

$\frac{1}{100}$ mg. of the new tuberculin. His condition then was as regards physical signs: impaired movement of the upper third or more of the right side of the chest, and over this part of the lung there was marked dull percussion, the respiratory murmur was harsh both in expiration and in inspiration, and the harsh sound of the former was markedly audible from beginning to end of the act. Vocal resonance and vocal fremitus were both much exaggerated in amount over the dull patch, and for a considerable distance beyond its limits. For a month before the injection was given the temperature never rose above 99.5° F., and had on three occasions only, about midnight, passed 99° . Between 9 and 11 A.M. the temperature was always either normal or subnormal; between noon and 4 P.M. it was never higher than 99° , and only on three occasions passed 98.4° ; between 6 P.M. and midnight the temperature as a rule was either upon or within a couple of points of 99° . He had hardly any cough, and only very occasional night sweats when I first saw him, though I was told he had them profusely a month or so before that time. He had lost 24 lbs. in weight in about four months. I show you this young man's temperature charts, which tell also how many doses of the remedy he has had, and how each one of them has affected him. The dose has now reached 20 mg., and when this large quantity was injected there was, as you see, a rise to 99° about twenty-four hours after it was given on the 4th inst. During the last four days the temperature has been normal. I propose, at intervals of a month, to continue the use of tuberculin in this case. Of the diagnosis of this patient's condition there can be no doubt, for I found tubercle bacilli in his sputum early in November last; and his temperature under the influence of tuberculin was, as you see, that which is, when found with the physical signs I have mentioned above, characteristic of tuberculosis of the lung.

This case was seen on January 25th of this year by Dr. Patrick Manson, who gives me permission to tell you that after having carefully examined the patient, he would unhesitatingly have passed the young man into any service where sound physical condition is essential, had he not known the history of the patient's illness.

It may be worth while to mention that the hypodermic injections were always given in my wards with the antiseptic precautions stated in detail in my paper in vol. xiv of the *Transactions of the Medical Society of London*. These injections are now close on 2,000 in number, and there has never been in any one of them evidence of abscess nor of any other septic infection.

The mode of administration of the new tuberculin is by hypodermic injection, and it may be injected where loose skin can be taken up and the needle easily introduced. For the most part I have given the injections under the skin between the shoulder blades and the spinal column.

The regulation of the dose of the new tuberculin is most important. The use of the old tuberculin was characterised by what were called "reactions." These consisted of a rise of temperature following the administration of the drug at an interval of six, twelve, twenty-four, thirty-six, or forty-eight hours, and of nervous symptoms when the reaction was severe, expressed by rigors and headache. The temperature in the severe form of reaction not infrequently reached 104° . In giving the new tuberculin no one of these severe symptoms should occur. The dose should be so regulated that the rise of temperature will be confined within the limits of 1° F., and there should be at the very most, and that only because it is perhaps unavoidable, a slight amount of occasional headache. In some cases headache does not occur; but in certain cases I believe it is unavoidable. The dose at the beginning of treatment should, in a case of tuberculosis of the lung, be not more than $\frac{1}{100}$ mg. Even so small a dose as this has, I believe, produces considerable rise of temperature with headache. This, however, has not occurred in my experience. If the temperature rises more than half a degree as a result of the administration of any dose of the remedy, then that same dose should be repeated until practically no rise of temperature follows its injection. The dose should not be repeated until the temperature has fallen either to normal, or to the temperature which was usual to the patient before treatment was commenced. The temperature usual to the patient is ascertained

by keeping a careful record of it during one week before commencement of treatment. In no circumstances should tuberculin be used for the first time unless this week's record has been made for the seven days preceding the giving of the first injection. My practice has been to increase the first doses by $\frac{1}{100}$ mg. at a time, always subject to the rule above stated relating to temperature.

