

*A Preliminary Report on the Treatment of Human Trypanosomiasis and Yaws with Metallic Antimony.*

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(From the Yei Camp, Sudan Sleeping Sickness Commission.)

The use of precipitated metallic antimony, in a state of finest division, was devised by Plimmer for the treatment of trypanosomiasis, and the results of his and other experiments with this substance have been published.\* After a long series of experiments on subcutaneous and intramuscular injections of this form of antimony suspended in water, oily media, egg yolk, etc., all of which caused great irritation, he found that it was possible to inject it intravenously with safety, and without causing any irritation of the tissues. A large number of animals were cured of trypanosomiasis by this means, and in May, 1910, Major W. B. Fry gave a dose intravenously to a late case of Kala Azar, thus demonstrating that it could also be used safely in this manner on human beings.

Captain R. J. C. Thompson, R.A.M.C., gave this preparation by intravenous injection to the cases first admitted to the Yei Sleeping Sickness Camp between January and March, 1911. Eighty-one injections were given to 38 cases, but pressure of administrative work prevented these cases being fully treated and investigated, and they were all transferred to atoxyl treatment. Captain Thompson states that from a clinical standpoint some of these cases showed great improvement.

Later I had the honour of being appointed to the Sudan Sleeping Sickness Commission for work at Yei in the Lado Enclave, and since October, 1911, I have collected a series of cases treated by metallic antimony alone and in conjunction with other drugs. This report is consequently only preliminary; but it demonstrates that antimony in this form is a safe drug to employ in the treatment of sleeping sickness, if used with reasonable precautions, and that the results obtained so far certainly call for extended use and further investigation.

During the past year 76 newly admitted cases have been treated with antimony, alone and combined with salvarsan and atoxyl, and shorter courses of antimony have been given to 143 old cases previously treated with atoxyl,

\* 'Roy. Soc. Proc.' B, vol. 80, p. 483; B, vol. 81, p. 354; and B, vol. 83, p. 140.

atoxylate of mercury, etc. Over 1400 intravenous injections have been given, and three deaths have occurred which can be attributed to the treatment. All these fatal cases were amongst the first 150 injections.

The method of administration is the same as that of an ordinary intravenous injection of saline solution given hydrostatically through a needle of somewhat large bore.\*

The dose of antimony is stirred with about half an ounce of normal saline in a small glass mortar and becomes a temporary suspension. Two ounces of saline are then poured into the funnel and tubing, the needle is inserted into any vein in the forearm and the clip opened. As soon as it is seen that the saline is flowing freely into the vein, and there is no swelling round the site of the puncture, the suspension of antimony is poured into the funnel and the mortar is washed out, with a little more saline, into the funnel in order to leave no residue. The antimony is allowed to run into the vein, the funnel being gently shaken from time to time, and, when it is on the point of becoming empty, more saline is poured in. The window in the rubber tubing should be watched, and after all traces of antimony have passed it some more saline is allowed to run in to clear it out of the part of the tubing below the window; the clip is then closed and the needle withdrawn. About six ounces of saline seems to be a sufficient quantity, and the time occupied in giving an injection varies from three to seven minutes—depending on the calibre of the vein and the bore of the needle employed.

I have found it possible, without any hurry, to give as many as 10 injections in an hour; I mention this to show that this method of treatment is feasible on a large scale.

The question of dosage is one of considerable importance. The dose usually given was one grain. Large doses up to three grains have been given, but these seem to be attended with risk and have been given up for the present; it is probable, however, that in good, selected cases one and a half, or even two, grains may be safely given. Several cases of extreme susceptibility have been met with, however, so that the initial dose should be one grain. The interval between the doses seems to be of the greatest importance. Four days would seem to be most suitable, but injections have frequently been repeated on the third day after a dose; they should certainly not be postponed any later than the fifth day. A few of the earlier cases were treated with weekly doses; two of these were very susceptible and were unable to take doses at shorter intervals; both cases have relapsed.

