three-fifths of the full dose may be required. In all cases ten days must be allowed to elapse after the primary four-fifths B dose has been administered. If this precaution is rigorously adhered to there is no risk of overdosage. The appearance of an erythema is the signal for cessation of x -ray application to that particular area; the final effect of the treatment cannot be accurately gauged until all reaction has passed away. A cure can be anticipated in the majority of the cases in which it has occurred; for slight and invisible cutaneous atrophy, in which the sebaceous glands particularly are implicated, will ensue. It is again emphasized that the atrophy of the sebaceous gland is neither physiologically desirable nor a factor in the treatment. Inhibition of an excessive activity is all that is required to cause involution of the comedo. In every case of facial acne treated by x rays the eyebrows, eyelashes, and mucous membranes must be effectively protected by strips of malleable lead foil, which can be fixed *in situ* by rubber strapping.

In stage (2), when pustulation and dermatitis are marked, an effort should first be made to allay them by the application of mild antiseptic and detergent lotions of lead, calamine, or mercury oxycyanide (1 in 4,000). A few days later the areas can be treated by x rays. Two-fifths of the B tint can be given at intervals of ten days, and repeated as found necessary. "Erythema reaction" should be carefully avoided in the pustular stage.

While there are conceivable alternatives to radiotherapy in (1) and (2), the presence of intradermic and subdermic nodules and cold abscesses, periglandular fibrosis, and keloidal tissue (stage 3) is a direct indication for x -ray treatment, for by no other agency can their involution be permanently achieved. The deeper situation of all these lesions calls naturally for the use of harder or more penetrating rays. These can be obtained in two ways: either (a) by the use of a "hard" tube, with a spark-gap working at a distance of 5 to 6 in., or by (b) interposing a screen of sheet aluminium, which cuts out the soft erythema-producing rays altogether. The filter should have a thickness of 0.5 mm., and with this in position a full pastille dose (tint B) may be given at the first session without risk. (The pastille holder must be used on the proximal side of the screen.) Considerable improvement will usually be noticed in ten days or a fortnight, and filtered half-pastille doses may be repeated at this interval until involution is complete. The use of a filter will prevent or delay the development of erythema reaction, and in most cases a satisfactory result will have been obtained before this develops.

Local relapse after efficient treatment by x rays has, in my experience, rarely occurred. A case I treated in 1913 will suffice to illustrate the contention. The patient, an unmarried lady of 26, had suffered from the deep nodular variety with recurrent suppuration and hypertrophic cicatrization for many years in spite of vaccine treatment, local applications, ultra-violet rays, and yearly visits to a sulphur spa. The case was undertaken with considerable trepidation, as at that time my experience was not extensive. During the seven years which have since elapsed there has been no recurrence, nor is there now the slightest suggestion of cutaneous atrophy, although, as a result of treatment, the patient developed temporary erythema at the time.

X-ray Stigmata.

The ill effects produced by overdosage of x rays are well known, and may be either permanent or temporary.

An x -ray burn is a serious disability; it can be caused only by massive or repeated and uncontrolled doses of x rays. In the most intractable cases painful ulcers may develop. More usually there is parchment-like atrophy of the skin, pigmentation, and minute vascular stigmata (telangiectases), with permanent, partial, or total destruction of hair follicles. Such appearances are still occasionally the result of inaccurate dosage in epilation treatment for tinea of the scalp and chronic sycosis barbae, and more excusably after massive doses for lupus vulgaris and epithelioma. Modern refinements, however, have rendered the accident relatively uncommon, even in cases in which massive doses are essential. If the rules insisted on for acne cases are rigorously followed such accidents will not occur in the treatment of this disease. It is therefore with

the results of mild irradiation only that we are concerned. These are temporary, as a rule, and consist, as far as evident at all, of disturbances in the physiological distribution of pigment. As might be expected, blonde individuals are more susceptible in this respect than dark, and these should always be warned in advance of the possibility of the temporary appearance of "freckles" as a result of the x rays. In no case do they result in anything approaching the acne nodule or pustule in degree of disfigurement, and in a few weeks they vanish. The only treatment called for is the occasional application of calamine lotion, which is also useful in cases which develop erythema reaction. Grease in any form is never well tolerated, and ointments should therefore not be prescribed for patients undergoing radiotherapy.

CONCLUSIONS.

