physicians and surgeons who have admitted patients to the ward, and in particular Professor J A Davis for his encouragement.

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Today's Treatment

Diseases of the urinary system

Management of chronic renal failure

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The principal diseases responsible for chronic renal failure in Britain are glomerulonephritis, pyelonephritis, polycystic kidney disease, nephrosclerosis, and analgesic nephropathy. In respect of management it is important to realise that there is considerable variation in the rate at which primary renal disorders usually progress. Pyelonephritis tends to progress more slowly than glomerulonephritis, polycystic kidney disease also progresses slowly, and analgesic nephropathy may even improve provided analgesic abuse ceases. Depending on the nature of the primary disorder and on the efficiency with which reversible factors such as hypertension are controlled, the time taken for renal function to fall from the range of moderate impairment to potentially terminal may vary from a few weeks or months to many years.

Rate of progression

The rate of progression may conveniently be followed by relatively simple measurements. Serum creatinine concentration (normal range 35-115 $\mu\text{mol/l}$ (0.4-1.3 mg/100 ml)) is a better index of function than the serum urea concentration (normal range 2.5-7.0 mmol/l (15-42 mg/100 ml)) and is much simpler to obtain than serial measurements of glomerular filtration rate (GFR) (normal value 90-125 ml/min). Generally a rise in the serum creatinine concentration to between 150 and 250 $\mu\text{mol/l}$ (1.6-2.8 mg/100 ml) indicates that the GFR has fallen to 50-25 ml/min; 250-700 $\mu\text{mol/l}$ (2.8-7.9 mg/100 ml) corresponds with a GFR between 25 and 10 ml/min; while a serum creatinine concentration of 700 $\mu\text{mol/l}$ (7.9 mg/100 ml) or higher indicates that the GFR is likely to be below 10 ml/min.

Nearly all patients with slowly progressive renal failure have no symptoms related to the renal insufficiency per se until it is quite far advanced—that is, until renal function is reduced to 25% of normal or less. They may, of course, have symptoms related to accompanying problems such as fluid retention and hypertension. Until, therefore, the GFR has fallen to about 25-30 ml/min the management of the patient is essentially a question of identifying and correcting any reversible factors. As the GFR falls to between 30 and 5 ml/min it is also necessary to introduce dietary management and other measures. Once the GFR has fallen to around 5 ml/min it is imperative to take active steps to have the patient assessed for suitability for maintenance dialysis and transplantation if this has not already been done, and to make appropriate plans such as the creation of an arteriovenous fistula if the patient is suitable.

Reversible factors

The most important of the reversible factors in patients with chronic renal failure, no matter what the level of renal function, are as follows.

Obstruction within the urinary passages due, for example, to prostatic enlargement or renal stones, should always be considered. Clinical appraisal should usually be augmented by radiography. High-dose infusion pyelography has obviated the need in most cases for retrograde pyelography even in patients in whom renal function is seriously impaired.

Analgesic abuse—A careful history should always be taken about analgesic abuse and if present the patient must be advised that continued analgesics, particularly those containing phenacetin, are harmful.

Potentially nephrotoxic drugs—Other potentially nephrotoxic drugs that should be considered both as a possible cause and as an aggravating factor in patients with renal failure include tetracycline, methicillin, amphotericin B, neomycin, gold, and cephaloridine (especially if frusemide is also being given in high dosage).

Dehydration and hyponatraemia—Correction of any water or sodium deficit is extremely important since dehydration and hyponatraemia will further prejudice renal function, often severely. Dehydration may result from intercurrent diarrhoea and vomiting; from excessive use of diuretics; during any intercurrent illness, particularly if it has an infective basis; or during hospital admissions

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for surgery if the existence of chronic renal failure is not appreciated. Sodium depletion will commonly occur in association with water depletion, but on some occasions the patient may be sodium depleted even in the presence of water excess. Pronounced degrees of salt and water deficiency will need temporary intravenous replacement treatment; lesser degrees may be corrected by increasing oral fluid intake and by giving extra salt—for instance, as slow sodium tablets.