At first the injections are given not oftener than once in two days. It must not be forgotten that a rise of temperature of even half a degree, following upon the injection of a small dose of tuberculin, is practically diagnostic of the presence of tuberculosis in the patient. In certain cases of tuberculosis of the lung, tubercle bacilli may not be found in the expectoration, or there may be no expectoration. Should this happen in one's experience, the injection of a small dose of tuberculin which was followed by a rise of temperature would show the patient concerned had tuberculosis. The strongest possible confirmation of this important fact is given by the evidence forthcoming from many countries, and which shows that the presence of tuberculosis in cattle, which may even seem to be healthy, can be detected with practically absolute certainty by means of this tuberculin test. It seems to me that this diagnostic value of tuberculin has not been sufficiently utilised in our dealings with doubtful cases in the human subject.

To return to the regulation of the dose. When by rises of $\frac{1}{100}$ mg. the dose reaches $\frac{1}{10}$ mg., my practice has been to increase the dose by $\frac{1}{10}$ mg. until $\frac{1}{2}$ mg. is reached, and then by $\frac{1}{2}$ mg. up to 1 mg. All this, however, must be strictly subject to the law of temperature I have already mentioned. After a dose of 1 mg. the doses may be increased by $\frac{1}{2}$ mg. at a time or more, according to the temperature shown after each dose. When 5 mg. doses are reached, not more than two injections should be given in a week. With still larger doses there should be but one injection in a week. The injections should be increased up to 20 mg. of the tuberculin, that is, the contents of two bottles of the fluid as it is now sold. When this large dose has been given, and has not been followed by rise of temperature, the treatment is at an end as regards increase of dose, and this large dose need not be repeated more than once a month, for safety's sake.

This, gentlemen, is a fairly full account of almost all my experience of the use of tuberculin both old and new. I have, I repeat, never seen in my own practice harm done by the use of this remedy. I have seen it do good in the treatment of lupus, and, in my opinion, it is of value in helping consumptives on the way to recovery provided the disease is in a very early stage. In advanced stages of the disease I do not think the discomfort inseparable from the use of the hypodermic syringe, and to which many persons are exceedingly sensitive, is sufficiently outweighed by the slight chance there is of possible good that might come from the use of tuberculin. Of the cure of tuberculosis by tuberculin it is impossible for me yet to speak, because I am not sure there may not be relapse in any one of the most promising of the cases that have come under my observation. I incline to the belief that the new tuberculin is of more use than any other drug in the curative treatment of very early stages of tuberculosis affecting the lungs or the skin.

REFERENCES.

¹ *Trans. Med. Soc.*, vol. xiv. ² The details of L. B.'s treatment are stated under those initials in my paper published in *Trans. Med. Soc.*, vol. xiv.

ON THE TREATMENT OF OBESITY AND MYX- CEDEMA BY A NEW PREPARATION OF THYROID ("THYROGLANDIN").

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THE extensive use of thyroid gland, or its active ingredients, in the treatment of certain morbid conditions makes it very desirable that a preparation of uniform strength and quality be at all times employed. The gland is possessed of such powerful properties that the more nearly its preparations approach the "standardised" the safer and more satisfactory will their employment be.

A large variety of preparations of thyroid is employed in the treatment of obesity, myxœdema, and other ailments. Perhaps the tablets of the dried extract are the most popular. But none of the extracted preparations commonly used contain all the active ingredients in the same form or proportion as they are found to exist in the gland itself.

Last spring I obtained from Mr. E. C. C. Stanford, F.I.C., F.C.S., whose researches on iodine are so well known, a new preparation of the active ingredients—thyroglandin. I have made numerous trials of this substance in a number of cases of obesity, and in one case of myxœdema.

CASE I. *Obesity*.—B. McR., aged 21, married, complained of rapidly increasing gain of flesh, with debility and great shortness of breath on exertion. She was put on 1 grain of thyroglandin thrice daily for a few days. The dose was then rapidly increased until 9 grains in the day were being taken. The decrease in weight was as follows: June 1st, 12st. 4lb.; June 12th, 11st. 10 lb.; July 10th, 11st. 2 lb.; August 10th, 10st. 6lb.; September 4th, 10st. 5 lb.; September 29th, 10st. 1lb. Since last date this patient has been taking about 1 grain daily, and her weight remains fairly stationary.

