, was assigned to us as a most suitable place for our investigation. The Government Bacteriologist Dr. Walravaens, and later the Entomologist Mr. Ch. Seydel, assisted us in our work and looked after our requirements.

Sleeping sickness in the Congo basin is transmitted by G. palpalis, and not as in Nyasaland and Rhodesia by G. morsitans. The causal agent is probably identical. Clinically, at any rate, there are no fundamental differences, though in general in the Congo, where the disease has occurred for a long time, it appears to be in a more chronic state.

#### DIAGNOSIS.

The diagnosis was made by microscopical determination of living parasites in the secretion of the enlarged glands of the neck. If no glands were present the blood was examined in large thick wet stained smears. As lately authors have reported many negative results in the blood examinations of sleeping sickness patients, whilst the gland examinations gave positive results, we have made several comparisons. Of 32 patients 24 showed trypanosomes in the glands and in the blood; 4 only in the glands and not in the blood; and 4 not in the enlarged glands though in the blood. Of each patient only one blood smear and one gland smear was examined. If the number of the smears is increased, our experience in many sleeping sickness districts shows an agreement between the finding in the glands and the blood, i.e., if parasites are present in the glands they are also easily found in the blood. Different results must be attributed to defective technique. We used the method of blood examinations as described in the report of Koch's Sleeping Sickness Expedition. So far as we know, the first to apply it - as a modification of the Ross method - was Kudicke. Lumbar puncture was

unnecessary for the diagnosis of untreated patients.

To find out whether trypanosomes occur in the cerebro-spinal fluid without causing any appreciable nervous symptoms in the patient lumbar punctures were made on 24 mentally sound cases. The findings were negative throughout. This is worthy of notice in view of Uhlenhuth's finding of spirochaetes in the early stages of syphilis. For various reasons we were unable to inoculate the cerebro-spinal fluid into monkeys and were only able to examine the centrifugate under the microscope. Even in sleeping sickness cases that are not quite normal mentally one does not always find trypanosomes in the lumbar fluid; but the number of the lymphocytes is then always unusually great, which justifies the conclusion that the nervous system is infected.

#### TREATMENT

In the Congo we mostly adopted intravenous injections, which are less unpleasant for the patient. The patients receive on the 1st, 3rd and 13th day respectively, 1 gm. Bayer 205 diluted in 10 com. of rain water injected into a vein in the arm. The children were given a correspondingly smaller dose (0.4 - 0.6 gm.) and the site of application was the jugular vein. Patients with parasites in the cerebro-spinal fluid or showing serious clinical symptoms (paralysis, maniacal behaviour) were again treated in 10 day intervals. Also in the case of children a more intensive treatment was sometimes indicated. But we never exceeded 5 injections.

In view of Martin Mayer's numerically small but therapeutically brilliant results, we aimed at reaching our goal with a few injections as possible, especially as we were not so much concerned with the treatment of individuals as to test the possibility of the extermination of the disease on a large scale. The more injections required for the curing of the patient or for sterilising his peripheral blood, the more complicated becomes the campaign against the disease under the conditions prevailing in Africa. For the same reason we avoided intralumbar infusions. They were, by the way, quite impossible under our working conditions. We were

satisfied that for diagnostic purposes we were able to make lumbar punctures. The natives dislike their frequent use. We are of opinion that they are surprised and mistrust the fact that a clear fluid flows from the back of the patient.

#### RESULTS.

At Kiambi we had 91 patients under treatment, mostly second stage (enlarged glands); to these were added 40 that had been under the observation of the Government Medical Officer. Dr. Conzémus at Bukama. The blood of our patients was examined at 8 day intervals as far as possible. As the patients could not always be fetched from their villages at precisely the right time, we had to take into consideration delays and irregularities. The treatment began at the end of December '22. In all cases the neck gland swellings quickly diminished. The majority declared after a short time that they had regained their original strength and were completely well. On 9.5.23 of 90 fairly regularly examined patients we only found trypanosomes in the blood of 2 children, and this 2-3 months after the third injection. Whether these were cases of actual relapse or reinfection must remain undecided, as we could not concern ourselves with the habits of our patients (fishing in palpalis-infested rivers) in their absence from our place of treatment.