Hypokalaemia, hypercalcaemia, and hyperuricaemia—Other biochemical abnormalities that can prejudice renal function include hypokalaemia, hypercalcaemia, and hyperuricaemia.

Severe uncontrolled hypertension is a very adverse factor in the progression of chronic renal failure, and its management will be discussed later.

Cardiac failure may complicate chronic renal failure, particularly if there is hypertension and associated myocardial ischaemia. Renal perfusion is diminished and renal insufficiency increased. Digoxin dosage must be carefully regulated in such patients otherwise there is danger of toxicity in view of impaired excretion, and diuretic dosage (see below) usually needs to be higher than normal.

Active urinary infection may be present in patients with chronic pyelonephritis, polycystic kidney disease, and analgesic nephropathy and should be treated after determining the drug sensitivity of the organisms, remembering the need to avoid potentially nephrotoxic drugs and to reduce the dosage of drugs that are largely excreted by the kidneys.

Systemic infection, such as an intercurrent pneumonia, also needs treatment. The increased catabolism associated with infection can cause significant deterioration in the biochemical state of the patient.

Dietary aspects

Modification of the dietary protein is seldom necessary until renal insufficiency is relatively far advanced—that is, a GFR around 25 ml/min or less. At this juncture nausea and vomiting tend to develop and considerable symptomatic improvement can often follow restriction of dietary protein. A useful general guide is to reduce the intake gradually to around 0.5 g nitrogen/kg body weight—that is, a 35–40 g protein diet for most individuals. With such a level there is general agreement that negative nitrogen balance is unlikely to occur. If there is a continuing high urinary protein loss the restriction of dietary protein need not be so great. Even lower protein intakes—for example, down to 0.3 g nitrogen/kg body weight are sometimes needed in severe cases of renal failure to control troublesome symptoms but a negative nitrogen balance is likely to ensue with such levels of intake given time. As the dietary protein intake falls it is imperative to ensure that an adequate energy intake (10–45 MJ; 2500 kcal) and an adequate intake of vitamins is maintained. Non-protein energy is usefully obtained from such foods as cream, butter, sugar and jams, and from special products such as liquid glucose, dextrin, and Calonutrin (lactose and sucrose-free mono- and poly-saccharide), which are available on prescription. It is also important to use so far as possible protein foods of high biological value—that is, with a high content of essential amino-acids. With very low protein intakes amino-acid supplementation may be desirable.

The decision to put a patient on a considerably restricted protein diet should be made only after full consideration, including assessment as to the likely duration of survival. For example, in an elderly patient for whom maintenance dialysis is not envisaged and whose duration of life is limited, a relatively simple approach to dietary management is desirable. The patient should be advised that the main protein-containing items in the diet are meats, fish, milk, eggs, and cheese and be guided to take half quantities of these foods and, perhaps later, third quantities. Adequate symptomatic control can often be achieved with such a simple approach.

The sodium content of the diet may need to be reduced if the patient tends to retain fluid or is severely hypertensive. In the first instance salt should not be added at table and if this proves an insufficient restriction the salt used in cooking should be curtailed and the content of the diet modified. It is possible to reduce the sodium intake to 40 mmol(mEq)/day

and yet retain palatability, but stricter restriction is difficult without loss of palatability and therefore a risk of losing patient compliance. The need for continuing sodium restriction requires careful monitoring in patients receiving diuretics, otherwise a salt depletion state may be unwittingly produced.

If the patient is a salt loser, as may happen in chronic pyelonephritis or analgesic nephropathy, the dietary salt intake may need augmenting—for instance, with slow sodium tablets containing 10 mmol(mEq) of sodium and of chloride. The presence of postural hypotension, unexplained tiredness, and muscle cramps should alert the doctor to the possibility of sodium depletion.

Most patients with chronic renal failure retain the ability to excrete adequate amounts of potassium at least until the renal failure is very far advanced. They are at risk, however, of hyperkalaemia if they inadvertently take a sudden considerable dietary excess of potassium, if they receive potassium supplements, or if they receive potassium-sparing diuretics such as spironolactone. It should also be remembered that in many commercial salt substitutes the sodium has been replaced with potassium. Substances rich in potassium include fresh fruit juices, soft fruit, chocolate, brown sugar, potatoes (including crisps), instant coffee, evaporated and condensed milk, and Coca Cola.

