THE TREATMENT OF SLEEPING SICKNESS.

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IN the present paper the various methods of treatment in use at Kyetume Camp, Uganda, are discussed.

Therapeutic Effects of Arsenicals.

As to the ultimate curative results, no one method seems to have so far shown the least superiority over any other in any given class. As regards early therapeutical effects, good seems to result from all organic arsenical compounds, save possibly kharsin (Burroughs and Wellcome). It so happens that Class "A" have, as a rule, been under soamin, and therefore this drug has had the advantage of having to combat the disease in an early stage. By "A" cases I designate those only who on examination show trypanosomes in their glands or blood, but who otherwise show no clinical symptoms whatever; in fact, they themselves say that they feel perfectly healthy. In some respects soamin is undoubtedly superior to any other of the organic arsenicals in use, for reasons which are given in detail later.

As far as one can judge, short of animal experiments, the trypanocidal effects of all organic arsenicals seem similar, and all appear to be trypanofuges, using the term to mean that one is able by a single hypodermic injection to banish trypanosomes from both glands and circulation, where they possibly swarmed, to such an extent that the parasites, after twelve hours, cannot be demonstrated microscopically in the usual way. That this is not a complete or real trypanocidal effect—that is, sterilization—is shown by the fact that the parasites have reappeared in the blood, and in one case the glands sooner or later, and also that patients die from typical sleeping sickness while under treatment.

However, in some "A" cases the sterilization seems to have been complete. These few patients have never, since treatment was stopped, shown the least advance in symptoms, nor have they appeared at any time other than well; one is almost tempted to say they are cured.

Toxic Effects.

As regards the toxic effects of the various drugs I at once find a wide divergence.

Kharsin.—This drug seems to be so toxic that death follows all save possibly very small doses, and to be unfit for use in the human subject. I have had no experience of it, but am judging from the camp records. In view of the fact that we have much safer drugs it does not seem worth while to try it further, even in small doses.

Atoxyl.—This, while some samples have proved satisfactory, has proved so much less stable than other organic arsenicals and so uncertain in the qualities of the various samples sent to us, that I consider its use as a therapeutic agent entirely unjustifiable, unless the risk of subsequent total blindness is considered of no moment, and because here again in soamin (Burroughs and Wellcome) we have a drug equal to atoxyl in therapeutical effects but entirely pure.

Soamin.—This I consider is the best form of organic arsenic which I have yet experimented with, as its trypanocidal and trypanofuge characteristics are equal to all others put forward as yet. I have found no reason to alter the opinion I stated more than a year ago that it is entirely non-toxic in doses up to 1 gram; moreover, every sample supplied has been of an entirely uniform quality, pure and reliable. I use this drug entirely, to the exclusion of all other organic arsenicals, in the routine treatment of this camp. I find from the records that the former medical superintendent came across one case in which he seems to have concluded that serious optical symptoms (total blindness) followed the use of soamin; but there were no notes as to the eye conditions on admission. This I consider an important point, for I find that in this disease we have a certain number of patients who complain of poor vision without any treatment whatever. In one case I found complete optic atrophy. In all such cases it seems as if the eye conditions were aggravated by the treatment unless care be taken in the dosage; this does not mean that a diminished dose is required, for I am firmly convinced that eye

symptoms are an incident in the disease itself, though aggravated by any impurities in the drug used. Some other four cases are also reported as having eye symptoms following on the administration of soamin, but the fact was overlooked that these also received atoxyl. As I stated before, I have yet to find untoward symptoms after the administration of soamin.

Asodyl or Orsudan (the 3-methyl 4-acetylaminophenyl-arsonate of sodium) seems similar in action to soamin, though I understand that Messrs. Burroughs and Wellcome claim it to be four times less toxic than atoxyl. We have had only one case treated by it, owing to the small amount of the drug supplied. The former medical superintendent notes that eye symptoms occurred, but I see that this patient also had atoxyl prior to the said symptoms. I am giving this drug a more extended trial at present.

Arsacetin has been tried in a few cases by Captain Gray. I find no notes as to its being a trypanofuge, but he remarks on five cases which showed eye symptoms after being treated with this alone. In three cases the symptoms appear to have been transitory, as the patients are now well, but in two I note total blindness. Personally, I have had no experience with this drug.

Antimony cream I have had no personal experience of, but Gray reports as follows:

The treatment with antimony cream has not been very successful. Every patient who has had the injection has complained very much of the great pain and tenderness which followed. An indurated mass could be felt at the seat of injection for a fortnight after the dose was given. Very few patients would allow me to continue giving them injections. (Monthly report, Kyetume, March, 1909.)