The usual course of treatment has been five doses at intervals of four days,

\* The size of the one I have used is No. 19 of Imperial Standard Wire Gauge internal diameter and No. 15 external.

covering a period of from 17 to 20 days; after an interval of six weeks a short course of three doses extending over nine days has been given.

The table on pp. 206-7 gives in shortest form the results of the treatment with antimony alone. Thirty-five cases have been so treated: in 15 of these there were no symptoms other than enlargement of the cervical glands, except varying degrees of debility; 17 had also fine tremor of the tongue and five œdema of eyelids. The cases were not especially selected for treatment, but were taken just as they came.

Up to the present it has not been possible to procure susceptible animals for inoculation from the cases treated, so microscopical examination has been the only available method of controlling the results. Blood and gland juice have been examined in all cases. Three observers have undertaken each examination, and the total time of each examination has been one and a half hours. Many of the cases have been repeatedly examined.

Of these 35 cases four are dead and two have deserted. Trypanosomes have reappeared in the blood of four cases and another has relapsed clinically. The remaining 24 are all improved and all microscopical examinations are negative up to date of writing.

(a) *Deaths*.—Two only of the four deaths can be connected directly with the treatment. Both were advanced cases and had been given larger doses than usual. No. 2, a boy of 10 years, had 2 gr. on one occasion and 1½ gr. twice. He showed no symptoms till 48 hours after the last dose, when meteorism appeared accompanied by acute abdominal pain, and he died seven hours later. I have seen a somewhat similar death here in a case treated only with atoxyl.

No. 24 was also an advanced case; he took two injections of 1 gr. without discomfort and then had a dose of 2 gr. Twelve hours later epileptiform symptoms set in quite suddenly; the patient became unconscious and died six hours later.

Of the other two deaths—No. 7 was due to broncho-pneumonia; the patient was debilitated and broncho-pneumonia was very prevalent at that time. No. 47 died from an epileptiform attack, but had not had any form of treatment for a week.

(b) *Deserters*.—One, No. 38, had recently completed his course of treatment and had shown great improvement. The other, No. 3, belonged to a district 100 miles from Yei. He had been without treatment for five months and had done very well—taking large doses without untoward symptoms. All examinations had been negative, though repeated very frequently.

(c) *Relapses*.—No. 27 is a clinical relapse. He was a soldier and his

## Abstract of Cases Treated with Antimony only.\*

No.	Sex.	Age.	Glands.	Trypano- somes.	Treatment.	Present Condition.			General Condition.
						Blood and gland juice.	Glands.	Mental.	
1	F.	Adult	++	++	5 doses .....	—	Much smaller. Puncture ne- gative	Much improved	Much improved; better nourished.
2	M.	10	++	++	3 " (2 of 1½ gr., and 1 of 2 gr.)	—	Disappeared	Good	Died 18 days after commencement of treatment; a very advanced case. Deserted, as he lived 100 miles away.
3	M.	Adult	+	+	4 doses (1 to 3 gr.)	—	Disappeared	Good	Very much improved.
4	M.	"	++	++	3 " (1 gr.)	—	Just punctur- able	"	In very good condition. Has recently been confined of a living child, and is quite well.
5	F.	"	+	+	3 " (3 gr.)	—	Disappeared	"	Very susceptible to antimony. Remained in good condition for 5½ months, when he had a relapse.
6	M.	"	+	++	5 " (1 gr.)	—	Disappeared	Good	Old and debilitated; died of broncho- pneumonia, which was prevalent.
7	M.	"	++	++	3 " after relapse (1 gr.)	—	Disappeared	Good	Very good.
9	F.	"	++	++	5 " .....	—	"	"	Very good.
13	M.	"	+	+	5 " .....	—	"	"	Old; poor condition.
14	F.	"	++	++	3 " .....	—	Scarcely notice- able	"	Had oedema, which disappeared.
21	M.	"	++	++	5 " .....	—	Small and hard	Very good	Very good. Had tongue tremor, which disappeared.
22	M.	"	++	++	3 " .....	—	Much reduced	Good	Advanced case, in poor condition. Died with epileptiform seizure about 12 hours after 2-gr. dose.
24	M.	"	++	++	3 " (1 to 2 gr.)	—	"	Good	Very good. Tongue tremor disappeared.
25	M.	"	++	++	5 " .....	—	Only one small hard one left	Good	Improved.
26	F.	10	++	++	3 doses (½ gr.)	—	Much smaller	Much brighter	This case was verging on the third stage; for 3½ months there was great improve- ment, so that he could act as assistant. He has now oedema, and is "mental."
27	M.	Adult	++	++	3 " .....	—	Much less ...	"	Blood, glands, and cerebro-spinal fluid are negative.