1. Acne vulgaris in its early stages can be relieved by vaccines and the application of lotions and ointments containing sulphur, resorcin, or mercury.
2. As far as the author knows, cure can only be attained by the judicious application of x rays.
3. The nodular and keloidal varieties of the disease are not amenable to relief or cure by any other method.
4. Relapse after apparent cure by x rays is rare. Should it arise it can be dealt with by further irradiation.
5. There are no permanent contraindications to the treatment by x rays.
6. Temporary cosmetic stigmata are sometimes met with, especially in blonde subjects; but permanent disfigurement of any kind is the result of faulty technique.

TREATMENT OF SLEEPING SICKNESS BY SALVARSANIZED SERUM.

BY

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THE history of the treatment of sleeping sickness in the past has been one of optimistic hopes resulting in failure, as each new method tried has been found to be nearly the cure, yet to have just fallen short of success. This applies more especially to African patients, for while certain Europeans and Asiatics have been undoubtedly cured of the disease, no such success has followed the treatment of natives. The reason may be that the African native is seldom seen in the very early stages, and being also more susceptible to the poisonous effects of the arsenic preparations used, is unable to stand the large doses employed to kill the trypanosome in the cases of non-natives.

For nearly a year after its introduction atoxyl was hailed as a definite remedy, only to prove not quite successful, while more recently Drs. Rodhain and Broden in the Congo have shown that salvarsan produces great improvement in early cases, although they do not claim it to be a cure, and definitely state that it is of little value if the trypanosome can be found in the cerebro-spinal fluid (Manson).

Quite early in the disease the trypanosome appears to gain an impregnable position in the central nervous system, and when attacked by drugs which drive it from the blood stream, remains undefeated in the spinal cord, in the same way as syphilis, which in the early stages is easily cured, but once it has established itself in the central nervous system complete cure is more problematical.

It would appear therefore that if sleeping sickness is to be cured, except in the earliest stages, the trypanosome must be attacked in the spinal cord, as well as in the blood stream. With this idea I commenced treating cases by intraspinal injections of neo-kharsivan; unfortunately the first case so treated died as a result of the injection.

Case I.—W., a man aged about 40 years, was examined on September 26th, 1918. The glands were small, but typical. Trypanosomes were present in the gland juice. An intravenous injection of 0.6 gram neo-kharsivan was given on September 27th, and on October 1st an intraspinal injection of 0.025 gram neo-kharsivan, after 10 c.cm. of cerebro-spinal fluid had been drawn off. The patient died on the following day.

Though doubtless this method will not necessarily cause death, I decided to employ neo-kharsivanized serum for future injections into the spinal cord instead of the drug itself.

The patients treated were divided roughly into five classes according to the stage of the disease, as follows:

CLASS A.—Early cases with distinct glands, the juice of which contains scanty trypanosomes, but with no other signs. The patients consider themselves quite well, and are only discovered by systematic examination of a large number of natives.

CLASS AB.—The glands are well marked and contain numerous trypanosomes. The patients do not feel well, and complain of pains and sleeplessness.

CLASS B.—In addition to above signs there are finger and tongue tremors, increased knee-jerks, headache, and pain in the limbs. Impotent.

CLASS BB.—Advanced cases, unintelligent, spastic, and uncertain gait.

CLASS C.—Almost comatose. Unable to walk or reply to questions.

With this classification it is suggested that the central nervous system has been invaded in the AB class, though it is possible that this may occur even earlier.

Method.

1. An intravenous injection of neo-kharsivan is given, and after one to two hours 10 c.cm. to 40 c.cm. of blood are drawn off from a vein into a sterile vessel.
2. The vessel containing the blood is kept cool by being placed in a beaker of cold water for from twelve to sixteen hours, by which time the clear serum has separated from the blood clot.
3. A lumbar puncture is performed, and 15 c.cm. to 20 c.cm. of cerebro-spinal fluid drawn off, and a corresponding quantity of the serum, obtained as above, slowly injected into the spinal cord through the lumbar puncture needle by means of a large all-glass syringe.

This method has been used in a series of 12 selected cases, with the results tabulated below. Several patients have only been observed a short time since the treatment; the longest period of observation has been sixteen months.

While no absolutely definite results can be looked for till several years have elapsed after the patient has been treated, it must be borne in mind that these cases have only had one injection of the serum and were then sent back to their homes without further treatment of any kind, except in one case, No. 9, to whom two injections of serum were given.