Particularly striking was the recovery of 2 absolutely maniacal patients (Inkaria (no. 75) and Bulaya (no. 82). The former who had always to be kept chained down, could be allowed to go free 10 days after the third injection. Bulaya, a boy of about 12 years old, became absolutely calm a few days after the third injection. Both cases, as stated above, were treated further.

Seven patients (No. 1, 2, 3, 4, 5, 9 & 10) in the 3rd stage (nervous symptoms), of whom a few had for a long time received atóxyl and antimony without results, presented a more or less unhealthy appearance in spite of continual treatment with Bayer 205.



The blood of all, however, remained free from trypanosomes, although in 2 cases parasites were found in the cerebro-spinal fluid. Of great interest was Ulinengo (no.3). Although his stupor and ataxia were very marked, lumbar punctures showed neither higher pressure nor trypanosomes nor increased lymphocytes. As an explanation of this condition we assume that, though the parasites had been killed in the brain, the pathological disturbances of the substance were irreparable.

When our observations are concluded, Dr. Walravaens will watch the progress of the patients in the following year and make fresh experiments. It is hardly to be doubted that the therapeutic results may be still further improved by more individually suitable treatment, or perhaps even by the aid of other drugs.

The most important definite results of the application of Bayer 205 are, we consider, the possibility of sterilising for a long period the blood of even those patients that are not clinically cured. If in districts infected with sleeping sickness all suspected natives received treatment at the hands of travelling doctors or a responsible sanitary staff, the source of infection for the natives would gradually disappear and in time the disease must die out. Naturally, sanitation of the villages and by hand in hand with medical treatment. The success of a campaign against sleeping sickness becomes a question of sanitation.

It is of theoretical as well as practical interest to consider for a moment the varying susceptibility of the trypanosomes to Bayer 205 in different species of animals. We see that the drug is of great use in trypanosomiasis of rats, mice, guinea-pigs, rabbits, monkeys and man, but less so in the disease of cattle. The animals that are not exposed to natural infection are the most easy to cure. In our opinion the various species of trypanosomes are the result of hereditary adaptation to the mammals to which in the course of time they have continually been transmitted. The kind of animal that is regularly infected with trypanosomes under natural

conditions gradually produces the most suitable nourishment for the parasites, and their growth in this favourable medium is most difficult to treat by drugs. Thus Trypanosoma oederae in the goat and Tr. bovis in cattle, for instance, are particularly resistant. Tr. brucei, which under normal conditions is found in the buffalo, is more suited to the related conditions of life in cattle than to those in the rat, mouse, rabbit, monkey, etc., and is therefore difficult to influence in cattle.

That human trypanosomiasis yields more readily to treatment must be attributed to the fact that man has not harboured the parasite for very long. Mal de oederae, the form of trypanosomiasis in which Bayer 205 has had such brilliant therapeutical results, is supposed to have first appeared in 1834. In this connection it should be remembered that Kolle and Ruppert could treat human syphilis in rabbits much more easily with salvarsan than the true rabbit spirochaete.

Katentania, Belgian Congo, 6th June 1923.

Director:  
 SHAW, C.M.G., M.B.,  
 D.P.H.

## TROPICAL DISEASES BUREAU,

Assistant Director:  
 W. ALCOCK, C.B.E.,  
 M.B. (retd.),  
 and Librarian:  
 J. SHEPPARD.

28, ENDLSHUGH GARDENS,

LONDON, N.W. 1.

PHONE No.:  
 2324.

Dec. 18 / 23

Mr. Parkman

I return the draft attached  
 with five additional sentences, intended  
 to make it clear that the car is in  
 my opinion the barrier to the general  
 adoption of this drug for reserves.

Yours sincerely

Clifford H. Parkman

## Imperial Bureau of Entomology

Head Office at—

Director,  
 MARSHALL, C.M.G., D.Sc., F.R.S.

BRITISH MUSEUM (NATURAL HISTORY),

Assistant Director,  
 C. A. REARD, D.Sc.

CROMWELL ROAD, LONDON, S.W. 7

15th December, 1925.