28	M.	11	++	+	5 3 3 3 3 3 3 5+ 3	( $\frac{3}{4}$ gr.)	—	Small and hard	Very good	Was in poor condition, with oedema.
29	M.	Adult	++	+	3	.....	—	Nearly gone...	Good	Very good. Had bronchitis after first course.
30	M.	"	++	+	3	.....	—	"	"	Very good.
31	M.	"	++	++	3	.....	—	"	"	Had relapse two months after last dose. Trypanosomes appeared again in blood. Very sensitive to antimony.
33	M.	"	++	++	5 doses 3	.....	—	Only one perceptible	Good	Came in bad condition, and showed great improvement. Oedema and tongue tremor disappeared.
34	F.	"	+	+	5	.....	—	Quite soft ...	"	Much improved.
35	F.	"	++	++	3	.....	—	Not noticeable	"	Very good.
36	M.	"	+	+	3	.....	—	Much smaller	"	Improved.
37	M.	"	++	++	3	.....	—			Trypanosomes reappeared after two months.
38	M.	"	++	++	5 3 3	.....	—			Patient deserted six weeks after course of treatment in much improved condition.
40	F.	"	+	+	5	.....	—	Very small ...	Good	Very good.
41	F.	"	++	+	3	.....	—	Much smaller	"	Improved.
42	F.	"	++	++	5 3	.....	—			Trypanosomes reappeared after 2½ months.
45	M.	"	++	++	3	.....	—	Much smaller	Good	Good.
46	M.	"	+	+	5	.....	—	"	"	Came very thin; now much improved in condition.
47	M.	"	+	+	3 3	.....	—	"	"	An old emaciated man, in advanced stage. Died a week after last dose in an epileptiform attack, not apparently connected with the treatment.
48	M.	"	++	++	5	.....	—	Much smaller	Better	Had oedema, which disappeared. Slight improvement.
50	M.	"	++	++	3	.....	—	Small	Good	Good.
51	M.	"	+	++	5 3	.....	—	"	"	Toluidin blue, 1 gr., was given before first, third and fifth doses at suggestion of Dr. Balfour. Tongue tremor disappeared; much improved.

\* Too much importance should not be attached to the size of the glands or number of trypanosomes, as these factors do not give an accurate indication of the severity of the case.

† At intervals of one week.

condition on arrival at the Camp was alarming, and he was quite unable to walk. A full course of antimony, in doses of 1 gr., was successfully given and there was a great improvement in his condition. The large masses of glands were very greatly reduced in size. The tremor was unaffected, but he became much stronger. He was able to act as a "native assistant" in the laboratory and a "headman" in the camp. His improvement was maintained for three and a-half months, when suddenly he relapsed and became a third stage case. Blood examinations have been negative. The cerebro-spinal fluid was examined also and the cellular elements were increased, but trypanosomes were not found.

In four other cases trypanosomes have reappeared in the blood. Two of these were very susceptible to antimony and were unable to take doses at shorter intervals than a week. After the relapse attempts were made to give them another course of antimony, but it had to be given up owing to their unusual susceptibility to the drug. The other two had heavy infections, but did not seem to improve. They have all been transferred to atoxyl.

