Drug Treatment of Disease

TREATMENT OF CHRONIC HEART FAILURE

BY

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When the heart first shows signs of failure the right side or the left side generally fails first, but these problems of acute heart failure are to be discussed in a later article. In chronic heart failure both sides are affected, and there is the general picture of congestive heart failure with a rise of venous pressure, oedema of the ankles and a sacral pad, enlargement of the liver, and congestion of the lungs. Sometimes, however, signs of left ventricular failure may still form an important part of the picture.

Occasionally, failure that appears to be chronic is due to a cause that can be remedied, such as thyrotoxicosis, a large patent ductus, or some cases of mitral stenosis. Such causes should be looked for and the patients should be relieved of their failure so far as possible and then cured of its underlying cause.

General Principles

In chronic heart failure limitation of exertion to an amount compatible with the state of the patient's heart must be the first consideration. Some patients with adequate treatment can be kept at work with minimal signs of failure, and this is obviously the ideal. Others, in spite of every form of help, can only do a little in the house or are almost confined to bed. In the more favourable cases, it is important to find what the patient's capacity is and to keep him within these limits.

Digitalis and Aminophylline

Some form of digitalis is still a most important part of treatment. There are many forms and the doctor should use one or two of which he has experience and should not change them frequently. Mackenzie almost confined himself to tincture of digitalis, for he said that his life had not been long enough to learn all he wanted to know about it; and, with the increasing number of drugs of all types available, this has become even more important.

Tincture of digitalis, 15 minims (0.9 ml.) three times a day, tab. digitalis fol., 1 gr. (65 mg.) three times a day, or digoxin 0.25 mg. three times a day, are well-proved remedies that can be relied upon to produce good effects, and the amounts mentioned should be adequate and not too much in most patients, though the right dose has to be learned for each one individually. Unlike most drugs, the largest amount of digitalis that can be taken without toxic symptoms generally produces the best results, and most patients getting about will be better with a little more than they needed when resting in hospital.

In heart failure with normal rhythm, as in many cases of hypertension, less good results can be expected from digitalis than, for example, in cases of mitral stenosis and auricular fibrillation. It should be used in these cases and I think in the same amount, but some of my colleagues think more cautiously and in smaller amounts, as there is some risk of inducing auricular fibrillation. If a patient is on the correct amount of digitalis, it can be taken for years, but he should be familiar with the signs of overdosage—nausea, vomiting, and a slow pulse. If this occurs, all digitalis should be stopped for 48–72 hours, and then resumed at a rather lower level.

Aminophylline has its main use in the treatment of acute left-sided failure, but by lowering the venous pressure and stimulating respiration it may prove beneficial in chronic failure as well, especially if there is paroxysmal nocturnal dyspnoea or Cheyne-Stokes breathing. It is far more effective intravenously, 250 mg., but can be given by mouth, 100 mg. three times a day or more if a patient can tolerate it without nausea. If paroxysmal dyspnoea is troublesome at night, a suppository containing aminophylline may help.

Diuretics

The doctor's task may be made easier, and stricter treatment postponed, if, as is discussed later, salt is reduced in the cooking and taken sparingly or not at all with meals, and if the fluid intake is limited to 30 or at the most 40 oz. (0.9–1.1 litres) daily. If, at a later stage, stricter limitation of sodium is needed, fluid need not be so limited.

An important advance was made when mercurial diuretics were introduced, and this was bettered when theophylline was combined with the organic mercurials, as in mersalyl ("salyrgan"), "neptal," and "esidrone." These diuretics act on the renal tubules by preventing the reabsorption of sodium, and so the urinary output is increased. After a test dose of 1 ml. the usual dose is 2 ml. intramuscularly, and this contains 80 mg. of metallic mercury and 100 mg. of theophylline. After the first few days it is rarely wanted more than twice a week. Many patients get adequate diuresis with these injections once or at the most twice a week, or may need them only from time to time. When they are in regular use, the daily urinary output should be checked to see if the weekly output is any higher when the diuretic is given twice a week than when it is given once a week.