My dear Parkinson,

Thanks for your letter of yesterday's date, enclosing the draft of a despatch dealing with Professor Kleins's report on his experiments with "Bayer 209". Until reading Bagshaw's comments, I had no idea that the drug was so very expensive, and in view of this information, I should like to make a slight modification in my comments, to the effect that wholesale treatment would only be possible if there was a substantial reduction in the cost of the drug. I have indicated the way in which the alteration could be made on the draft of the despatch, which I now return.

Yours sincerely,



Director.

Draft

A. G. C. Parkinson, Esq.,  
 Colonial Office,  
 Downing Street,  
 S.W.1.

# Imperial Bureau of Entomology

Head Office at—

Director:  
MARSHALL, C.M.G., D.Sc., F.R.S.  
Assistant Director  
A. NEAVE, D.Sc.

BRITISH MUSEUM (NATURAL HISTORY),  
CROMWELL ROAD, LONDON, S.W. 7

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Yours sincerely,



Director.

Draft.

A. C. C. Parkinson, Esq.,  
Colonial Office,  
Downing Street,  
S.W.1.

DRAFT

Downing Street,

December, 1923.

No.  
Mr CoryndonEast Africa Protectorate No.  
Mr ArcherEast Africa Protectorate No.  
Mr Administering the  
Government.East Africa Protectorate No.  
Mr British ResidentEast Africa Protectorate No.  
Mr Byatt.East Africa Protectorate No.  
Mr Summers.East Africa Protectorate No.  
Mr Clifford

Sir,

With reference to my despatch

No.

(1)	348
(2)	131
(3)	80
(4)	46
(5)	169
(6)	69
(7)	305

of the 6th of March, I have the honour to transmit to you, for your information a copy of a translation of a further report by Professor Klein of his investigations in connection with the efficacy of "Bayer 205" in the treatment of trypanosomiasis in men and animals

2. The Director of the Tropical Diseases Bureau, to whom the report was referred, comments on it as follows:-

"The report, which was published in the Deutsche Medizinische Wochenschrift of August 10, contains much

much that is of interest, but in my judgment further experience and experiment are necessary before the use of this expensive remedy for infected natives on the scale contemplated by Professor Kleine can be advised. It is yet uncertain whether his results are so much better than those following the use of atoxyl, employed since 1912 on a large scale by the French, or of trypanamide, one of the promising newer drugs, as to justify the selection of "Bayer 205" for this purpose to the exclusion of the others, for it has to be remembered that "Bayer 205" costs at present £2 - £3 for each native treated and atoxyl about 1/4d; trypanamide is not yet on the market.

It seems that "Bayer 205" is of little value in the treatment of trypanosome infected cattle and

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and its employment for the protection of stock when passing through tsetse areas is hardly likely to become general if it does no more than maintain them in condition for a longer period than untreated animals.

I understand that Professor Kleine is now in Europe. Doubtless he is writing a third report to contain such conclusions as his experiments justify. It will be well to await this report before deciding what, if any, action should be taken."

3. The following are comments on the report by the Director of the Imperial Bureau of Entomology:-

"The results obtained in these experiments appear to be extremely promising so far as human trypanosomiasis is concerned

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concerned, even though relapses have occurred in certain cases; but sufficient time has not yet elapsed to make it certain that the curative effect of the injections is really lasting. However, the rapidity with which the drug is able to clear the trypanosomes from the peripheral blood for a considerable time should make it of great practical value in checking the spread of an epidemic, and if the treatment could be administered on the wide scale suggested by Dr. Kleinf, it might even serve to break the cyclical transmission of the disease."

I. have etc.,

included in dft.  
 as sent ↓  
 will not be possible if the  
 very high cost of the drug  
 (substantially reduced)

Imperial Bureau of Entomology

British Museum (Natural History)

Cromwell Road, London, S.W.7.

10th November, 1923.

Sir,

I have the honour to acknowledge the receipt of your letter of the 31st October (No. 50271/1923) transmitting a copy of a despatch from the High Commissioner for South Africa together with a report, in German, by Professor Kleins on his investigations into sleeping sickness.

2. This report has now been translated into English and I enclose three copies of the translation as requested together with the original.