(d) The other 24 cases have shown improvement. In three it is slight and these are being kept under close observation. In some cases the improvement has been very striking; in others who were admitted in fairly good condition, it has not been so evident, but the whole appearance of the patients is different. After a course of antimony there is not uncommonly depression and debility. This, however, passes off in a few days; the patient becomes more active, feels and looks better, and loses the languor that is so often seen in patients just admitted. They put on weight and the skin becomes healthier; this is no doubt due in part to the regular feeding in the sleeping sickness camp, but the improvement would not occur were it not initiated by the treatment. In some cases the tongue tremor has disappeared under treatment. Probably some other cases will relapse, so these cases are being kept without further treatment at present, as it is desirable to test the effect of this treatment with antimony alone.

## II. *Antimony and Salvarsan.*

Ten cases have been treated with these two drugs, but a regular course has not been carried out; the salvarsan was given, in the majority of cases, when a patient was unable to take a complete course of antimony.

No information has been obtained as to the best line of treatment to be followed with this combination of drugs, but a further series has been commenced.

The results up to the present are: Eight out of the ten cases are very well and have shown definite improvement; one deserted, but was in very good

health and had been without treatment for four months. She was one of the few who had a complete course. The tenth case had one injection of salvarsan and was unable to take antimony on account of extreme susceptibility. Atoxyl was substituted, but the patient developed toxic symptoms. She is now having small doses of atoxyl, but is getting steadily worse.

The salvarsan has been given both as an intramuscular injection in olive oil, and by intravenous injection in alkaline solution.

### III. *Antimony and Atoxyl.*

The patients in this series have been treated as follows :—

- (1) Five doses of antimony 1 gr. at intervals of four days.
- (2) Atoxyl 5 gr. every three days for 40 days.
- (3) Three doses of antimony 1 gr. at intervals of four days.
- (4) Atoxyl 5 gr. every three days for one month.

There is no interval between these courses, so the patients have continuous treatment over a period of rather more than three months. An interval of a month is then given and atoxyl treatment is then continued, as a tonic and precautionary treatment.

Thirty-one patients have been treated; but three were unable to take the complete course of antimony.

This is the most recent series, and the three months' course has just been completed; it is too early to speak of results. At the time of writing all have done well; the improvement, in many instances, has been striking; some, however, were advanced cases, and it is not expected that the improvement can be maintained permanently.

### IV. *Old Atoxyl Cases, Treated with Short Courses of Antimony.*

After we had seen that intravenous injection of antimony was bringing about improvement in the newly admitted cases and could easily be carried out on a large scale, it was decided to give short courses of antimony to the old cases that had been under treatment with atoxyl, atoxylate of mercury, etc. The majority of the patients so treated have had two separate courses of three doses of antimony, 1 gr.

In some instances, patients have not had all these six doses on account of susceptibility, intercurrent affections, bronchitis, etc., but 813 injections have been given to 143 patients.

In this series there has been one death. The two fatal cases in the first series had doses which have been found to be inadvisable in advanced

cases. In this case only two injections of 1 gr. had been given. The patient was a man in good health; he showed slight depression after the first dose, but had quite recovered and was ready for a second dose four days later. He was sick after this and soon developed alarming symptoms, and died. There were no late effects in any of the other patients.

#### SYMPTOMS FOLLOWING THE INTRAVENOUS INJECTION OF ANTIMONY.

Antimony has a powerful depressant action and, as the preparation employed is very active, it is only to be expected that a course of treatment should cause the appearance of some symptoms. It has been found that some patients have a high degree of susceptibility to antimony, and they have suffered somewhat severely; also, at the beginning of this work, when attempts were being made to obtain some information as to the dosage, larger doses were given and the effects were, in some cases, more marked. With further experience symptoms of any degree of severity have become very rare.

The following are the symptoms which may be seen in patients who are not unusually susceptible:—

1. Fever: The “*réaction thermique*.”
2. Pulse: Is not much accelerated; but, so far as can be ascertained by digital examination, there is a fall in blood pressure.
3. Diuresis: There is variable diuresis.
4. Cough: This occurs in the majority of cases. It begins a few minutes after administration and lasts for 5 or 10 minutes. Very rarely it has persisted for 12 or 24 hours, but only in cases which have had slight bronchitis.
5. Pain in the xiphisternal region: This is a common occurrence and is most severe the day following an injection. It is probably of gastric origin.
6. Headache is not uncommon, but is not severe.

