

ENDOCRINES IN THEORY AND PRACTICE

This article is one of a series on Endocrinology contributed by invitation

THYROID EXTRACT IN CONDITIONS OTHER THAN MYXOEDEMA

BY

D. MURRAY LYON, M.D., F.R.C.P.Ed.

The discovery that a drug acts successfully in one disease inevitably leads to a trial of its powers in other conditions. At first it will be tried in allied disorders in which it may be expected to produce some benefit, and later it will be given empirically in many other complaints. Such has been the history of thyroid extract. A survey of the literature will show that it has been employed in almost every department of medicine and that it has been recommended for the most unlikely conditions.

The active principle of the thyroid possesses definite pharmacological actions both in the healthy body and in disease. Thyroxine increases general metabolism and raises the activity of many organs and tissues in the body. Among other important actions it stimulates the sympathetic nervous system, it has secondary effects on the circulation, and it plays some part in controlling the water content of the body. The extract is probably most successful in therapeutics where some definite pharmacological action is made use of. It must be remembered, however, that it is not possible to isolate the different actions, and when the drug is given for one specific purpose other unwanted side actions are apt to appear.

Subthyroidism and Obesity

Mild degrees of subthyroidism not sufficiently marked to warrant a diagnosis of myxoedema are probably more common than is generally thought. One or more of the following symptoms may suggest such a condition: dry skin and hair, mental depression or dullness, forgetfulness, loss of energy, a tendency to chronic constipation, a predisposition to colds, and some vasomotor disturbances; a useful confirmatory sign is a thinning or loss of hair from the outer third of the eyebrow. Such signs will indicate the administration of small doses of thyroid, and the improvement in the general health of this class of patient under such treatment is often remarkable.

Thyroid has been much used in the treatment of obesity, which may be caused by different factors in different individuals. Some obese patients are definitely subthyroid, showing some of the signs mentioned above and often having a characteristic "round moon" face; in these thyroid extract is obviously indicated. It is also given in cases with no signs of thyroid insufficiency, and in those in which there is disturbance of the other endocrine glands. Here the idea is that the thyroid extract will stimulate the general metabolism so that the patient may be able to use up some of his excessive stores of fat. It must be remembered, however, that in obesity the basal metabolic rate is not abnormal. It is usually within the normal range, and since the basal metabolic rate is calculated on the area of the body surface, which, of course, is increased in these subjects, the metabolism may be actually in excess of that of a person of average proportions.

Thyroid extract given to obese individuals must tend to raise the metabolism above normal, but it cannot be

relied on by itself as a treatment for excessive weight. Given alone it is often unsuccessful, for it increases the appetite, which neutralizes its action on the general metabolism. As an adjunct to carefully chosen subcaloric diet (say 1,000 calories) it has a most important place in therapy. Obesity in some patients, particularly those who have been large eaters, can be successfully reduced by dieting alone. In others dieting fails to accomplish all that is desired. For a time they lose weight on the low diet satisfactorily enough; then the metabolism adjusts itself at a new level and loss of weight gradually ceases. When this point has been reached the diet should be continued as before and thyroid treatment should be started, the dose being slowly increased till a satisfactory rate of fall has been again secured. In this way the patient may continue to reduce in weight for many months. When thyroid is begun there is little evidence of its action on the weight for three or four days, then a rapid drop takes place during the next few days, apparently due to displacement of fluid from the system. The fall after this is less rapid, but continues steadily for a time. Under continued administration of thyroid the pulse rate will quicken and the basal metabolic rate gradually rises. A value of +20 to +25 may be reached before cardiovascular symptoms appear. The amount of thyroid which obese patients can take without trouble varies with each individual. Some appear to be excessively sensitive, while others can tolerate very large doses without discomfort. When reduction of weight has been completed a few patients can keep their weight down without further treatment; some must continue to restrict their diet; and others must take small doses of thyroid extract if they are to prevent reaccumulation of fat.

Use of Thyroid in Various Disorders

The thyroid gland has important interrelations with the rest of the endocrine system, acting with some of the hormones and against others. Thyroid extract has been employed in place of other hormones which were not available on the market, but the successful commercial production of an ever-increasing number of endocrine substances will limit this use of it. It is still often given in certain cases of pituitary insufficiency and in such conditions as amenorrhoea and the disturbances of the menopause. It is also a common ingredient of pluriglandular compounds, and in some may be the *only* active agent. In most cases it is probably best to administer the thyroid separately, so that the most appropriate quantity may be more accurately judged.

Thyroid extract is sometimes of value in the treatment of asthma. When the patient is grossly overweight and the excessive fatty covering of the chest embarrasses the breathing its use can be readily understood. In cases of asthma thyroid extract may act in another way. It may stimulate the adrenals and it increases the sensitivity of the sympathetic elements on which adrenaline acts. Because of the stimulating action on metabolism thyroid extract cannot be freely given in the thin type of asthmatic.

The striking improvement in the skin of myxoedematous patients under treatment has suggested the use of thyroid extract in dermatology. It has been tried in a large variety of skin lesions, but is now mostly advised in chronic conditions of a non-inflammatory nature. The skin may be kept in a tolerable state in some cases of

ichthyosis by small doses of thyroid taken regularly. In others it is less successful, but the remedy is worth persevering with. Claims have also been made for thyroid extract in psoriasis, but the evidence of a beneficial action here is not so clear. In other skin conditions indications for thyroid extract are less definite.

The improved cerebation of the myxoedematous patient under treatment has led to the employment of thyroid in certain mental disorders, especially those associated with dullness or depression, and good results are often obtained in such cases.

