Drug Treatment of Disease

ACUTE AND CHRONIC GLOMERULAR NEPHRITIS

BY

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ACUTE GLOMERULAR NEPHRITIS

There is no known way to prevent acute glomerular nephritis from developing into chronic glomerular nephritis, though at one time antihistamine and nitrogen mustard derivatives were given for this purpose. The aim of treatment is to prevent the patient dying from the three immediate complications of the disease—namely, acute renal failure, heart failure, and hypertensive encephalopathy.

It is customary to keep the patient in bed, and in most cases this induces a brisk diuresis within 24–48 hours. A course of penicillin, 250 mg. twice a day by intramuscular injection for 3–5 days, is begun after swabs from the throat or any obviously infected area have been taken. For the first day no food is given and the intake of fluid is limited to 500 ml. At the end of this time it is usually clear which direction the illness is taking. If the 24-hour urine volume is greater than 1,000 ml., no further dietary or fluid restrictions are necessary; if it is between 500 and 1,000 ml. the intake of fluid is increased by an amount equal to that of the urine excreted, and a low-salt and low-protein diet is given; if the urine volume is below 500 ml. the patient is considered to have acute renal failure. This is not the place to discuss the treatment of that emergency.

Most patients with acute nephritis have heart failure, but this rarely needs special attention. Occasionally acute attacks of left heart failure make it necessary to give digitalis—digoxin $\frac{1}{2}$ to 1 mg. intravenously, followed by 0.25 mg. six-hourly. If there is bradycardia before the administration of digitalis it may be difficult to gauge the dose.

Hypertensive encephalopathy will usually respond to intravenous injection of sodium amobarbitone, 0.3 to 1 g., followed by 0.4 to 0.6 g. six-hourly. Alternatively, sodium thiopentone, 0.1 to 0.5 g., can be used for the initial injection. Hypotensive drugs are also useful, though the patient needs greater supervision; in an emergency, however, 25 mg. of hexamethonium bromide intravenously may be life-saving.

The administration of adrenal steroids and mercurials in acute nephritis is contraindicated. Steroids may precipitate heart failure, aggravate the rise in blood pressure, and delay the onset of the diuresis; they are also ineffective in the treatment of acute renal failure when it is a complication of acute nephritis. Mercurials rarely increase the flow of urine, and the attempt to obtain a diuresis in this way in acute nephritis has little to justify it. After the initial course of penicillin, treatment is continued with phenoxymethylpenicillin (penicillin V), 125 mg. daily by mouth until the proteinuria has ceased.

CHRONIC GLOMERULAR NEPHRITIS

The cause of chronic glomerular nephritis is unknown, but it is a reasonable precaution to put the patient on daily oral penicillin V in the hope that acute

exacerbations after infections with haemolytic streptococci may be avoided. The dose should be 125 mg. once a day indefinitely. But destruction of the renal parenchyma usually proceeds more or less rapidly. As renal function diminishes it is often possible to prevent those acute deteriorations in function which accompany sudden changes in electrolyte and water balance (diarrhoea and vomiting) or blood volume (acute haemorrhage), or which are associated with renal infection. The treatment of acute disturbances of electrolytes, acute haemorrhage, and superimposed renal infections in chronic glomerular nephritis are not discussed here. The following symptoms and complications can sometimes be relieved by drugs.

Gastro-intestinal Symptoms

The patient with anorexia can be helped by frequent small meals, and, when there is an unpleasant ammoniacal halitosis, by frequent mouth washes. The most important advance in the relief of misery in the end stages of chronic renal failure has been the use of chlorpromazine ("largactil") 25–100 mg. by mouth to relieve vomiting. More recently perphenazine ("fentazin"), 2–4 mg. by mouth, has been used with equal success; it is less stupefying than chlorpromazine and is sometimes better for those patients who can still get about. Chlorpromazine may occasionally cause acute hypotension, but with the small intermittent amounts which are given the other complications, such as jaundice and neurological signs, are unusual. It is most useful in helping to relieve apprehension and in reinforcing the effect of other sedative or analgesic drugs.

It is important to avoid treating the constipation of chronic renal failure with magnesium sulphate, for it may cause magnesium intoxication.

Anaemia

The anaemia of chronic renal failure is due principally to depressed erythropoiesis. In advanced cases there may also be haemolysis and occasionally there is iron deficiency from a slow gastro-intestinal haemorrhage or from menorrhagia. Before treating the anaemia it is important to remember that patients with renal failure are often unaffected by moderately severe anaemia. It is therefore unnecessary in many instances to try to treat the anaemia unless the haemoglobin falls below approximately 70%, when it may precipitate cardiac failure. It should also be remembered that in chronic renal failure a rapid rise in the haematocrit (packed cell volume) after a transfusion may cause a sudden deterioration in renal function.

Depressed erythropoiesis can be corrected by transfusion of packed cells or treated with the administration of cobaltous chloride.

Packed red cells are given in small amounts, 100–200 ml. at intervals of two to three days, during which creatinine clearances and the blood urea are

measured. The total number of transfusions needed is determined by their effect on renal function and the haemoglobin concentration. Cobaltous chloride, 100 mg. by mouth or by intramuscular injection, three times a day, has been given with some success, but its side-effects severely limit its use. It has little effect on erythropoiesis unless treatment is continued for over a month, and in the interval there may be vomiting, paraesthesiae, and nerve deafness.