The following symptoms have only occurred in cases of great susceptibility to the drug:—

7. Sickness and vomiting: This has occurred six times; once it occurred in a fatal case (No. 32A).
8. Fainting: Only one case.
9. Meteorism: Was seen in one case (No. 2), which was fatal. Captain Thompson saw a similar case 18 months ago.
10. Herpes: There have been seven cases. In six it was seen on the face and lips, and in the seventh along the ribs. This condition is probably similar to the herpes that occurs in certain forms of arsenical poisoning.



11. Stomatitis: Two cases; one was vesicular, but the other was more severe and ulcerated. In both cases the lesions were limited to the anterior portion of the hard palate, and the condition may perhaps have been herpetic.

It is of interest to note that very similar symptoms were observed in experimental dogs treated in this manner.

Short mention must be made of the effect of antimony on the temperature and upon the leucocytes.

#### I. *Temperature.*

A "réaction thermique" has been described, occurring about 20 minutes after injection of salts of antimony. This subject may be of greater interest owing to the large amount of work done on the subject of salvarsan fever.

Temperatures have been taken in over 100 cases: (1) at short intervals on the day of an injection; and (2) morning and evening temperatures for three days after treatment.

There is no effect on the temperature till two or three hours after treatment, when it rises  $1^{\circ}$  F., and at four hours after treatment the average rise is  $1.4^{\circ}$  F. The same evening, 10 to 12 hours after treatment, some cases have fallen to normal, while others have gone up to over  $101^{\circ}$ . For the next two days there is an average evening temperature of  $100.2^{\circ}$  and  $99.7^{\circ}$ , and the temperature returns to normal. The results are identical in treated and untreated cases; trypanolysis and the disposal of dead trypanosomes do not, therefore, cause this rise of temperature.

The initial rise may be due to antimony, but the temperature for the two following days is probably due to the saline solution. With the apparatus available here it is impossible to get pure distilled water; it would be of interest if some injections could be given with water twice distilled in a good apparatus.

The temperature does not seem to have any effect on the general condition of the patients.

#### II. *Leucocytes.*

The action of leucocytes on this preparation has been described.\* Blood films, taken from animals after treatment, were stained and the leucocytes found to be crammed with the minute particles of antimony. They show a great avidity for this preparation, which they discharge, presumably in soluble form, into the blood-stream, the action being thus spread over a longer period.

A series of 200 leucocyte counts has been made to determine the effect of

\* 'Roy. Soc. Proc.,' B, vol. 83, p. 140.

treatment on the numbers of leucocytes. The cases selected were all under treatment, but some enumerations were made on untreated cases and the same changes observed.

Immediately after injection of antimony there is a considerable reduction of the leucocytes in the peripheral blood and in half an hour they have fallen to 60 per cent. of the number obtained on enumeration just before administration. In some cases the count is still lower an hour after the injection. From this point the leucocytes began to rise in number and in the majority of cases have returned in four or six hours to the level of the first count. This increase continues and 24 hours after treatment there is an average count of over 16,000; this is maintained for another 24 hours, but four days after treatment the numbers have fallen to approximately the original count. The estimations were continued over a series of three doses, and showed the same changes after each.

### III. *Action of Antimony on Trypanosomes.*

The exceedingly rapid action of the salts of antimony in man has been reported (4), but it was not anticipated that the metal would have an almost immediate trypanocidal action. Trypanosomes were never found in cases examined a few hours after treatment, so observations were made to determine the time required for an intravenous injection of antimony to clear the glands of trypanosomes. Only heavily infected cases were selected, a case being considered suitable if 10 trypanosomes were found in five minutes in the gland juice, but in many instances they were much more numerous, two and three trypanosomes being often seen in one field. The time was taken from the moment the antimony suspended in saline solution entered a vein in the arm, and at periods from 3 to 30 minutes after this time glands were punctured and wet preparations made. These were examined both by dark ground and ordinary illumination. In all cases 15 minutes was allowed for each film, and in many cases the search was prolonged up to 30 or 45 minutes.