Another interesting and little-known use for thyroid extract is in the chronic oedemas of renal disease. Some diuresis is commonly observed in myxoedemas and other cases under treatment with thyroid extract, which has been strongly recommended for the persistent oedema of the nephrotic syndrome, and it may be of definite assistance. It is interesting to note that this class of patient can tolerate relatively large doses of the drug without inconvenience.

Formerly the extract was employed in diseases of the thyroid gland itself; but such treatment is especially dangerous, for overaction may be very easily induced. When subthyroidism develops in a case of goitre, thyroid extract is of course indicated. Other uses are less easily explained and may be entirely empirical. It has been prescribed in those chronic disorders in which potassium iodide is given—arteriosclerosis, fibrositis, chronic rheumatism, etc.—probably with the idea of stimulating local metabolic changes and increasing the removal of waste products. Thyroid extract has been put forward as a means of preventing the development of eclampsia, and in the fully developed case enormous doses have been taken. The list of diseases for which it has been recommended might be indefinitely extended, but this would serve no useful purpose.

Method of Administration

The secretion of the thyroid gland is a very powerful agent, and serious harm may result if its action is not carefully controlled. In no circumstances should the drug be left to a patient to take freely. Treatment must be closely supervised by the medical attendant, and the patient should be seen at least once a week. The dangers are the development of hyperthyroidism and in particular cardiac symptoms, and the risk is increased by the fact that these may appear slowly. A point of great importance is that the full effects of the drug are not seen for several days after it has been begun or the dose has been increased. This fact is in keeping with other metabolic phenomena. For example, an increase or reduction of protein or of carbohydrate in the diet does not exert its full effect on metabolism for about four days. The results of administering thyroid extract can be readily followed in an obese patient who is weighed daily. The influence on the weight is seldom noticed before the third or fourth day, and the maximum increase in pulse rate does not occur for some time longer. The full increase in the basal metabolic rate is also slow in developing. For this reason it is a good rule not to order an increase in the amount of the drug at intervals of less than a week. Further, it is impossible to foretell exactly how much thyroid an individual will require or how much he will be able to tolerate. In all cases, therefore, the initial dosage should be small. Obese subjects are especially intolerant of the drug, and for them the initial dose should not exceed half a grain twice or three times a day. Other patients may begin with double this amount. Owing to the very slow development of the action there is no reason why the daily

quantity prescribed should not be given in a single dose, but the practice of taking medicine three times a day is firmly established in the lay mind. If the drug is to be taken for a prolonged period it is often advised that it be discontinued for a few days each month so as to lessen the possibility of overaction developing.

Small doses are often adequate for certain purposes, but in other cases it is often desirable to push the drug to the limit of tolerance in order to get its maximum effect. In these circumstances signs of overaction must be constantly looked for. The earliest evidences of intoxication vary in different patients. Some complain of palpitation, tremor, nervousness, or headache when taking only small amounts. Patients with fatty hearts are particularly prone to develop cardiac symptoms, and the possibility of auricular fibrillation must be kept in mind. The drug must be reduced or discontinued at once if any symptoms appear. The physician's best guide for controlling cases under thyroid treatment is the rate of the pulse. It is usually perfectly safe to continue administration so long as the pulse rate remains under 100 beats per minute. Obese patients who are otherwise in good health will often tolerate 6 to 9 grains of thyroid (*B.P.*) daily, and I have given for a time as much as 18 grains to a woman of 30 who weighed 28 st. Patients with the nephrotic syndrome are especially tolerant to thyroid, and can continue relatively large doses with impunity.

The doses mentioned above are in terms of thyroid *B.P.* (thyroid extract), and this is probably the best preparation for general use. Thyroxine has no special advantage except that it can be given intravenously and may come into action more rapidly. There are also on the market other preparations of thyroid substance for which special claims are made, such as being less liable to upset the heart than the official preparation. With these, as with the standard drug, the most suitable dose has to be determined by the method of trial and error.

BRITISH EMPIRE CANCER CAMPAIGN

In the absence of Viscount Hailsham, Sir Cuthbert Wallace, President of the Royal College of Surgeons of England, presided at the sixty-first quarterly meeting of the Grand Council of the British Empire Cancer Campaign, held at 12, Grosvenor Crescent on January 11.

The Council was informed that Viscount Hailsham had sent a letter to the King tendering loyal and humble thanks for the services which His Majesty had rendered the cause of cancer research as the president of the Campaign since 1924 to the time of his accession to the throne. A message in reply from His Majesty was read.

The Council tendered its sympathy to Lady Bland-Sutton in her recent bereavement. The late Sir John Bland-Sutton was one of the founders of the Campaign, and was vice-chairman of the Grand Council for ten years. Mr. Stanford Cade, F.R.C.S., of the Westminster Hospital, was invited to become a member of the Grand Council, and Sir Harold Mackintosh, Bt., and Mr. B. T. Clegg were also invited to become members to represent the Yorkshire Council in addition to the Earl of Harewood.

The following grants, in addition to those totalling £28,995 which were made at the annual meeting in November, were approved on the recommendation of the Scientific Advisory Committee: £200 to cover the cost of special physical investigations being carried out under the direction of Dr. F. G. Spear at the Strangeways Research Laboratory, Cambridge; £500 for one year to Dr. H. J. Phelps, whilst carrying out experiments in connexion with Dr. Lumsden's anti-cancer serum under the supervision of Dr. Gye and Professor McIntosh; and £440 for one year to Miss C. F. Fischmann, working in the Bernhard Baron Institute of Pathology at the London Hospital.