Two cases are recorded in detail, and the others are shown in the table.

Case 2.—A woman, aged about 30, Class AB, was examined on September 9th, 1918. There was a large typical chain of glands in the neck and trypanosomes were present in the gland juice. On October 1st an intravenous injection of 0.6 gram of neo-kharsivan was given; 2 oz. of blood were drawn off after three hours. Twenty minims of serum were injected into the spinal cord next day. On December 14th, 1918, the glands at re-examination were found to be few and pea-like. One cubic centimetre of the patient's blood was injected into a monkey, which on December 24th escaped and was not recaptured. On the 30th the glands were as before and another monkey was inoculated. On February 8th, 1919, this animal was well; as I left the station on four it was not seen again, but I understand it remained perfectly well until it escaped some time later. The patient was re-examined on May 29th and September 2nd, 1919, when she was quite well and the glands were very small. A monkey inoculated on the latter date was quite well at three subsequent examinations (the last on January 7th, 1920). The patient was last seen on November 29th, 1919, when she was quite well; two pea-like glands were present, the juice of which contained no trypanosomes.

Case 4.—A woman, aged 27, Class AB, had one large soft gland in the neck on January 9th, 1919; trypanosomes were present in the juice. On January 10th, 1919, 0.6 gram of neo-kharsivan was injected into a vein, 40 c.cm. of blood being drawn off. Intraspinal injection of 20 c.cm. of serum was performed next day. At her next examination, on September 2nd, 1919, no glands were palpable, and inoculation of 2 c.cm. of blood was made into a sheep, which was found quite well on October 30th, 1919, and January 7th, 1920. At subsequent re-examinations on November 12th, 1919, and January 7th, 1920, the patient was well and her glands were not palpable.

Note.—This woman disappeared during the severe famine in the early part of 1919, and was not seen for nearly nine months.

These two cases had only one injection and no other treatment. After sixteen and twelve months respectively they show no signs of relapse, declare themselves to be perfectly well, and are certainly in better health than when they first came under treatment.

Table showing Twelve Cases Treated.

No. of Case.	Sex.	Class.	Dose of Serum.	Months since Treatment.	Result.
2	F.	A B	20 min.	16	Well.
3	M.	A	3 c.cm.	1	Disappeared.
4	F.	A B	20 c.cm.	12	Well.
5	F.	A B	8 c.cm.	1	Died (cause unknown).
7	M.	B	15 c.cm.	6	Well.
8	F.	B	15 c.cm.	4	Well.
9	M.	C	20 c.cm.	1½	Died.
10	M.	B B	15 c.cm.	2½	Improved.
11	M.	B	21 c.cm.	1½	Well.
12	F.	A B	7 c.cm.	1½	Well.
13	F.	B	20 c.cm.	1½	Well.
15	F.	A B	24 c.cm.	1½	Well.

Of the cases quoted above, Case 3 showed no signs of relapse when last seen, but he was lost trace of during the famine, and is said to have died of hunger and dysentery in April or May.

Case 5 was treated on July 11th, 1919, and showed considerable improvement. She died suddenly on August 18th, 1919, from some unknown cause. I did not see her as I was away on tour, but I understand that she was well and working on the cultivation in the morning, but was found dead in her hut next day. There appears to be no reason to suppose that her death was due either to sleeping sickness or to the serum injection.

Case 9 was very advanced; on admission he could not give his name and was unable to walk, and could only stand with difficulty. This patient was a man, aged about 22, Class C; he was examined on September 25th, 1919. A very large chain of typical glands was found on both sides of the neck, and the gland juice contained numerous trypanosomes. Trypanosomes were also found in the blood but not in the cerebro-spinal fluid. Next day 0.6 gram of neo-kharsivan were injected intravenously. On the 27th an intraspinal injection was made of 20 c.cm. of serum, and on the 29th he appeared better. On October 12th he was much improved and more intelligent; the glands were harder and smaller and their juice contained no trypanosomes. The same observation was made two days later. On October 16th 0.6 gram of neo-kharsivan were given; this was repeated on November 1st, on which date no trypanosomes were found in either the blood or the gland juice. Next day 22 c.cm. of serum were injected intraspinal, and no trypanosomes were found in the cerebro-spinal fluid, of which 3 c.cm. were injected into a dog. The patient died on November 3rd; on January 7th, 1920, the dog was well.