3. A paragraph appears to have been omitted in the original report after paragraph 3 on page 2 of the translation for no account is given of the details of the experiment with Bullock No. 14 which is stated to be particularly instructive.

4. The results obtained in these experiments appear to be extremely promising so far as human trypanosomiasis is concerned, even though relapses have occurred in certain cases; but sufficient time has not yet elapsed to make it certain that the curative effect of the injections is really lasting. However, the rapidity with which the drug is able to clear the trypanosomes from the peripheral blood for a considerable time should make it of great practical value in checking the spread of an epidemic, and if the treatment could be administered on the wide scale suggested by Dr. Kleins, it  
might

ZL might even serve to break the cyclical transmission of the disease.

I have, etc.

(sgd.) Guy A.K. Marshall.

Director.

The Under Secretary of State,

Colonial Office.

Downing Street,

S.W.1

Tropical Diseases Bureau

23 Endsleigh Gardens,

London, N.W.1.

30th November, 1923.

Sir,

I have the honour to acknowledge the receipt of your letter of November 16th (54306/23) forwarding a translation of a further report by Prof. Kleine on his experiments with "Bayer 205" in Tropical Africa and a letter from the Director of the Imperial Bureau of Entomology.

2. The report, which was published in the Deutsche Medizinische Wochenschrift of August 10, contains much that is of interest but in my judgment further experience and experiment are necessary before the use of this expensive remedy for infected natives on the scale contemplated by Prof. Kleine can be advised. It is yet uncertain whether his results are so much better than those following the use of atoxyl, employed since 1912 on a large scale by the French, or of tryparsamide, one of the promising newer drugs, as to justify the selection of "Bayer 205" for this purpose to the exclusion of the others; for it has to be remembered that "Bayer 205" costs at present £2 - £3 for each native treated and atoxyl about 1s and 4d; tryparsamide is not yet on the market. Doubtless all the natives treated in Rhodesia are being kept under observation and reports on their state will be rendered at regular intervals to the Secretary of State.

3. It seems that "Bayer 205" is of little value in

X ] in the treatment of trypanosome infected cattle and its employment for the protection of stock when passing through tsetse areas is hardly likely to become general if it does no more than maintain them in condition for a longer period than untreated animals.

4. The printed version shows that Dr. Marshall is not correct when he states that a paragraph has been omitted; for "Bullock No.14" one should read "Bullock No.11".

X ] I understand that Prof. Kleine is now in Europe. Doubtless he is writing a third report to contain such conclusions as his experiments justify. It will be well to await this report before deciding what, if any, action should be taken.

I have, etc.,

(Sgd.) Arthur J. Bagshawe.

Director.

The Under Secretary of State,

Colonial Office,

Downing Street,

S.W.1.

Ms. 59150/23 E.H. wa

(This draft for concurrence of W. Marshall & B. Shaw) X

2<sup>c</sup> of draft

Dec 1923

Hawaii No

W. Long adm.

Hawaii No

Dr. Archer

Hawaii No

Dr.

Hawaii No

Dr. H. H. H.

Jan 7 - 40

H. H. H.

Hawaii No

Dr. C. C. C.

Hawaii No

Dr. B. B. B.

Dec 10

lines 11, 12 atomic

12 DEC 1923  
copy to [unclear] 7/4/23

with ref to my desp No

- 1) 345
- 2) 131
- 3) 5
- 4) 4
- 5) 169
- 6) 24
- 7) 205

of the 6<sup>th</sup> of March, covers 6  
 lines and is for use of  
 a copy of a translation of a  
 further report by Professor  
 Nieme on his investigations  
 in connection with the efficacy  
 of "Bayer 205" in the treat-  
 -ment of typanosomiasis  
 in men & animals.

translation of report  
(attached)

W.H.P.



