Practical Points of Diagnosis and Treatment in Medicine.

MEDICAL TREATMENT OF GRAVES' DISEASE.

BY GERALD M. SLOT, M.D., M.R.C.P., D.P.H.

Physician, Royal Waterloo Hospital; Royal Hospital, Richmond; Consulting Physician, Hammersmith Hospital; late Harmsworth Research Fellow, &c.

IN the following article it is proposed to confine the text strictly to the treatment of Graves' disease, and no attempt will be made to enter into a discussion on the pathology or ætiology of the disease.

In dealing with a case of exophthalmic goitre a very long view must be taken; it must be remembered that every system of the body may show signs of disorder, and that the resulting illness is similar to a combination of a toxic disorder to which has been superadded an irritative lesion of the sympathetic nervous system. The distinction between primary and secondary goitres is very artificial, the latter condition merely being toxic manifestations appearing in a previously enlarged thyroid gland.

The first essential in the medical treatment is to secure adequate rest. This must include both physical and mental rest. The patient should be in bed most of the time and when possible in an atmosphere in which he is removed from the cares and troubles of his life. For this reason it is usually preferable to remove the housewife to a clinic or hospital.

Apprehension, mistrust, worry over financial or domestic matters, all need the sympathetic treatment of the doctor. The important part played by marital or sexual difficulties must not be forgotten, and this aspect of a case often will need careful and tactful handling. Little progress will be made until all efforts at mental rest have been attempted and some success in this direction achieved. It is realized that where the subject is the breadwinner or has serious responsibilities, it is difficult to reassure him, but it can be pointed out that it is only by relaxing that his cure will be hastened.

A comfortable room and a comfortable bed should be chosen. Indeed where space permits it is sometimes an advantage to have two beds in the room, in one of which the patient can sleep by day and in the other by night. This arrangement allows for a change and is greatly appreciated.

Kindness and sympathy help greatly in quietening the patient and some firmness of handling is occasionally required. One has often seen a very anxious restless patient changed completely by a few kind words from an understanding doctor and tactful treatment by the nurse. It may help considerably to "have their own things round them," and where this is not contra-indicated it is wise to acquiesce in this desire. Some patients, however, will not respond to any such treatment and will sink rapidly.

Diet. The general principle of diet is that it should contain a maximum of carbohydrates. It is best to avoid meat, tea, strong coffee and cocoa. The diet should be attractive and easily digested.

The following diet adapted from Lapp and Schoenbauer (*Wien. Mediz. Woch.*, 3, 1932) may form a useful basis.

Breakfast.—Coffee with milk (10 oz. milk and added sugar). Café vierge is very useful for flavouring. 2 Rolls ; 1 oz. butter ; $\frac{1}{4}$ oz. jam ; 1 egg.

Lunch.—Soup made perhaps with $1\frac{1}{4}$ oz. oatmeal ; $1\frac{1}{2}$ oz. butter ; 1 roll, with $\frac{1}{2}$ oz. butter.

Midday Meal.—5 oz. meat ; 3 oz. rice ; $\frac{1}{4}$ oz. butter ; 5 oz. peas, with $\frac{1}{2}$ oz. flour and $\frac{1}{2}$ oz. butter ; $2\frac{1}{2}$ oz. milk pudding ; 8 oz. stewed fruit.

Tea.—10 oz. milk, flavoured with cocoa ; 2 rolls and 1 oz. butter.

Dinner.—Soup, with $1\frac{1}{2}$ oz. barley and $1\frac{1}{2}$ oz. butter noodles au gratin (3 oz. noodles, $\frac{1}{2}$ oz. butter) ; 1 egg ; $\frac{1}{2}$ oz. cheese ; 6 oz. of carrots, cooked with $\frac{1}{2}$ oz. butter and $\frac{1}{2}$ oz. flour ; 1 roll ; $\frac{1}{2}$ oz. of butter ; $1\frac{1}{2}$ oz. Gruyère cheese and 10 oz. of milk.