It appears quite possible that this man died from the effects of treatment, but at the same time the disease was so far advanced that even supposing the trypanosomes in his system had been killed their effect prior to treatment might still have caused death. It is interesting to note that there was no rise in temperature above normal after the first injection.

In order to confirm the experiments of Drs. Rodhain and Broden, as well as the one or two similar cases which have occurred in Uganda, I quote the following cases to show that the improvement noted in the patients tabulated above is not due to the injections of neo-kharsivan alone:

Case 6.—A large dog was brought to me suffering from keratitis, and on examination its blood was found to be swarming with trypanosomes of the *gambiense-brucei* type (Duke). On July 11th, 1919, it received an intravenous injection of 0.3 gram of neo-kharsivan; on the 13th it was much improved, the eye symptoms being better and the dog eating well. On the 22nd the trypanosomes returned to the blood, and on August 1st the animal was very ill, and refused all food; 0.4 gram of arsenophenyglycin was given intravenously, and three days afterwards no trypanosomes could be found in the blood. They returned, however, on the 14th, and on the 26th the animal, which was blind and refused food, was shot.

Case 7.—M., a man of about 30, Class B, had a few small glands with trypanosomes in the juice when first examined on June 1st, 1919. He disappeared for a month, but when he returned similar findings were observed (July 1st). On the 10th, 0.6 gram of neo-kharsivan was injected intravenously, but no serum was given. On the 27th the glands were small and hard, and trypanosomes could not be found in the juice; 20 minims of cerebro-spinal fluid, containing no trypanosomes, were withdrawn by lumbar puncture on September 29th, and injected into a monkey. On October 25th the patient was greatly improved, and stated he could do work of which he was not previously capable. All glands but one (very small and hard) had disappeared. The monkey was quite well. Three days later trypanosomes were found after prolonged search in the

centrifuged deposit from the man's cerebro-spinal fluid, 3 c.cm. of which were injected into a sheep. Next day 0.6 gram of neo-kharsivan was injected intravenously, and 15 c.cm. of serum were given intraspinally. On January 7th, 1920, the patient, the monkey, and the sheep were found to be quite well.

In these cases the patients made undoubted progress under neo-kharsivan alone, but in neither case was the disease cured.

The fact that the cerebro-spinal fluid in Case 7 showed no trypanosomes on first examination, and that both the sub-inoculated animals remain well, I am unable to explain except as due to faulty technique.

In conclusion, I would suggest that these experiments tend to show:

1. That intra-spinal medication causes improvement in the patient, and may prove to be a complete cure.
2. That it has a greater beneficial effect than intravenous injections alone.
3. That in advanced cases, even if the actual disease is arrested, the damage already done to the central nervous system is probably beyond repair.

I wish to express my thanks to Dr. C. A. Wiggins, Principal Medical Officer, Uganda Protectorate, for permission to publish these notes.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

A CASE OF ENCEPHALITIS: LETHARGY AND MYOCLONUS.

A STEEL dresser in a shipyard was admitted to the Royal Victoria Hospital, Belfast, under the care of Dr. William Calwell, on April 26th.

He had been a soldier for eleven years (one year in Africa, no illness; six years in India, enteric; four years in France, influenza, 1916). On April 2nd he felt ill, complaining of headache and double vision and pain and stiffness of the neck and right shoulder; the following day his right eyelid dropped and he developed a double internal squint. About a week later the muscles of the neck and right side of the face were twitching.

He was admitted in a drowsy condition; temperature 99.4°, pulse 84, systolic blood pressure 130; urine, heart, and lungs normal. He lay indifferent to his surroundings, and would only answer questions if vigorously roused, when he was, however, quite intelligent, though slow of cerebration. When the stimulus of the raised voice was withdrawn he sank back into lethargy. Although lethargic he did not sleep at night.

There were striking myoclonic movements of the face and neck; the twitchings, rhythmical, at the rate of 60 a minute, involved the levator anguli oris, the masseter, the temporalis, the sterno-mastoid, and the upper part of the trapezius of the left side. The diaphragm was not involved. The sphincters were normal; the knee-jerks were brisk; there was no ankle clonus; the abdominal and epigastric reflexes were absent. The pupils responded to light, but not to accommodation. There was ptosis of the right eyelid (N.3), double internal strabismus (N.6), and inability to close the left eyelid (N.7). The discs were normal.