2 To Director of the  
Tropical Diseases Bureau,

to whom the report was referred,

concerning the <sup>it</sup> report as follows:—

The report, which was published  
in the Deutsche Medizinische Wochenschrift  
number 410, contains much that is of  
interest, but in my judgment further  
experience & experiment are necessary  
before the use of this expensive remedy  
for malarial natives on the scale con-  
templated by Prof. Kline can be advised.  
We still <sup>yet</sup> uncertain whether his results  
are so much better than those following  
the use of atoxyl, employed since  
1912 on a large scale by the French,  
or of tryparsamide, one of the promising  
newer drugs, as to justify the selection of  
"Bayer 205" for this purpose & the exclusion  
of all others; for it has to be remembered  
that "Bayer 205" costs at present £2-3  
billion for each native treated and atoxyl  
about 1/4; tryparsamide is not yet on  
the market.

It seems that "Bayer 205" is of little  
value

To the Director of the  
Imperial Diseases Bureau,

to whom the report was referred,  
concerning the <sup>it</sup> report as follows:-

The report, which was published  
in the *Zeitschrift für Tierärztliche Medizinische Vochenschrift*  
No. 10, contains much that is of  
interest, and in my judgment further  
experiments & experiments are necessary  
before the use of this expensive remedy  
is recommended either on the scale con-  
templated by Dr. Vufft Kieune can be advised.  
It is <sup>not</sup> clear in certain whether his results  
are so much better than those following  
the use of atoxyl, employed since  
1912 on a large scale by the French,  
or of triparasamide, one of the promising  
newer drugs, as to justify the selection of  
"Bayer 205" for this purpose to the exclusion  
of others; for it has to be remembered  
that "Bayer 205" costs at present £2-£3  
per <sup>gallon</sup> for each native treated and atoxyl  
about 1/4<sup>d</sup>; triparasamide is not yet on  
the market.

It seems that "Bayer 205" is of little  
value

value in the treatment of  
trypanosome infected cattle  
& its employment for the  
protection of stock <sup>when</sup> passing  
through tsetse areas is  
hardly likely to become general  
if it does no more than maintain  
them in condition for a longer  
period than untreated animals.

I understand that Vufft-  
Kieune is now in Europe.  
Doubtless he is waiting a third  
report to contain such conclusions  
as his experiments justify.  
It will be well to await this  
report before deciding what,  
if any, action should be taken.

3. The following are com-  
ments on the report by the  
Director of the Imperial  
Bureau of Entomology:-

The results obtained in these  
experiments appear to be extremely  
promising so far as human  
trypanosomiasis is concerned.

even though relapses have occurred in certain cases; but sufficient time has not yet elapsed to make it certain that the curative effect of the injections is really lasting. However, the rapidity with which the drug is able to clear the hypanosomes from the peripheral blood for a considerable time should make it of great practical value in checking the spread of an epidemic, and if the treatment could be administered on the wide scale suggested by Dr. Wilson, it might even serve to break the cyclical transmission of the disease.

JTC

even though relapses have occurred  
in certain cases; but sufficient  
time has not yet elapsed to  
make it certain that the curative  
effect of the injections is really  
lasting. However, the rapidity  
with which the drug is able to  
destroy the trypanosomes from the  
peripheral blood is a considerable  
fact which should make it of great  
practical value in checking the  
spread of an epidemic, and if  
the treatment could be administered  
on the wide scale suggested by  
Dr. Nogueira, it might even serve  
to break the cyclical transmission  
of the disease.

Jrc

59150/23 Ea wa

Jan  
(On quarter for  
the Panama Dept)

C. D.  
R 11 DEC  
D 11

DRAFT.

12 Dec 1923

Mr. H. K. Marshall  
Sup. Bureau of Entomology

Dear Marshall  
Bagshaw

I enclose the draft

MINUTE.

- Mr. Bagshaw
- Mr. Top. Dep. Bureau
- Mr. Brett - Dec 10
- Mr. Jeffries 10/12/23
- ~~Mr. ...~~

of a test which it is  
proposed to send to the

- Mr. C. Davis
- Mr. G. Grindle
- Mr. H. Rhoad
- Mr. J. Minterston Smith
- Mr. Ormsby Gore
- Mr. ...

... dependencies of  
Africa, sending copies of  
the translation of Prof  
Klein's report on his  
investigations into ...

Jan Draft test  
(Hermon)

20/26

No. 9  
59150/23

Ea  
wa

509

Just

(On quarter for  
In Service of  
Sigsbee)

C. D.  
R 11 DEC  
D. H.

DRAFT.