Mercurial diuretics are generally more effective if ammonium chloride is given just before them. At first, when 30 gr. (2 g.) was given three times a day for one or two days before the injection, the patient was often upset by it, and now as a routine less is given and sometimes it is omitted. It does, however, generally add to the diuretic effect, and 30 gr. (2 g.) given once two hours before the injection, or twice two and four hours before, is advisable unless diuresis is adequate without it.

Mercaptomerin ("thiomerin"), a combination of the organic mercurial with a mercaptide group, has much the same effect. Attempts have been made for a long time to produce an effective oral diuretic of this group, but not very successfully. Chlormerodrin ("mercloran") was used a good deal, but generally it failed to produce a good diuresis regularly when given in amounts that the patient could tolerate. Some newer diuretics will be discussed later. Mersalyl has been proved reliable over years of experience. Though a few patients reach a stage where it ceases to be effective, often because the balance of the electrolytes is upset, this need not be expected, and, provided there is no serious renal disease, it can often be taken for years with great benefit.

Apart from the mercurial diuretics which act by preventing the reabsorption of sodium in the renal tubules, there is another group that act by inhibiting the enzyme carbonic anhydrase. Normally, this helps the reaction in the distal tubules when sodium alkaline phosphate and carbonic acid are changed to acid phosphate and sodium bicarbonate;

the latter is reabsorbed and so half the sodium is saved. If this is inhibited more sodium is excreted.

Acetazolamide ("diamox"), a sulphonamide derivative, is sometimes a useful oral diuretic, but one cannot rely on it being effective in all patients. The usual dosage is 250-400 mg. daily. It causes a metabolic acidosis from which it takes about three days to recover, so it should not be given at intervals shorter than this. Braveman *et al.* (1957) found that when all treatment was kept the same except that 250 mg. of diamox daily by mouth was substituted for mercurial diuretics intramuscularly the result was satisfactory for long periods in most of the patients. If all diuretics were stopped the patients gained weight owing to oedema, but improved again when diamox was resumed. Side-effects were not observed. Most workers, however, have found that diamox is not always as effective as this.

Aminometradine ("mictine") is another helpful oral diuretic, but, again, effective only in some patients and sometimes only for a time. It is best given for two or three consecutive days each week, 3 or 4 tablets of 200 mg. daily. It is apt to cause nausea and vomiting.

Amisometradine ("roliction") seemed to Jose and Wood (1958) after most carefully controlled observations a better diuretic and one less apt to cause vomiting. In most of their patients, 400 mg. was given three times a day for two days consecutively and alternately with mersalyl. The increased output lasted over 48 hours rather than the 24 hours after mersalyl, and was sometimes greater on the second and third days after than the first and the second. They concluded that this amount had rather less than half the diuretic strength of a single injection of 2 ml. of mersalyl. They did not observe any toxic results, though nausea and rarely skin reactions, and once leucopenia, have been reported. It produces an equal excretion of sodium and chloride and some increased potassium loss. In some other patients the same amount given continuously for ten days produced a good diuretic response without any side-effects.

Urea was used as a diuretic a long time ago, but recent reports have drawn attention to its value in patients who are proving resistant. Papp and Shirley Smith (1957) have tested it carefully on patients with chronic heart failure, in several of whom mercurial diuretics had become ineffective. They gave 15 g. of urea dissolved in 60 ml. of water three times a day, and most patients could take this without anorexia and vomiting. Those who found the sickly taste intolerable were able to take it dissolved in grapefruit juice. These physicians found great improvement in more than half of 17 patients, and in a few it had been effective for years and had enabled them to resume some quiet activity.