The cerebro spinal fluid was clear under pressure, and the cell count under 10. The Wassermann reaction, blood and cerebro-spinal fluid, was negative.

On May 14th the patient's condition was unchanged except that there was a slight decrease in the lethargy and abatement of the ocular symptoms.

The case is therefore hybrid between lethargic and myoclonic encephalitis. It conforms to the lethargic syndrome with the dominant exception of the myoclonus.

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A BUST has recently been erected by the Faculty of Medicine and Pharmacy of Lille to commemorate Joseph Willot, a Roubaix chemist, who by the publication of a journal known as *L'Oiseau de France* did much to keep up the courage of the population of Northern France during the German occupation, and subsequently died during imprisonment in Germany.

Reports of Societies.

TREATMENT OF TUBERCULOSIS.

At a meeting of the Medico-Chirurgical Society of Edinburgh, held on May 5th, with Emeritus Professor F. M. CAIRD in the chair, Professor Sir ROBERT PHILIP opened a discussion on the treatment of tuberculosis. He showed how the Hippocratic conception of the disease was a terminal phenomenon, and explained the modern outlook on the subject by which all efforts were directed to the early recognition of bacillary infection. He outlined the essential facts as to invasion of the organism, tissue reaction and systemic intoxication, drawing an analogy between tuberculosis and syphilis. He urged a broad outlook in dealing with a general disease with local manifestations. In the past too much had been made of the local phenomena in the various organs without taking sufficient notice of the systemic disturbances, these latter being very frequently in advance of the local signs. The value of the various special diagnostic tests was briefly reviewed. He then dealt with the advances that had been made in the recognition of the tractability of the disease if taken in hand sufficiently early and sufficiently firmly. He urged strongly the importance of keeping the patient under surveillance once the disease had been definitely determined. Tuberculosis took a long time to come and a long time to go, even with the best results. Once the patient was tuberculinized there was always the risk of further spread in acute or chronic form. So-called "fresh outbreaks" were simply caused by further spread in an already infected individual. He showed from the Registrar-General's returns the very steady decline in the mortality, although there was an increase in the cases coming for diagnosis and advice. He also reminded his audience how the age of death had gradually been postponed, as shown by the mortality tables. Finally, he urged the need for continuous intensive observations, both clinical and experimental, with a fuller training of men on the modern lines. There was ample reason for sound optimism.

Sir HENRY J. GAUVAIN dealt with the conservative as opposed to the radical treatment of non-pulmonary tuberculosis. He pointed out that tuberculosis was a general disease with local manifestations, and the aim of conservative treatment was to make use of every means in our power to assist in the formation of Nature's fibrous barriers. Conservative treatment was not to be confounded with convalescent treatment. He considered his lines of treatment under four main headings:

1. General treatment, which included (a) climate; (b) hygiene; (c) occupation, on which he laid considerable stress, and told how he had five educational establishments, at Alton, beginning with a nursery school and going on in stages to continuation classes for cripples; (d) dietetic; (e) specific, including drugs.
2. Local treatment. This included orthopaedic and other measures designed to secure local rest and prevention and correction of deformity. He explained the vital importance of minute attention to detail in carrying out these procedures.
3. Adjuvant methods of treatment, including (a) heliotherapy, which was used by gradual increasing exposure to the sun—he found those who did not take on pigment readily did badly; (b) x rays; (c) vaccine-therapy; (d) chemio-therapy; and (e) surgery.
4. Treatment of complications. He gave in detail the gradual change which had taken place in our views as to the treatment of tuberculous abscesses.

Finally, figures were given to show the results obtained by the conservative method as practised at Alton, and he explained how a considerable length of time was required to attain satisfactory results.

Professor GULLAND, in thanking Sir Robert Philip and Sir Henry Gauvain, mentioned the importance of the time factor and good will of the patient in treatment.

Mr. JOHN FRASER, from his study of the pathology of bone and joint tuberculosis, declared himself a strong believer in conservative methods of treatment, but urged that certain conditions made operation necessary—namely, (1) social conditions, (2) age of the patient, (3) in bone tubercle, when the disease was near a joint, removal of disease would save the joint.

Dr. IAN STRUTHERS STEWART spoke of sanatorium difficulties. He found the question of occupation of his patients of vital importance, as the tendency to staleness