A NOTE

ON SODIUM MORRHUATE IN TUBERCULOSIS.

BY

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TUBERCULOSIS is the greatest medical problem of the day, being one of the most frequent causes of sickness and death in tropical as well as temperate climates. If anything like a cure for this disease could be discovered, the losses of the great war would be replaced within a very few decades. During the last year I have been working at a new line of treatment of tuberculosis on similar lines to that which has proved of great value in my hands in the case of the other human disease produced by an acid-fast bacillus, namely, leprosy. By a similar process to that by which sodium gynocardate is made from chaulmoogra oil a preparation has been made of the sodium salts of the unsaturated fatty acids of cod-liver oil after extraction by ether. This I have termed "sodium morrhuate." A 3 per cent. watery solution is sterilized in an autoclave and $\frac{1}{2}$ per cent. carbolic acid added. This may be injected subcutaneously with very little pain, and also intravenously. I had previously shown in 1916¹ that intravenous injections of sodium gynocardate in leprosy produced febrile and local reactions with breaking down of the bacilli and had suggested its trial in tuberculosis as that disease is also produced by an acid-fast bacillus. As, however, in rare cases of leprosy prolonged febrile reactions with temporary exacerbation of the disease may follow sodium gynocardate given intravenously,² I hesitated to use it in tuberculosis by that method. Given by the mouth in phthisis some gain in weight only resulted, and it causes painful local induration hypodermically. Several attempts I made to investigate the use of the drug in tubercle infected animals failed for want of a virulent bovine culture. It was in these circumstances that I was led to prepare sodium morrhuate from cod-liver oil. Its subcutaneous injection proved to be nearly painless, and a year's experience has shown it to be of great value in leprosy. This is a most important point, as it proves that there is nothing absolutely specific in the products of chaulmoogra oil in that disease, and supports my view that the sodium salts of the unsaturated fatty acids of these two oils act in some way on the coating of the acid-fast bacilli, that of tuberculosis having been shown to contain palmitic and other unsaturated fatty acids. During the past year sodium morrhuate has also been used with very promising results in tuberculosis having been shown to contain palmitic and other unsaturated fatty acids. During the past year sodium morrhuate has also been used with very promising results in tuberculosis having been shown to contain palmitic and other unsaturated fatty acids. During the past year sodium morrhuate has also been used with very promising results in tuberculosis having been shown to contain palmitic and other unsaturated fatty acids.

Sodium morrhuate has now been under trial for a year, and from my own limited experience and the more extensive experience of Dr. E. Muir, M.D., F.R.C.S.E., of the Kulna Mission Hospital in the unhealthy Burdwan district of Bengal; of Captain R. Knowles, I.M.S., director of the Pasteur Institute, Shillong; of Dr. Caleb Davies, M.B., Ch.B., in Eastern Bengal, and of Lieut.-Colonel A. W. R. Cochrane, M.B., F.R.C.S., I.M.S., of the Bhowali Sanitarium, Kumaon Hills, to all of whom I am greatly indebted for trying the new treatment. I am satisfied that it is harmless. The three first named observers are convinced of its great value, although the last, with a shorter experience, is not satisfied that it has produced any permanent effects either for good or evil. Their reports will be published in full, together with my own more limited experience, in an early number of the *Indian Journal of Medical Research*, with details of the method of preparation, which is essentially the same as that of making sodium gynocardate already recorded.³ Limits of space will only allow of a brief summary of the results so

far obtained being recorded here to enable others to give the method a trial.

Dosage and Reactions.

In a case of old-standing lupus of the face, kindly sent to me by Miss Webb, of the Calcutta Dufferin Hospital, intravenous injections of sodium morrhuate produced a slight febrile and a definite local congestive reaction, similar to those obtained in leprosy. In phthisis similar febrile reactions occur, while occasionally there may be slight haemoptysis, indicating a local reaction in the affected lung tissue, which clearly point to a definite action on the tuberculous lesions. No harm has followed such reactions; frequently the temperature and other symptoms have improved decidedly after them. Their occurrence indicates the necessity for the precaution of increasing the doses very gradually. I usually begin with $\frac{1}{2}$ c.cm. of the 3 per cent. solution, and increase by 2 to 4 minims at each injection, which may be given two or three times a week until any reaction occurs; then a week's interval is left and the dose reduced. The injections are given subcutaneously until they reach an inconvenient size, such as 2 c.cm., when intravenous injections can be begun with $\frac{1}{2}$ c.cm., gradually increased in the same way as with the subcutaneous ones. Dr. Muir finds he gets the best results by pushing the dose until a febrile reaction occurs and then returning to a small dose and gradually increasing it again. In febrile cases the doses should be smaller and more slowly increased than in afebrile ones. He has gone up to 4 c.cm. intravenously two or three times a week.