Stoc

12 Dec 1923

Mr. Marshall

Dear Marshall  
Bryant

Conf 215

I enclose the draft

Sup. Bureau of Entomology

MINUTE.

Mr. ~~B. Shaw~~ C. H. J.  
Mr. Trop. Dir. Bureau  
Mr. Bell - Dec 10

of a letter with a list of

Mr. Jeffries 10/12

proposed to send to the

~~Mr. ...~~

Department of Agriculture &

Mr. C. Danks

requesting you to send a copy of

Mr. G. Grubbs

the translation of the

Mr. H. Road

document to his

Mr. J. M. Sterton Smith

investigation. He would

Mr. Orinby Gore

Director of Dept. -

Fair draft list  
(Herewith)

246

59150/23  
Jud

Ed  
Wa

(On quarter for  
In Parson's  
Signs)

C. D.  
R 11 DEC  
D-11

~~Doc~~

DRAFT.

12 Dec 1913

Mr. H. Marshall

Dear Marshall  
Baltimore

Comp. M.B.  
Imp. Bureau of Entomology

I enclose the draft

MINUTE

Mr. Brewster - Dec 10

of a letter which it is

Mr. Jeffries

proposed to send to the

~~Mr. ...~~

relevant agencies of

Mr. ...

signing, sending a copy of

Mr. ...

the conclusions of Prof

Mr. ...

Allen's report on his

Mr. ...

investigation. I should

Mr. ...

Two drafts lost  
(Kearney)

Ed

To Bayes 205.

I send the draft  
for your concurrence as  
it contains ~~the~~ <sup>the</sup> comments  
made  
in the report of the

Special Committee of the  $\text{10}^{\text{th}}$   
 $\text{30}^{\text{th}}$

of Nov. I am

writing similarly to

Bayshawe

Marshall

Yours sincerely

(sd) acc. Parkin



102/59150/23



S. Af.  
to Afr.  
g.c. dist. to all

DRAFT

Wa No. Verner Coryndon

anda Protectorate No. Governor Archer

aland No. 6. Officer Administering the Government.

umber No. 5. Acting British Resident

anyika Territory No. 522 Governor Nyanteh

smalland Protectorate No. 2 Governor Summers

geria No. 26 Governor Clifford.

Downing Street,  
11 December, 1923.

Sir,

With reference to my despatch

No. -

- (1) 348
- (2) 131
- (3) 80
- (4) 45
- (5) 169
- (6) 69
- (7) 305

of the 6th of March, I have the

honour to transmit to you, for your

information a copy of a translation

of a further report by Professor

Kleine on his investigations in

connection with the efficacy of

"Bayer 205," in the treatment of

of trypanosomiasis in men and animals

2. The Director of the Tropical

Diseases Bureau, to whom the report

was referred, comments on it as

follows:-

X "The report, which was published in the Deutsche Medizinische

Wochenschrift of August 10, contains

much

20.12.23

24/12/23

21/1/24

Report 105198/0/23

embodies both Dr. Bagshaw's and Dr. Marshall's amendments.)

had got to TBE r B LFP

corr<sup>d</sup> ought also

go to the other

a. Colonies. All

got S.S. cases, & we

had enquiries for '205'

E. Coast.

Send them copies of full despatches & say they can get only with C.A. 1/24

Report 105198/0/23  
No. 24-14 Jan 24 - 10  
4874/23  
copy (with send) to 388 - 14 Jan 24 - 10

Review  
or  
Latin

much that is of interest, but in my judgment further ~~experiments~~ and experiments are necessary before the use of this expensive remedy for infected natives on the scale contemplated by Professor Kleins can be advised. It is yet uncertain whether his results are so much better than those following the use of atoxyl, employed since 1912 on a large scale by the French, or of trypanocide, one of the promising newer drugs, as to justify the selection of "Bayer 205" for this purpose to the exclusion of the others; for it has to be remembered that "Bayer 205" costs at present \$2 - \$3 for each native treated and atoxyl about 1/4d; trypanocide is not yet on the market.