The calorie value of this diet is approximately 5,000, and it contains roughly 500 gm. carbohydrate, 324 gm. fat, and 155 gm. protein. If this diet is not easily assimilated, carbohydrate can be given in the form of 50 gm. of lactose added to a glass of lemonade. This adds approximately 200 cal. per glass. Owing to their rapid rate of metabolism, it is desirable that these patients ingest the maximum amount of food compatible with their digestion.

Anorexia is sometimes a problem. It is then that the resources of the cook must be sought. Small appetizing dishes may tempt the patient, as will also a teaspoonful of bitters before the meal. Usually, however, the patient has a large appetite, and hence this problem does not arise.

Drugs. Many drugs have been used in the treatment of Graves' disease, and most clinicians now rely on iodine. This drug has the effect of diminishing symptoms, particularly in that class of case which is toxic from the start. Iodine is usually prescribed as the French tincture, which is a 10 per cent. solution of iodine in alcohol. The average dose is 5 minims (that is 10 drops, because owing to the surface tension 1 drop of iodine is equivalent of $\frac{1}{2}$ minim) in a teaspoonful of milk thrice daily after meals. The effect of the iodine is usually marked and may take a few days to develop, the pulse becomes slower, the restlessness less marked, and the gland becomes softer. The irregularity of the heart too is improved, and this will be discussed below. The good effect does not last indefinitely, and iodine therefore has its greatest value in preparing patients for operation. The dose can be cautiously increased, the physician keeping a careful watch on the pulse rate, weight and heart sounds and, when possible, checking the metabolism by weekly estimations of the basal metabolic rate. Should the thyroid become hard or the pulse increase, the iodine must be discontinued for some days, but it can be resumed later. I do not think it is a wise procedure to keep a case indefinitely on iodine. It is far better to get the maximal effect and then operate, or where operation is not being performed to drop it for a while.

Sleeplessness is a common trouble, and for this I have found luminal in full doses of $\frac{3}{4}$ to $1\frac{1}{2}$ gm. most valuable. Luminal is also a very valuable sedative drug. As the condition improves the dose of luminal can be reduced. Where patients are actually delirious, morphia may be indicated in $\frac{1}{4}$ -gr. doses, or if the movements permit 3i to ʒiiss of paraldehyde *per rectum*. I do not advise the routine exhibition of iodine, but

suggest that a course of three weeks be given, and then that it be discontinued for a period and if necessary recommenced.

Quinine hydrobromide in 5-gr. cachets at night is also very valuable as a sedative. Many physicians have found that a mixture of tincture of belladonna $\text{m}x$ and 7 gr. of potassium bromide administered three times a day is very helpful—and perhaps is most successful in those cases which arise at or about the menopause.

Cardiac Treatment.

The treatment and management of the heart is one of the most important aspects of the cases of Graves' disease. The main cardiac complications are: (1) Enlargement—this is clinically doubtful. (2) Auricular fibrillation—this occurs in 20 per cent. of the cases according to Williams and Boothby. (3) Tachycardia and palpitations—these occur in almost every case. (4) Auricular flutter—this is rare.

Auricular fibrillation, which is so often associated with the toxic type of goitre, needs careful treatment. The pulse in this condition may be rapid and is irregular in time, force and rhythm. Exercise increases the irregularity and beats may be heard at the apex which are not transmitted to the pulse.

In the first instance rest in bed and sedative drugs, together with iodine therapy, may prove enough in some cases. Iodine frequently, as has been mentioned above, restores to some extent, or even completely, the normal rhythm.

In cases where this is not restored and cardiac failure develops, recourse must be had to digitalis. Care must be taken to use a fresh tincture—as failures from old stocks which are inert have been recorded. As a useful guide of the amount of digitalis required per day: Take the patient's weight in lbs. and multiply it by $1\frac{1}{2}$ —this will give the number of minims required. This dose can be given in 30 to 40 m doses at four-hour intervals. A patient weighing 140 lb. would need 210 m a day.

When digitalisation is effected, as shown by a return to normal rhythm, slowing of the pulse-rate, satisfactory output of urine, lessening of the dyspnoea—a maintenance dose of 10 to 15 m of the tincture thrice daily is adequate.