Progress.

Improvement in phthisical cases is seen in reduction and cessation of the fever, diminution of the expectoration and cough, and steady gain in weight, the last being a very marked and satisfactory feature. In addition, the tubercle bacilli in the sputum greatly decrease in numbers, and may in time disappear. Moreover, they commonly show deficient acid staining and a granular or beaded appearance, indicating that they are actually being destroyed within the tissues. Captain Knowles has especially observed these changes, while Dr. Muir and I have also noticed them.

For example, the first phthisical patient I treated had extensive breaking down of the right apex, fever, profuse expectoration, and most distressing cough preventing sleep. When a 1 c.cm. dose was reached she had a reactionary rise of temperature, followed by a normal temperature for a week, and only a few rises to 100° F. later. The sputum and cough gradually subsided and she gained 10 lb. in weight in two months. Seven months later she wrote that she was keeping well in spite of having passed through an attack of influenza.

Another remarkable case was a missionary, sent to me by Dr. Caleb Davies, with slight affection of the right apex and early tuberculous epididymitis, both of which cleared up after twelve injections of sodium morrhuate. A patient with tuberculous disease of the knee put on 9½ lb. in four months and improved in his general health while having the injections, but of course he also had rest in bed with splints, and no conclusions can be drawn from a single case of joint tuberculosis.

Clinical Reports.

As my opportunities for clinical trials are necessarily very limited, the following abstracts from the reports which have reached me from reliable clinical workers are of more importance than my small experience.

Dr. Muir has had a year's experience of the new treatment and he reports that he is strongly convinced of the great usefulness of the drug. He has noted increased expectoration accompanying a febrile reaction and advises measuring the sputum in graduated bottles and taking the temperature frequently to detect slight reactions. In phthisis he considers the results to be far superior to those produced by tuberculin, and although he does not yet claim any cures, he thinks the results "are sufficiently encouraging to lead to the hope that the cases under treatment will be finally cured." His previous experience at Kulna makes him regard the climate there as exceedingly inimical to tubercle, so that spontaneous improvement can be eliminated, yet in all but the most

*Sodium morrhuate is being manufactured by Messrs. Smith Stanistreet and Co., Calcutta. Their London agents are Messrs. Evans, Son, Lescher, and Webb, Ltd., 60, Bartholomew Close, London, and of 92, William Street, New York.

advanced cases improvement was obtained under sodium morrhuate, and he thinks that even more favourable results might be obtained under better climatic conditions. In pulmonary phthisis he summarizes his results thus:

(a) Rapid diminution in the amount of the sputum in lung cases. (b) Rapid putting on of flesh and weight. (c) Diminution in the fever in febrile cases. (d) Increase in weight and strength. (e) Diminution in the number of the tubercle bacilli in the sputum.

In gland cases he noted reactions in the form of fever and local swelling, followed by very marked and rapid improvement, matted glands becoming discrete, and later all but disappearing.

Captain Knowles has also had nearly a year's experience of the treatment, and records valuable detailed accounts of his cases. He concludes as follows:

I am not yet satisfied that the drug is a specific cure for tuberculosis. I am, however, certain that it is at present the best line of treatment for tuberculosis in general. Tuberculin in unskilled hands is about as dangerous as prussic acid.

He regards

The marked increase in weight as the outstanding feature of the series; along with this, very often, goes a persistently normal temperature. The general health of the patient often shows a marked improvement. For early cases the treatment is an admirable one.

His first case was a serious one, with fever, cavitation, night sweats, repeated haemoptysis, paroxysmal cough, and sputum loaded with tubercle bacilli. This patient improved rapidly, and his sputum is now free from tubercle bacilli, while he has done full work for six months past. Captain Knowles also reports several earlier cases with very favourable results, and apparent cure in some. He has used comparatively small doses every fourth or fifth day, and has aimed at avoiding anything in the way of a severe reaction. In two of the cases clearing up of physical signs in the lung was demonstrated by means of x-ray observations before and after the course of injections.

Major C. Brierley, I.M.S., civil surgeon of Peshawar, has also kindly reported to me the two following remarkable cases. The first was a man with advanced phthisis, who was treated with 2 c.cm. doses of a 3 per cent. solution of sodium morrhuate intramuscularly three times a week for two weeks, and 2 c.cm. sodium gynecardate intravenously once a week for the next fortnight owing to sodium morrhuate running short, after which sodium morrhuate was again used. During the first week he was worse with high fever and increased expectoration—a severe reaction, after which he rapidly improved, and at the end of a month had gained 8 lb. in weight. At the end of six weeks no expectoration could be obtained, and he had gained 12 lb. during the last three weeks.