It seems that "Bayer 205" is of little value in the treatment of trypanosome infected cattle and

See Dr. Bagshaw's  
letter of 18/12



The possibility of reinfection, which  
Kleins admits, has also to be taken  
into account. Other things being  
equal, without question Bayer 205  
is the best remedy at the present time  
for human trypanosomiasis.

and its employment for the protection of stock when passing through tsetse areas is hardly likely to become general if it does no more than maintain them in condition for a longer period than untreated animals.

I understand that Professor Kleins is now in Europe. Doubtless he is writing a third report to contain such conclusions as his experiments justify. It will be well to await this report before deciding what, if any, action should be taken."

3. The following are comments on the report by the Director of the Imperial Bureau of Entomology:-

"The results obtained in these experiments appear to be extremely promising so far as human trypanosomiasis is concerned

concerned, even though relapses have occurred in certain cases; but sufficient time has not yet elapsed to make it certain that the curative effect of the injections is really lasting. However, the rapidity with which the drug is able to clear the trypanosomes from the peripheral blood for a considerable time should make it of great practical value in checking the spread of an epidemic, and if the treatment could be administered on the wide scale suggested by Dr. Kleins, it might even serve to break the cyclical transmission of the disease."

I have etc.,

(Signed) DEVLIN HIRZ

which will only be possible if the present very high cost of the drug is substantially reduced,

↑

See Dr. Marshall's letter of 13/12

~~S/59270/23 G.A.~~

M/59150/23 Ea.  
Wa.

28 JAN 1924

End

Sir

DRAFT.

- Good Coast NO 88.
- S. Leone NO 14
- Gambia NO 11.

MINUTE.

- Mr. Ford (6.1.)
- Mr. Parkinson (7.1.)
- Mr. Ellis (7.1.)
- Mr. G. Brown
- Mr. G. Brown

- Mr. H. Road 17
- Mr. J. Masterton Smyth
- Mr. Ormsby-Gore
- Truke of Devonshire.

Report in 48404/22

Report in 9174/23

Report in 59150/23

As attached to  
M/59150/23 G.A.

I have the honour to inform  
 to acquaint you, for  
 you that, following upon the  
 you visit,  
 practical tests conducted in Rhodesia  
 by Professor Kleins, supplies of  
 the drug "Bayer 205" can now  
 be obtained.

I enclose copies of reports  
 by Professor Kleins on the results  
 with "Bayer 205" in the treatment  
 of his work of trypanosomiasis,  
 which you will no  
 doubt bring to the notice of your  
 medical Dept., in case they should  
 wish to undertake experiments  
 with the drug. I am glad to  
 understand that the present price of  
 the drug is high and that the cost of  
 its sterilisation is great (2)

treating a single case is between two or three pounds for the drug alone.

The reports <sup>have been</sup> submitted to the Prof. Dr. has a <sup>very</sup> ~~very~~ <sup>country</sup> ~~country~~ <sup>and</sup>, I admit, and in connection with the last of them the Director of the Tropical Diseases Bureau comments as follows:-

The report which was published in the Deutsche Medizinische Wochenschrift <sup>abstract</sup> of the 10th of August, contains much that is of interest, but in my judgment further experience and experiment are necessary before the use of this expensive remedy for infected natives on the scale contemplated by Professor Kleine can be advised. It is yet uncertain whether his results are so much better than those following the use of atoxyl employed on a large scale by the French, (since 1912) or of typanamide, one of the newer promises drugs, as to justify the selection of 'Bayer 205' for this purpose to the exclusion of the others; for it has to be remembered that 'Bayer 205' costs at present £2-6-3 for each native

515  
treated and atoxyl about 1s. 4d. : typanamide is

not yet on the market. The facility of re-infection which Professor Kleine admits has also to be taken into account. Other things being equal, without question 'Bayer 205' is the best remedy for human typanosomiasis at the present time.

"It seems that 'Bayer 205' is of little value in the treatment of typanosome infected cattle and its employment for the protection of stock passing through tsetse areas is hardly likely to become general if it does no more than maintain them in condition for a longer period than untreated animals."

"I understand that Professor Kleine is now in Europe."

DRAFT.

MINUTE.

Mr.

Mr.

Mr.

Sir C. Davis.

Sir G. Grindie.

Sir H. Ross.