Orpiment alone does not appear to be a trypanofuge, but used along with one of the organic arsenicals is possibly of value in prolonging the effect. It is still under trial here, and in graduated doses up to 1 gram no untoward symptoms have been met with. It presents one great objection to my mind, when used as pills on natives—they find the daily attendance irksome, and as often as not, unless carefully watched, spit out the pills when outside, so one has to spend time seeing that each individual before leaving actually swallows his dose.

Soamin or Atoxyl, combined with Mercury, given Simultaneously.—For reasons given above I use soamin exclusively, but it is conceded by all, I think, that no single drug has yet been put forward whose sole use is justifiable in this malady; a combination of drugs is indicated, and, as organic arsenic has shown itself to be a certain trypanofuge, and also to some extent a trypanocide, it seems rational that it should form one part of the combination, and of the organic arsenicals we have seen that soamin has proved the most reliable. Mercury, of little value apparently in itself, seems undoubtedly of value when used simultaneously with organic arsenic. The statistics from the first quarterly report on the results of these camps, written by Gray, show that these drugs given simultaneously over the same period in the method originated by me gave by far the best results, although in common with every other method tried the later results were somewhat disappointing. However, one cannot avoid the impression that this method is the best we have at present, though it entails more laborious work.

Methods.

It is stated by the makers of soamin that it is not compatible with the salts of heavy metals, and should not be given too soon after injections of them. I have no hesitation in saying that this precaution is needless, for I have given mercury not only soon after soamin, but along with it in the one injection, thus reducing the number—an advantage when one has to give them to some hundred natives. A perfectly clear solution results if the sodium chloride necessary for the satisfactory solution of the sublimate is used slightly in excess, for this dissolves the first cloudiness formed on mixing the solutions.

Atoxyl has been given in various doses; Manson's method having been tried amongst others, but to my mind all these methods involving continuous or interrupted small doses are incorrect, and of absolutely no use in avoiding eye symptoms, etc., if the drug is impure; if it is pure, no symptoms follow even the large doses. I am convinced that we should attempt to get the maximum sterilizing effect as soon as possible, and

that small doses are useless. In my opinion we should endeavour to give the maximum quantity of arsenic in the first dose, as it seems probable that the parasite subsequently acquires an immunity to the drug; otherwise it is difficult to account for case after case no longer reacting to arsenic after a time. I give, therefore, as large a dose as is convenient for the first, followed by a second within twenty-four hours.

Mercury used alone has proved useless as a trypanofuge, whether given in injection by mouth or intravenously as the cyanide salt.

Contrary to the belief usually held that the Baganda have an idiosyncrasy for mercury, I find that they tolerate heavy doses in injections very well, though they react badly to inunctions or mercury by the mouth. Of course it is necessary to see that they keep their mouths clean to avoid sore gums, but this is not a difficult matter amongst natives. Abscesses forming at the site of injection are avoidable in most cases, if care is taken to see that the needle is dry before use, that it is made of platinum, and that the site of the injection is well massaged after injecting. The injection need not be intramuscular—a small point, but of importance when dealing with large numbers of natives. I find the posterior axillary fold as good a place as any.

Dr. Andrew Balfour's suggestion as to inoculations of the patient's own serum into the spinal canal has been tried in some six cases, but the results were not encouraging. I must add, however, that the method was tried only in cerebral cases, and these are usually too far gone for any other treatment. At present it is not, however, feasible to try this method in early cases in these camps.

THE TREATMENT OF PHTHISIS AND OTHER CONDITIONS BY ARYLARSONATES.*

BY

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MUCH has been written during the last few years regarding the use of arylarsonates in protozoal diseases, chiefly sleeping sickness, and, more recently, syphilis. We have been able to find no account of their employment in any bacterial infection except in a paper by Hallopeau,¹ where one case of renal tuberculosis and two of leprosy are narrated that benefited much under treatment by atoxyl. The idea that they might be useful in tuberculous conditions came to us from our friend Dr. van Someren, of the Uganda Medical Service, who told us in the autumn of 1908 that, shortly before he came home on furlough, he had seen remarkable improvement in two cases of tubercular leprosy under one of these drugs. His first case was a young man who came to be treated for sleeping sickness, with which he was convinced that he was affected. Careful examination failed to reveal any evidence of it; but the man was so possessed with the idea that he had it, and so persistent in his request to be treated, that a course of injections was administered. During its progress it was noticed that leprosy tubercles on the brow, etc., from which he was suffering improved rapidly and to a surprising extent. Dr. van Someren then sent for another leper at a more advanced stage of the disease who had consulted him some time previously, and subjected him to a similar course. Here also there was marked and striking improvement in the lesions, and it was noticed that there was a great diminution in the number of lepra bacilli present. Dr. van Someren had no time before leaving Uganda to pursue the investigation further, but he suggested to us that it would be worth while to try similar treatment in patients affected with tuberculosis. We have heard from him since his return to Uganda: "I have repeated my experiment in leprosy with the same results."