The second case was a boy of 15 with apical phthisis, very extensive breaking down of glands in the neck with numerous sinuses, which had resisted repeated operations, and a greatly disorganized and suppurating wrist-joint indicating amputation. He was also treated with 2 c.cm. doses intramuscularly, and at the time of writing, six weeks later, the lung signs had disappeared, many of the sinuses in the neck had healed without any surgical treatment after more rapid breaking down of the glands in some of them, and the condition of the wrist had decidedly improved.

Such cases as these afford great hope of the new treatment proving to have a permanent value in tuberculosis.

CONCLUSION.

I fully realize the great responsibility of bringing forward a new treatment for such a serious and widespread disease as tuberculosis. A year's trial by several careful workers has, however, convinced me that it is harmless in the doses recommended, which is more than can be said of that double-edged weapon tuberculin, regarding which, after over a quarter of a century's world-wide trials, scarcely two experts are agreed, either on the doses or the particular preparation to use, although no one doubts the great harm it often does in inexperienced hands. At the same time, the fact that sodium morrhuate causes febrile and local reactions necessitates great caution in pushing the drug beyond the limits which have so far proved safe, and a warning is required regarding the possibility of harm being done by its injudicious use. With this caution I feel that the results already obtained justify

me in bringing sodium morrhuate to the notice of the medical profession, to allow of the prolonged trials by many skilled workers which will be necessary before its permanent value, if any, can be decided, and the indications and contraindications for its use worked out.

REFERENCES.

¹ BRITISH MEDICAL JOURNAL, October 21st, 1916. ² *Ind. Journ. Med. Research*, October, 1917. ³ Ghosh, *Ind. Journ. Med. Research*, April, 1917, p. 691.

THE TEACHING OF OBSTETRICS AND GYNAECOLOGY TO MEDICAL STUDENTS.

A GENERAL SURVEY OF THE SUBJECTS TO BE TAUGHT AND OF THE METHODS OF TEACHING THEM.*

BY

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THE importance of a thorough training in obstetrics for students of medicine, who with few exceptions will enter general practice, is generally accepted. My duty this evening is to introduce a discussion on this subject in order that we who have the great responsibility of teaching may consider our aims and methods, so as to ensure that our training shall be as perfect as possible and our students made capable of rendering the great service to the nation that the efficient care of mother and infant can afford.

We who are teachers can help each other by comparing our methods; those who have profited more or less by our teaching can assist us even more by pointing out from their own experience of practice where our teaching methods have been deficient. We shall welcome candid criticism from any source, directed not to schools or individuals but to the methods which are more or less common to all.

Gynaecology is so intimately bound up with obstetrics that any attempt to teach these as separate subjects is futile, though there is much in each subject to be taught independently. It appears to me that our aims should be to give the student a good general knowledge of the special diseases of women in order that the practitioner may be able to deal adequately with the simpler cases, and to know when he ought to obtain more skilled assistance. Preventive gynaecology necessitates very thorough teaching—the prevention of infection, the prevention of the extension of infection, and the prevention and the early relief of various complications of pregnancy, labour, and the puerperium, such as lacerations and imperfect involution. While advanced and operative work is for the graduate who has the time and opportunity for further study, our aim should be to stimulate every student to take a keen interest and pride in the advancement made and to be made in our knowledge of these subjects, and so far as in him lies to do something towards the elucidation of the many problems which await solution.

I. SUBJECTS TO BE TAUGHT.

The obstetric anatomy of the pelvis must be taught by the obstetrician. The anatomy of the pelvic organs, not necessarily in minute detail, but the gross anatomy, must be taught with the greatest accuracy.

The Physiology of the Generative Organs.—Menstruation, puberty, and the climacteric: This subject, so fundamental to gynaecology, is generally neglected by the teachers of physiology, and must be taught by the obstetrician whose experience will enable him to give the student a view of its far-reaching importance in health and disease, mental and physical.

Pregnancy.—(1) The general structural changes in all parts of the body affected by pregnancy as well as the special organs and their functions, by which the symptoms and physical signs are recognizable in diagnosis. (2) The general development of the ovum into the mature fetus, placenta, and other parts. (Minute details of development are unnecessary in this course.) (3) Morning sickness. (4) Duration of pregnancy and the prediction of the probable day of confinement. (5) The various positions of the fetus and the means for recognizing them.

* An introduction to a discussion in the Section of Obstetrics and Gynaecology of the Royal Society of Medicine. Other parts of the discussion will be reported next week.