CASE II. *Obesity*.—R. C., aged 46, married, multipara, consulted me on account of her obesity and dyspnoea. She was put on 1 grain of thyroglandin thrice daily, and as this dose was well tolerated it was rapidly increased to 9 grains in the day. Her weight at different dates was as follows: July 16th, 14 st. 13 lb.; July 25th, 14 st. 10½ lb.; September 17th, 13st. 12 lb.; September 24th, 13 st. 10 lb.; October 8th, 13 st. 1 lb.; October 19th, 12st. 9 lb.; October 26th, 12 st. 5½ lb.; November 19th, 12st. 0½ lb.; November 26th, 11st. 9 lb.

CASE III. *Obesity*.—Mrs. M., aged 40, under 5 feet in height; had great difficulty in moving about, and complained of excessive dyspnoea on exertion. She was put on thyroglandin in doses similar to the two former cases, and her weight fell as follows: May 16th, 13 st. 11 lb.; June 14th, 12 st. 11½ lb.; July 6th, 11st. 6 lb.

In all of these cases the rapid loss of flesh was accompanied by few of the unpleasant symptoms so commonly experienced. There was no sickness, diarrhoea, sore throat, excessive sweating, or cardiac failure, and no persistent symptoms of thyroidism.

CASE IV. *Myxœdema*.—Mrs. P., aged 49. This patient first came under my observation in 1893. She was suffering from myxœdema of many months' duration. In June of that year the treatment with raw thyroid gland was begun. Four glands were given in the week. In two weeks a marked improvement began. Dyspnoea became less pronounced, insomnia disappeared, œdema of legs and arms diminished, and coldness of the extremities became less. Her weight, too, was considerably reduced, and she was able to move about with some ease. At the end of two months a most obvious change in her facial expression was recognised. She continued the use of the gland for six months, with occasional intervals, which were followed by relapses if the cessation was prolonged beyond two weeks. This patient's residence being in the country, it was found to be inconvenient to procure the necessary weekly supply of fresh and healthy glands. In 1894 treatment was continued with the tabloids of dried extract. Since then almost all the preparations of thyroid, including several fluid extracts of various makers, and thyroïdin (Bayer's) have had prolonged trials, but the results were not satisfactory, while these preparations were not nearly so therapeutically active as the raw gland. Early in 1897 thyroglandin was begun. The dose was 5 grains daily. This was continued for one month. Her general condition when she began this treatment was similar to when the raw gland was first commenced, except that œdema and breathlessness were not quite so marked. She responded at once to the thyroglandin, and in three weeks she became more comfortable, greatly improved in appearance, and swelling disappeared almost entirely from her arms and legs. From that time up till now the thyroglandin has been continued with occasional intervals of from two to three weeks. The therapeutic effect of this remedy seemed to me to be quite equal to that of the raw gland, while it produced no unpleasant symptoms.

In many cases in which I have employed similar preparations, prescribed at different dates, but under conditions as nearly as possible identical, the results have been far from uniform. I have been led to believe that these differences depend more largely on a want of uniformity in the preparation employed than on any inherent difference in the patient.

Most of the preparations on the market have some drawback, and, as far as I am aware, none of them contain the thyroïdin and the antitoxins in the same proportion, or of the same activity, as that in which they are present in the gland.

The thyroid gland may be administered either in the raw state or dried at a gentle heat under the coagulating point of albumen. To either of these forms there are obvious objections, because animal substances foreign to the essential active principles are almost certain to be present, and bacteria of a dangerous kind may be introduced into the system of the patient.