Hyperkalaemia may be corrected by ingesting an ion exchange resin either in the calcium or the sodium phase or, in an emergency, by the intravenous administration of concentrated glucose and soluble insulin, sodium bicarbonate to correct acidosis, and calcium gluconate to minimise the effect of the high potassium on the heart.

Restriction of dietary phosphate is now commonly advocated as a contribution to lessening the hyperphosphataemia of renal failure and thereby reducing the likelihood of skeletal changes from secondary hyperparathyroidism. Foods rich in phosphorus include dairy products, liver, kidney, and certain fish.

Skilled dietetic advice is invaluable in achieving and maintaining satisfactory dietary management of patients with chronic renal failure, particularly if a protracted period of management is envisaged.

Acidosis

The metabolic acidosis of chronic renal failure seldom produces symptoms until relatively severe, and few patients need sodium bicarbonate (commonly 0.5 g twice or thrice daily) until the plasma bicarbonate level is below 15 mmol (mEq)/l. When hyperventilation does develop, symptomatic control should be the aim rather than return to normal of the biochemical indices of acid-base balance.

The administered sodium may prejudice blood pressure control and correction of the acidosis may produce some evidence of tetany due to reduction of the amount of calcium in the blood present in ionised form.

Fluid retention

The importance of ensuring an adequate fluid intake to balance the polyuria of chronic renal failure has already been emphasised. Should the patient become oedematous, due either to cardiac failure or to a severe proteinuria causing the nephrotic syndrome, correction can usually be achieved with diuretics. Thiazide diuretics are ineffective once the GFR has fallen to 15–20 ml/min but frusemide, ethacrynic acid, bumetanide, and metolazone remain effective if a higher dosage is used than in patients with normal renal function. Of these very powerful diuretics, frusemide is the one most generally advocated in Britain. A convenient approach is to double the dose of frusemide from the orthodox range of 40–80 mg/day until adequate result is achieved. Many patients with chronic renal failure will need 250–500 mg of frusemide daily to correct

oedema; some will need even more. The advent of 500 mg tablets of frusemide has been very convenient for such patients. In an emergency—for instance, acute left ventricular failure with pulmonary oedema—intravenous frusemide is recommended, and the dosage may have to be as great as 250 mg given very slowly. If diuretics are employed it is important, as mentioned earlier, not to over-correct the condition and so produce water and salt depletion, and careful clinical supervision should be maintained with reduction of dosage to the minimum needed to keep the patient in normal fluid balance.

Potassium supplementation is not invariably needed despite the high dosage of diuretics that is often necessary. There is indeed some danger of hyperkalaemia due to impaired ability of the kidney to excrete potassium. If the dietary intake of potassium is not deficient and if there is no diarrhoea or malabsorption the patient may be tried without potassium supplements; if potassium supplements are given a careful watch should be maintained on the serum potassium concentrations. Particular attention should be paid to the potassium concentrations in patients receiving digoxin since hypokalaemia increases the sensitivity of the heart to digoxin.

Blood pressure control

It is of paramount importance to correct severe hypertension in patients with chronic renal disease. A useful aim is to ensure that the diastolic blood pressure is not above 100 mm Hg.

There are two major causes for the hypertension—namely, sodium and water retention and increased secretion of renin. These factors will be discussed more fully in another article in this series. At this juncture, however, it is emphasised that adequate control of blood pressure is unlikely to be achieved if salt and water overload is not corrected with appropriate dietary modification and diuretics.

Drug treatment of hypertension in renal failure has improved considerably in the past few years. Despite some initial anxieties, the beta-blocker drugs have proved valuable. In my experience most patients with renal hypertension can now be controlled using a beta-blocker drug alone or in combination with a modest dose of methyl dopa or hydralazine, or both. Occasional patients will need other antihypertensive agents including clonidine, prazosin, and minoxidil. In an emergency—for example, diastolic blood pressure 130 mm Hg or above, intravenous diazoxide has no equal. The drug is given as a bolus in 10 or 15 seconds in a dose of 150–300 mg. The effect is relatively short-lived (4–8 hours) but is a useful preliminary to control with oral treatment.