Sir J. Masterton Smith.

Mr. Ormsby-Gore.

Duke of Devonshire.

Doubtless he is writing a third report to contain such conclusions as his experiments justify. It will be well to await this report before deciding what, if any, action should be taken."

\* The Director of the Imperial Bureau of

Entomology has made the following remarks:

"The results obtained in these experiments appear to be extremely promising so far as human trypanosomiasis is concerned, even though relapses have occurred in certain cases; but sufficient time has not yet elapsed to make it certain that the curative effect of the injections is really lasting. However, the rapidity with which the drug is able to clear the trypanosomes from the peripheral blood for a considerable time should make it of great practical value in checking the spread of an epidemic, and, if the treatment could be administered on the wide scale suggested by Dr Kleine, which will only be possible if the present very high cost of the drug is substantially reduced,

Doubtless he is writing a third report to contain such conclusions as his experiments justify. It will be well to await this report before deciding what, if any, action should be taken."

\* The Director of the Imperial Bureau of Entomology has made the following remarks:

"The results obtained in these experiments appear to be extremely promising so far as human trypanosomiasis is concerned, even though relapses have occurred in certain cases; but sufficient time has not yet elapsed to make it certain that the curative effect of the injections is really lasting. However, the rapidity with which the drug is able to clear the trypanosomes from the peripheral blood for a considerable time should make it of great practical value in checking the spread of an epidemic, and, if the treatment could be administered on the wide scale suggested by Dr. Kleine, which will only be possible if the present very high cost of the drug is substantially reduced,

516  
it might even serve to break the cyclical transmission of the disease."

3.5 Supplies of the drug can be ordered through the C.O. for the Colonies, who will endeavour to obtain the quantities required from the manufacturers. The cost, however, is still high; it is understood that the manufacturers ~~so far the cost as to~~ act on the principle of supplying the drug as a <sup>charge</sup> ~~cost~~ wh. they regard as a contribution towards the ~~present~~ cost of investigation. It appears from Compt. that ~~the~~ passed between the Director of

DRAFT.

MINUTE.

Mr.

Mr.

Mr.

Sir C. Davis.

Sir G. Grindle.

Sir H. Read.

Sir J. Masterion Smith.

Mr. Ormsby-Gore.

Duke of Devonshire.

[of 10/1/1906/100]



... doubtless he is writing a third  
... report to contain such conclusions  
... as his experiments justify. It will  
... be well to await his report before  
... deciding what, if any, action should be  
... taken."

\* The Director of the Imperial Bureau of  
Entomology has made the following remarks:  
"The results obtained in these experiments  
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though relapses have occurred in certain cases;  
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it of great practical value in checking the  
spread of an epidemic, and, if the treatment  
could be administered on the wide scale  
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be possible if the present very high cost  
of the drug is substantially reduced,

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high; it is understood  
that the manufacturers  
~~to fix the cost as to~~  
act on the principle of  
supplying the drug  
as a <sup>charge</sup> ~~cost~~ wh. they  
regard as a contribution  
towards the ~~present~~  
cost of investigation.  
It appears from  
Coresp. that ~~the~~ framed  
between the Director &

DRAFT.

MINUTE.

Mr.

Mr.

Mr.

Sir C. Davis.

Sir G. Grindle.

Sir H. Read.

Sir J. Maesterton Smith.

Mr. Ormsby-Gore.

Duke of Devonshire.

[ 7/11/1906 ]

the Federal Diseases Bureau  
of the manufacturers <sup>that</sup> last year that  
the quantity needed  
for the treatment of each  
case is considered  
to be 10 grams,  
~~and~~ further that the  
manufacturers, ordinarily  
express that very  
doubt on the results  
obtained by the use  
of the drug and be  
communicated  
them

(SIGNED) J. H. THOMAS.

the Tropical Diseases Bureau  
of the manufacturers <sup>that</sup> last year that  
the quantity needed  
for the treatment of each  
case is considered  
to be 70 grammes,  
~~that~~ further that the  
manufacturers ordinarily  
express that only  
orders on the quantity  
obtained by the use  
of the drug should be  
communicated  
them.

(SIGNED) J. H. THOMAS.