*After 3 minutes* (slide made before the injection is completed).—Trypanosomes are still abundant; but some are already very obviously affected by the treatment. They show greatly exaggerated activity and dash rapidly across the field, so that they are difficult to keep in view. Frequently a trypanosome becomes anchored by the blunt end and lashes about most vigorously. This exaggerated motility soon passes into a state of fatigue, when the trypanosome wriggles more slowly and more and more feebly till movement ceases. Some retain their normal form, while others become swollen and bloated.

Occasionally a trypanosome comes rapidly to a standstill and dissolves away so that only a haze of protoplasm can be seen left behind.

*After 5 minutes.*—The exaggerated motility is not so frequently observed, but the trypanosomes are more often anchored and may be seen lashing about in an extreme state of activity. They appear to be somewhat reduced in number.

*After 7 minutes.*—Trypanosomes are more scanty. Exaggerated motility is not a feature of these preparations, but all the other changes occur as in the earlier preparations.

*After 10 and 15 minutes.*—In all preparations taken at these times a considerable search was required to find a trypanosome, but in the majority of cases one could be found in a search of 10 to 20 minutes.

*After 20 minutes.*—Very many preparations have been examined and have invariably proved negative.

An intravenous injection of antimony therefore kills the trypanosomes in the circulating blood in 20 minutes.

#### ON THE TREATMENT OF YAWS BY THE SAME METHOD.

Some cases of yaws have been met with in the course of this work.

In view of the successful results published by Strong, Castellani, and Alston, the first three cases were treated with salvarsan. One was given an intramuscular injection of 0.6 grm. in olive oil; the lesions—plantar ulcers—were healed in three weeks. The two others had an intravenous injection of 0.45 grm., they showed several small patches on the face and trunk and responded much more rapidly to intravenous treatment.

I had been much impressed with the rapid trypanocidal action of this metallic antimony, and decided to treat a case of yaws with this drug. At first doses of 1 gr. were given and the condition improved, but not very rapidly. With a larger dose the effect was much more striking; 1½ gr. seems to be quite efficient, but 2 gr. have been given to the last four cases. None of the 10 cases manifested the hyper-susceptibility to antimony that has been seen in sleeping sickness, and there have been no after effects.

In an adult of fair condition 1 gr. should be given as a first dose, and doses of 1½ gr. or 2 gr. repeated twice with intervals of four days. I have sometimes shortened the interval by one day. Three doses, I believe, is a quite sufficient course of treatment, but in the majority of our cases a fourth dose has been given to ensure, as far as possible, a permanent result, as most of these cases have been collected from different villages and pass out of observation when they are discharged from hospital. The antimony is administered as described above (p. 204) for trypanosomiasis.