We should have liked to begin with cases of lupus, as the form of tuberculosis most resembling tubercular leprosy, but no cases presented themselves, and we determined to make trial in other forms of the disease. We are much indebted to Dr. Bell and Dr. Affleck for allowing us

to treat some of the cases in the Longmore Hospital in this way, and to put on record our results.

We have used the same substance as was used by Dr. van Someren—namely, sodium para-aminophenylarsonate, as it is put on the market under the trade name of "soamin." This is a white powder very readily soluble in hot water, but liable to decompose if kept in solution. It is said to contain 22.8 per cent. of arsenium, so that our usual dose includes over 2½ grains of that metal. It has been dissolved immediately before use in boiling distilled water, and injected warm either subcutaneously or, more often, intramuscularly, generally in the buttock. Platinoid needles have always been used. We have given the injections early in the forenoon. The dose given has generally been 10 grains, but a dose of 5 grains has been tried in the first instance. In one case a dose of 10 grains was almost invariably followed by abdominal pain, with nausea and vomiting after from eight to twelve hours; here the treatment is being continued with 5-grain doses, which cause no inconvenience. Once 15-grain doses were tried, as noted below, with a similar result. In most cases we have followed Dr. van Someren's practice—a dose on each of two successive days, then a fortnight's interval. Sometimes we have given two doses weekly till 50 grains have been administered, and then waited ten days or a fortnight before commencing another course.

Our experience does not agree with that of Dr. van Someren when he says, "In the course of several thousand injections I have never yet had any untoward symptoms, not even pain and irritation at site of injection." Others have recorded similar experiences. In the published reports of the use of the drug pain is hardly mentioned, except as not occurring. For example, Dr. J. Johnston Abraham² says, "The injections are painless"; and Captain G. S. C. Hayes³ "Pain after injection is extremely rare." We have found that about one-third of our patients have, as a rule, local pain following the injections. In most the pain comes on about twelve hours after the injection. No redness, swelling, or other perceptible sign of irritation has been observed to accompany it; but the pain is sufficiently severe to interfere seriously with the night's rest. It usually lasts for some hours, but has always subsided within twenty-four hours of the injection. Local pain immediately following the injections also occurs—in some patients habitually, in some only occasionally. Pain has by no means been confined to tuberculous cases; one of those who complained most was suffering from syphilis. So far as we could see, the occurrence of pain neither favoured nor interfered with improvement following the injections. In two patients besides the one already mentioned abdominal pain, nausea, and vomiting followed injections, but there was not sufficient evidence to show that the injections were the cause of the disturbance.

We did not know of any case in which the injections did harm to the patient, beyond temporary inconvenience, until January 3rd, 1910, when we were met by the startling intelligence that one of the patients under this treatment, aged 51, had been discovered to be blind. How long she had been in this condition we cannot say—she lies quiet and rather apathetic in a corner of the ward, and has never taken much notice of what goes on—her own estimate is a fortnight; but, as she said she had not spoken of her loss of sight because she thought it was merely the effect of the darkness of the winter days, her statement must be accepted with reserve. On examination she proved to be totally blind. Externally the eyes appeared normal; on ophthalmoscopic examination it was found that in both eyes the discs were pale and the retinal vessels considerably diminished in calibre. She is known to have been able to read while in the infirmary, though she had never been seen to do so since she came from it to the Longmore Hospital on May 11th, 1909.

Many cases have been observed in which the administration of atoxyl has been followed by blindness, and in most of these the pathological process causing it is known to have been optic atrophy.⁴ Soamin has so far, though under suspicion, never been definitely proved to produce the same result.⁵ In this case the suspicion is so strong as almost to amount to certainty, particularly as there is no pathological evidence that the disease from which our patient suffers (pemphigus foliaceus) has any special tendency to cause nerve degeneration.

* Read at a meeting of the Edinburgh Medico-Chirurgical Society.