The thyroid gland contains two important principles: one of these is an iodoglobulin, the larger constituent, and the other is thyroïdin, discovered by Baumann. Both contain iodine, and both are requisite to produce the specific effects of the gland itself. Several chemical processes¹ have been

introduced with the object of separating the active principles from the animal substance—for example, boiling in dilute sulphuric acids, or in solutions of caustic soda, or digesting in closed vessels with water at a high temperature, or digesting with pepsin, or extracting with solutions of common salt and precipitating the solution with tannin.

It has been found, however, that none of these processes separate the active principles of the gland in the form or proportion in which they are contained in the gland; they all result in the destruction of the iodoglobulin entirely, or in the partial separation of the thyroïdin only, or in its association with other substances of a useless or objectionable nature. That the products of these processes have not the same medicinal effect as the gland itself is admitted by all who have employed them as substitutes on account of their greater convenience.

Thyroglandin is prepared by the following chemical process:

1. Selected and healthy glands are macerated in cold water, which extracts the soluble iodoglobulin. This solution is decanted or filtered off, and is evaporated to dryness at a temperature of 212° F. The resulting product is reduced to a fine powder.

2. The residual glands are then boiled for one hour with a weak solution of caustic soda which eliminates the thyroïdin. After filtration the solution is exactly neutralised with hydrochloric acid, evaporated to dryness, and powdered.

3. The two powders so obtained (iodoglobulin and thyroïdin) are mixed together and constitute thyroglandin.

It will thus be seen that this new preparation is made in such a way that thorough sterilisation is secured, and that it is freed from everything deleterious which might be derived from the other animal substances of the gland, while it contains the iodoglobulin and thyroïdin in the form and in the proportion in which they exist in the gland.

Thyroglandin keeps perfectly, if kept thoroughly dry, without deterioration. It may be administered in capsule or in tablets, and in doses of 3 to 5 grains, which are equal to half a gland of average size and weight.

The very active therapeutic properties which are exhibited by thyroglandin lead me to believe it is a preparation of great value. If it really represents all the active constituents present in the gland in their correct form and proportion, it may prove a very useful addition to our thyroid preparations.

REFERENCE.

¹ Vide articles by Robt. Hutchinson, M.D., BRITISH MEDICAL JOURNAL, January 23rd, 1897; March 21st, 1896; and *Journal of Physiology*, vol. XX, p. 474.

SHORT NOTES ON THE TREATMENT OF LUPUS VULGARIS WITH "T.R." TUBERCULIN.

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EARLY in September I selected four patients; one was treated entirely as an out-patient, the others were admitted to my wards. The following are condensed notes of the cases. The minimum dose injected was $\frac{1}{16}$ mg., and the maximum 10 mg.

CASE I. *Lupus of the Nose*.—J. J., a delicate girl, aged 15. The disease first made its appearance five years ago at the junction of the left nostril with the lip. When admitted on July 16th, the left cartilages, the septum, the columna, the right lower cartilage, together with the lobe, were in a state of ulceration, and numerous discrete nodules were seen at the base. The ulcerated surfaces were thoroughly scraped and cauterised and the nodules were bored with a wooden match dipped in liq. hydrarg. nit. acid. In a month the nose was soundly healed. At the beginning of September a few fresh nodules were observed beyond the area of operation, and for these the treatment with T.R. tuberculin was commenced on September 5th. September 26th. It was noticed that the nodules were disappearing, becoming depressed and scaly. September 30th. A few scales only marked the original site of the disease. October 15th. After six weeks' treatment the patient was obliged to return to her home in Wales, but with absolutely no trace of the disease. November 19th. She returned for inspection, when it was observed that a few fresh nodules had appeared. During her absence the treatment had been suspended, but it was subsequently carried out by Dr. Griffith of Castellmarch, Pwllheli, but without benefit. April 2nd. The patient returned a second time to hospital for further operative treatment, ulceration having again occurred on the right lower cartilage and base of nose; otherwise she had gained weight.

CASE II. *Lupus of Nose*.—E. W. aged 32, a domestic servant, has suffer