In some cases the patient will not tolerate digitalis; signs of digitalis poisoning, such as nausea, giddiness, vomiting, coupled beats or undue slowing of the pulse may occur. In these cases ouabain can be used or quinidine.

Quinidine is very valuable in two phases in exophthalmic goitre:—

(1) In treating those cases of auricular fibrillation which persist after cardiac failure has been restored.

(2) In treating those cases in which normal rhythm does not occur after operation. According to Chisley it should never be given until the patient has been digitalized.

The digitalis is discontinued for a day before quinidine is given. Then a test dose of 3 gr. of quinidine sulphate is given. Should no dizziness or tinnitus occur 6 gr. are given four-hourly, day and night, and the dose is halved as soon as the rhythm is regular, and after two or three days it is reduced to 3 gr. twice daily. It is wise to discontinue the drug should a regular rhythm not be established after three to four days' dosage with 6 gr. four-hourly, and it is also wise not to use the drug in cases with valvular disease, because several cases of embolism following its use have been recorded.

In treating the heart condition after operation, do not give digitalis to those cases of tachycardia without alteration of rhythm.

Where auricular fibrillation was present before operation, give them their maintenance dose of digitalis after the operation. It can be given hypodermically as digitalin ($\frac{1}{80}$ gr. digitalin = 15 m of the tincture) four-hourly, but owing to the irritating effect of the digitalin revert to the oral method as soon as possible.

Should auricular fibrillation return try digitalis for a while—then quinidine as outlined above—if this fails digitalis in 10 m doses thrice daily over a long period.

Often after operation the normal rhythm is restored, but there are some cases in which this happy condition does not occur.

Digestive Disturbances.

Anorexia may occur at the peak of the disease. Diarrhoea, particularly of the mucus-colitis type, occurs in severe cases. This improves as the toxic condition improves and with suitable sedatives. A few doses of a chlorodyne-catechu mixture is sometimes helpful.

Vomiting is a very serious symptom, and is usually due to a toxic cause and is central in origin. Morphia in adequate doses and large draughts of alkali (sodii bicarbonas 3ii to O may help). Pigmentation of the skin may occur and demands no special treatment. For the sweats which are common in this condition, atropin $\frac{1}{100}$ or genatropin in doses of $\frac{1}{80}$ t.d.s. are helpful, although the condition tends to clear up when the toxic process is removed.

Erythemas and itching may be relieved by linimentum calaminæ, while locally for the perspiring, applications of formaldehyde may prove useful.

The progress of a case may be estimated on (1) the weight; (2) the pulse rate; (3) the basal metabolic rate; (4) the general condition of the patient with special reference to his nervous and emotional characteristics. With regard to methods of treatment, I think every case should be treated on medical lines in the first instance. In those cases where auricular fibrillation has developed—or where there is gross evidence of toxæmia—surgery in experienced hands offers the best hope of cure, but the post-operative treatment of rest, diet and cardiac care is of paramount importance and must be firmly stressed.

I do not favour X-rays as a method of treatment. Early cases where X-rays are advised do better with surgery, and one effect of the X-ray therapy is to render a subsequent surgical operation more difficult because of adhesions which may form. In very advanced cases where the risk of surgery is considered too great and where medical treatment is not meeting with adequate response, they may have a slight use. I have no personal experience of radium therapy in this condition.

To Sum Up. Rest, diet, cardiac care and drugs. Avoid iodine in the treatment of acute toxic goitre, except in preparing the case for operation. Do not continue with iodine too long, because a phase of discomfort is sure to ensue.

The nervous aspect of the disease, which may even amount to delirium, needs special and sympathetic care.

Remember not to promise the disappearance of exophthalmos—it is often a very late symptom to disappear. Warn the patient to take a long view of a disease that is protean in its symptomatology, and for a successful issue demands the closest co-operation between himself and his doctor.

Acknowledgment is made to "Disease of Thyroid Gland," Hertzler.