The following short notes give an abstract of the cases:—

1. Lesions small, but generally distributed with septic or impetiginous patches in the beard. Four doses of antimony were given—two of 1 gr. and two of  $1\frac{1}{2}$  gr. Lesions were all healed in 12 days.
2. Lesions general and larger than in preceding case. Treatment, four doses of  $1\frac{1}{2}$  gr. All lesions healed in 11 days.
3. Extensive ulceration of scrotum. The ulcers had moist surfaces and an exceedingly offensive discharge. Treatment, four doses of  $1\frac{1}{2}$  gr. All healed in 11 days.
4. A large crusted patch on perineum and several small lesions on face. Treatment in four doses of  $1\frac{1}{2}$  gr. Healed in 10 days.
5. Extensive ulceration on soles of feet. Treatment four doses of  $1\frac{1}{2}$  gr.; local treatment, perchloride of mercury 1/1000 as a lotion. Quite healed in 14 days.
6. Discharging ulcers between toes. Treatment, four doses of  $1\frac{1}{2}$  gr. Healed in 14 days.
7. Generalised eruption. There were large confluent patches all over the face, trunk, perineum, and limbs. There was also a large primary ulcer on the scrotum 3 inches in diameter, with very foul discharge. The patient was debilitated, and three doses of 1 gr. were given. There was some improvement, but it was very slow, so a dose of 2 gr. was given, and all the lesions were completely healed in six days, except the ulcer, which was reduced to less than 1 inch in diameter.
8. Some patches on the face with thick raised limpet crusts, and many small lesions on the scrotum, perineum, and buttocks, with moist discharging surfaces. Treatment, one dose of  $1\frac{1}{2}$  gr., followed by two doses of 2 gr. and a fourth of  $1\frac{1}{2}$  gr. All healed in 10 days.
9. Small patches on scrotum, penis, and perineum. Treatment, one dose of  $1\frac{1}{2}$  gr. and two of 2 gr. All healed in 10 days.
10. Small patches on scrotum, penis, perineum, and axillæ. Treatment, one dose of  $1\frac{1}{2}$  gr. and two of 2 gr. All lesions healed in 11 days.

In all cases the lesions were characteristic of the various stages of yaws, from minute vesico-pustules up to confluent, crusted lesions, rupioid patches with limpet-shell crusts, or late plantar-ulcers.

The diagnosis was confirmed in the earlier cases by examination of scrapings from the deeper parts of the lesions. Films were examined by dark ground illumination and spirochaetes were found, sometimes in large numbers.

After the first dose the discharging ulcers showed signs of drying up and they skinned over rapidly. In 48 hours a distinct improvement was seen; the crusted lesions had shrunk somewhat and no longer contained fluid. The yellow colour disappeared and was replaced by a pearly grey; the underlying raw surface healed very quickly, and soon there was only a desquamating flake representing the site of the lesion. Accompanying the local changes there was improvement in the patient's general condition.

The number of cases treated is small, but they have been uniformly successful. The treatment can easily be carried out on a large scale, and it may be possible to cure large numbers of persons affected with this most unsightly, and hitherto long-enduring disease, without causing too

great a drain on the funds allotted to medical work in these colonies, etc., where this condition is prevalent.

This preparation of antimony was tried successfully in a few cases of syphilis\* by intramuscular injection, but the pain was so severe that the method was not continued. I venture to suggest that, as intravenous injection of the metal has proved feasible, a further trial may be warranted in this other spirochætal disease so closely allied to yaws.

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*The Liberation of Ions and the Oxygen Tension of Tissues during Activity.* (Preliminary Communication.)

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The hypothesis, that when cells become active ions are liberated, is frequently quoted in physiological writings, but measurements of the ionic changes are not given. The present research is an attempt to measure the ionic changes during tissue activity. A knowledge of these changes is desirable in order to compare the action of ions on colloids outside the cells with the changes that occur inside the cells.

On turning to the physiological literature one finds that little or nothing is given in the way of measurement of the ionic concentrations with which biology has to deal. Thus, neither the recent work on electrobiology by\* Bernstein,† nor that on the hydrogen ion in biological processes by Sorensen‡ contains any reference to the measurements of ions in tissues during rest or activity. Galeotti has, however, measured the hydrogen ion in heart muscle.§

*Method.*

The method used in the present series of experiments was to prepare a frog's sartorius muscle and arrange it for direct stimulation from an induction coil. A high resistance reflecting galvanometer was used and the muscle was tetanised. The muscle was tested with non-polarisable (Ringer solution, calomel) electrodes. Two of these were placed to touch the muscle directly

\* 'Roy. Soc. Proc.,' B, vol. 80, p. 481.

† J. Bernstein, 'Electrobiologie' (Braunschweig, Vieweg und Sohn), 1912.

‡ S. P. L. Sorensen, 'Ergebnisse der Physiologie,' 1912, vol. 12, pp. 393-532.

§ G. Galeotti, 'Archivio di Fisiologia,' 1904, vol. 1, p. 512; 'Zeits. f. Allge. Physiol.,' 1906, vol. 6, p. 99.