Chlorothiazide ("saluric"), an aromatic sulphonamide derivative, has been introduced more recently and promises to be a most effective oral diuretic. Like the mercurial diuretics, it acts mainly by inhibition of tubular reabsorption, but adds to its effect by inhibiting carbonic anhydrase. At first, 0.5 g. should be given four times a day for three or four days, and this amount may prove enough. It leads to a loss of potassium, and, if it is given in full doses for long, potassium 2-5 g. should be given daily. It has not perhaps been used long enough to find out its drawbacks, but it appears to be a most effective oral diuretic and can sometimes be tried in place of the mercurial diuretics intramuscularly.

Sodium Restriction

Limitation of salt has been mentioned as a treatment that helps without causing trouble or discomfort to the patient. Strict limitation of the sodium intake to 500 mg. is exceedingly effective and may enable the doctor to control congestive heart failure in a way that would otherwise be impossible. It should not be used as a routine at the start so long as simpler methods of treatment prove effective, because it is always a trouble and often a serious inconvenience to the patient and may make his food unattractive to him. When it is necessary, this strict limitation of sodium

can generally be carried out better and more intelligently by the patient if he has been taught in hospital by the dietitian how to do this. It can, however, be started without this, and there are many detailed instructions available (e.g., Wood, 1956). Shortly, the principles are that no salt should be taken at meals and no salt or baking powder used in the cooking, and that the patient must learn about the foods that contain sodium. Most meats can be taken, but not bacon, ham, sausages, salted beef, duck, grouse, meat paste, or tinned meats. All fish can be taken except kippers, bloaters, smoked haddock, smoked salmon, lobster, crab, shell-fish, tinned fish, and fish paste. Most vegetables can be taken, but not beetroot, carrot, spinach, celery, or watercress; and most fruit except figs and sultanas.

The main difficulty arises with bread, butter, and cheese. Fresh unsalted butter can be taken or the salt should be removed from ordinary butter by mashing it in luke-warm water and pouring away the water three times. Unsalted cream cheese, lard, suet, and olive oil are allowed, but ordinary butter, margarine, and most bought cheeses must be avoided. Milk should be limited to a pint (570 ml.) a day, including what is used in cooking, and will go further if it is diluted with half its volume of water. Ordinary bread, cakes, pastries, and cornflakes must be avoided, but oatmeal, macaroni, rice, and sago are allowed. It is becoming less difficult to buy special salt-free bread, and hospital almoners may be able to help by suggesting where it can be obtained. Home-made bread, cakes, and pastries can be taken provided they are made without salt or baking powder.

Drinks can be taken normally except for cocoa, "bovril," and milk beverages. Condiments can be used normally except for salt: "neo-selaron," which is made with potassium, can be taken and serves as a palatable substitute for some patients.

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THE DIABETIC SCHOOL-LEAVER

Because, in the experience of the medical advisory committee of the British Diabetic Association, school-leaving reports do not always give a true indication of what a diabetic child can do, the committee has prepared a note on the subject for inclusion in leaving reports. The committee's note is as follows:

"The great majority of occupations can safely be undertaken by the young diabetic, and it is, therefore, easier to consider those which are unsuitable. Regular meals and insulin injections form the basis of good control of diabetes, and occupations in which these cannot reasonably be maintained are unsuitable. This will rule out most forms of shift work, jobs in which the hours of work and mealtimes are subject to considerable variation, and occupations in which physical exertion is severe and also variable. The other group of occupations unsuitable for diabetics on insulin is that in which the consequences of a hypoglycaemic attack may be serious to themselves or other people. In this category must be included the driving of public transport vehicles, such as trains and buses, signal operating, steeple-jacking, window-cleaning, and occupations connected with dangerous machinery. Diabetics are not accepted by the fighting Services, and the Merchant Service is not well suited to the requirements of the diabetic.

"These suggestions apply to 'average' diabetics—using the term 'average' to cover both severity of the diabetes and the patient's intelligence and understanding of his condition. There are a number of diabetics engaged in some at least of the occupations listed above and carrying out their duties both safely and successfully."