Haemolysis will sometimes respond to the administration of steroids—cortisone 50–100 mg., prednisone 10–20 mg., or triamcinolone 2–4 mg. Iron deficiency is best treated with intramuscular injection of iron ("imferon").

Calcium Deficiency

In prolonged chronic renal failure the intestinal absorption of calcium is diminished, and this may lead to osteomalacia in adults and rickets in children. The bone changes can be reversed by giving large doses of calciferol, 1–3 mg. per day. The dose must be carefully adjusted for each patient. Sometimes even greater quantities of calciferol are needed, but it is essential to estimate the plasma calcium at regular intervals and to be alert for symptoms of hypercalcaemia—namely, polyuria, thirst, and weakness.

Hypertension

In chronic renal failure a rapidly rising blood pressure is often the beginning of the end. There is some evidence, however, that if the blood pressure is controlled the deterioration of renal function which usually follows such a rise may be prevented. An attempt to lower the blood pressure must be made when there is malignant hypertension, and it may sometimes be useful in the treatment of hypertensive cardiac failure.

The success of treatment will depend to a great extent on the response of the renal vasculature to the fall in pressure. If there is an accompanying vasodilatation, renal function either will remain unchanged or may improve. If the pressure falls but there is no vasodilatation, renal function will deteriorate. As a rough guide, the dividing line between these two responses seems to be when the blood urea is around 70 to 100 mg. per 100 ml. If the blood urea is greater than this, a fall in blood pressure may cause the renal failure to become worse, and treatment will have to be discontinued. The hypotensive drugs which are least likely to produce this effect are those that lower the pressure gradually. These are reserpine, 0.25–1 mg. daily by mouth, hydralazine, 50–200 mg. daily by mouth, and occasionally chlorpromazine, 25–100 mg. daily by mouth. If these substances do not lower the blood pressure, meprobamate, 5–30 mg. daily by mouth, or pentolinium tartrate, 6–30 mg. daily subcutaneously or intramuscularly, are also given. Occasionally phentolamine, 50–100 mg. by mouth, will lower the blood pressure in chronic renal failure in the absence of a phaeochromocytoma.

Hiccups

The inhalation of carbon dioxide and the administration of various antihistamine derivatives continue to be the only treatment of any value for hiccups. Suitable drugs are perphenazine, 2–8 mg. per day by mouth; chlorpromazine, 25–200 mg. per day

by mouth; and meprobamate, 100 mg. four-hourly. In intractable cases phrenic crush may be effective.

Central Nervous System

The treatment of hypertensive encephalopathy has been mentioned earlier. At first sleeplessness can be treated with chloral 0.5 g. at night. Later, barbiturates such as sodium amobarbitone 0.2 to 0.6 g. may be needed. Terminally, sleeplessness, restlessness, and dyspnoea may respond only to large amounts of paraldehyde, 4–8 ml. by intramuscular injection. Sometimes it may be necessary to combine the administration of paraldehyde with that of morphine, chlorpromazine, and a barbiturate before the patient obtains any rest. In some terminal cases the tolerance to opiates and barbiturates is remarkable and is difficult to explain.

Muscular twitches usually appear only in the terminal stages and do not need to be treated specifically unless they cause the patient some distress. They can be subdued temporarily with the intravenous administration of 10% calcium gluconate 10 ml.

Retention of Waste Products and Acidosis

At the present time it is not the custom to try to control the level of blood urea by restriction of protein unless the blood urea is rising rapidly or is greater than about 100 mg. per 100 ml. A temporary reduction in blood urea can be achieved by the use of anabolic steroids, either norethandrolone ("nilevar"), 50 mg. per day by mouth, or norandrostenedione phenylpropionate ("durabolin"), 25 mg. intramuscularly twice a week.

It is also debatable whether the acidosis of chronic glomerular nephritis should be treated. It depends on whether the patient feels any better after treatment. Sodium bicarbonate, 3–9 g. per day, or sodium citrate, 15–30 g. per day, may produce a temporary improvement in general well-being and appetite and diminish headache. Occasionally, however, the patient feels worse, and he may develop cardiac failure. Sodium lactate (1/6 molar) is sometimes given intravenously. Again the result obtained should decide whether to repeat the treatment. Some patients with long-standing acidosis are made acutely ill, and may develop severe vomiting and confusion.

"A problem which faces all Management Committees is that of the storage of medical records. An idea of the magnitude of the task locally [in the Portsmouth Group] can be gathered by the fact that each year there are something like 30,000 admissions and 100,000 new out-patients and casualty records. In 1954 an experiment was undertaken at Saint Mary's Hospital to see if micro-filming would provide a practical answer to the problem. It was found, however, that the photographing of the records would take approximately seven months, and, including the additional indices necessary, would cost something in the nature of £300 per annum. Over a period of, say, seven years this would amount to £2,000, whereas suitable racking to cover the same period could be provided for about £400. Provided, therefore, that there is physical room, economically the storage of original records is much the better proposition. Additionally it is preferable, since medical staff prefer original notes and it is speedier to produce them rather than reproduce from a microfilm in the event of the readmission of a patient. As space was available in Portsmouth it was decided to proceed with racking and abandon the microfilm experiment." (*Report for the Period July 1948 to December 1958, Portsmouth Group Hospital Management Committee.*)