Anaemia

Generally the degree of anaemia will increase as chronic renal failure progresses, and haematocrit values around 20 are commonly seen when the GFR is in the 5–10 ml/min range. Patients with polycystic kidney disease, however, commonly maintain rather higher haemoglobin concentrations despite severe renal failure. On the other hand, patients with kidney failure due to myeloma will have even greater degrees of anaemia.

The anaemia is basically due to depression of bone marrow activity by the abnormal biochemical environment of uraemia and to deficiency of erythropoietin production by the diseased kidneys. The anaemia is generally refractory to haematinics unless there is a coincidental deficiency of iron, folate, or vitamin B₁₂, which should always be borne in mind. Some improvement in the anaemia may follow the use of androgens or cobalt chloride, but neither of these preparations is free from danger and their use cannot be generally advocated. The possible value of oral histidine supplements is still being assessed.

Blood transfusions should be used with great discretion in patients with chronic renal failure because of the potential

hazard of serum hepatitis with its subsequent serious implications for renal dialysis units, the possibility that cytotoxic antibodies may develop prejudicing future renal transplantation, and the risk of haemosiderosis.

Renal osteodystrophy

The complex problems of renal osteodystrophy are discussed more fully in another article in this series. With regard to management there are two main approaches—namely, the control of hyperphosphataemia and correction of deficient calcium absorption. Restriction of dietary phosphate has already been referred to and hyperphosphataemia may be further controlled by taking a phosphate binder such as aluminium hydroxide either as a liquid gel (Aludrox) in a dosage around 100 ml/day or in powder form in capsules (Alucap). Calcium balance may be improved by ingesting 20 g calcium carbonate daily and also, once the hyperphosphataemia has been corrected, by an active preparation of vitamin D such as 1,25-dihydroxycholecalciferol or its more readily available analogue 1-alpha-hydroxycholecalciferol.

Symptomatic measures

Anti-emetic preparations such as metoclopramide (Maxolon) are extremely useful in controlling the nausea and vomiting of uraemia, although it may be possible to dispense with their use once a low-protein diet has been instituted. Pruritus, which can be very troublesome in advanced renal failure, may be alleviated in some patients with an anti-pruritic cream. Nitrazepam is a suitable preparation for relieving insomnia in patients with renal failure.

General management

Most patients with chronic renal failure, and their relatives, are now aware of the limited prognosis and of the possibility of maintenance dialysis and renal transplantation. It is important that the suitability of the patient for such treatment is assessed in time by referral to a renal unit before the renal failure is far advanced. The care of the patient who does not achieve a place on a maintenance dialysis programme is a demanding exercise requiring the skillful use of symptomatic measures in an atmosphere of trust and understanding.

ONE HUNDRED YEARS AGO A new and substantial addition to the Hospital for Sick Children, Great Ormond Street, consisting of an extra wing, was formally opened to the public on July 2nd, a considerable number of those interested in the charity visiting the building during the day. The wing is an isolated building, erected from designs by Mr E M Barry, RA, and consists of four wards containing sixteen beds, viz, eight on the first floor, and eight on the second, each having a ward-kitchen, bath-room, and linen store-room, also nurses' day-room and dormitories. Open windows are depended upon for fresh air, but a simple system of tube-ventilation is super-added, in order to regulate the admission of cold air in the winter. The roof of the building is laid with asphalt, to form an airing-ground for convalescent patients, while the large open space at the rear is being prepared as a recreation-ground and garden, which will add much to the comfort and welfare of both nurses and children. The funds for carrying out this latter scheme are yet required, the expenses of furnishing the new wing, which also includes a mortuary and museum, having yet to be met. The portion of the hospital newly opened is known as the North Wing; but it is in contemplation to erect a South Wing, containing wards for about eighty more patients, when funds for such a purpose are forthcoming, and rooms for the staff and other officers. (*British Medical Journal*, 1877.)