Current Practice

GROWING POINTS

Renal Disease—II*

J. S. CAMERON,† B.SC., M.D., M.R.C.P.

Chronic Renal Failure

In Britain about 7,000 people die every year with uraemia. This makes chronic renal failure the major problem facing nephrologists. Three advances have been made in the last few years in coping with the problem—namely, ultra-low-protein diets, intermittent dialysis, and renal transplantation.

Dietary Management

Protein restriction has been one of the cornerstones of the conservative management of chronic renal failure for many years. It has also long been realized that the level of blood urea depends upon the intake of protein (Fig. 4). At very low filtration rates small differences in the intake of protein make very large differences in the level of blood urea, and in its turn this affects haemopoiesis and the general well-being of the patient.

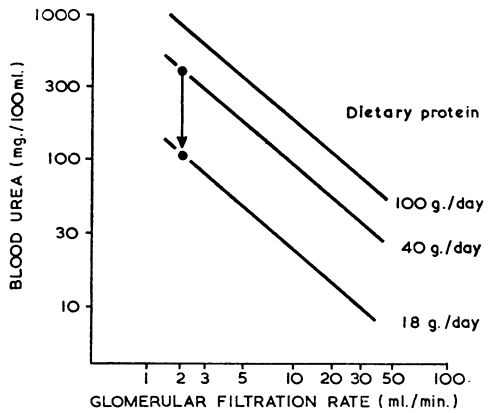

FIG. 4.—The relation between glomerular filtration rate and blood-urea levels at various protein intakes. At a glomerular filtration rate of 2 ml./min. reduction of protein intake from 40 g. to 18 g./day reduces the blood urea to levels where well-being and normal blood formation are possible.

The recent advance has been to use very low-protein diets, containing 20 g. of protein or less per day, supplemented if necessary with essential amino-acids. In this fashion it has been possible to keep patients with glomerular filtration rates of 1.5 to 5 ml./minute reasonably well for many months or even a year or more. The disadvantages of this type of management are that some patients may become very emaciated and protein-depleted (despite the quality of the protein received in the diet) and acidotic because of the high sulphur content of the protein.

Dialysis

Patients in chronic renal failure often present with an acute worsening of their uraemia ("acute on chronic" renal failure), particularly if they become depleted of salt or hypotensive, or develop an acute urinary infection. It is now standard treatment to offer such patients at least one peritoneal dialysis while the exacerbating condition is treated, and they can often be saved for months or even years of useful life. This is particularly true of patients with polycystic kidneys.

More recently haemodialysis has come to play a much larger part in the management of chronic renal failure. If the patient's intake of salt and water is restricted and he is given a high-calorie diet containing moderate amounts of protein (60 g./day)

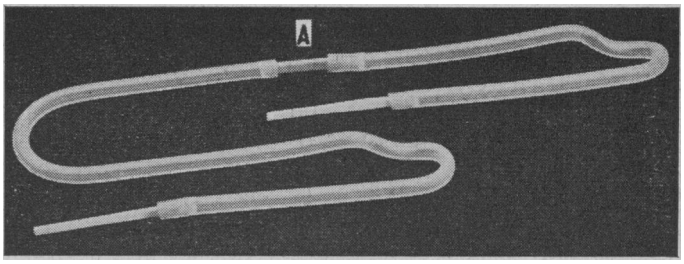

FIG. 5.—A modern Teflon-Silastic "single break" arteriovenous shunt. The vessel tips are Teflon, the tubing Silastic. The joints are simply etched Teflon gripped by the Silastic. The shunt is buried in the arm up to the step in the tubing, and the external part may be broken at A for connexion to the artificial kidney.

it is possible by performing dialysis twice a week not only to keep him alive but to return him to virtually normal health. One initial problem was to provide access to the blood-stream for the twice-weekly dialysis; this has been solved by the introduction of the Teflon–Silastic arteriovenous shunt, which is opened for each dialysis (Fig. 5). The situation is not yet ideal, since the average life of the shunt is only about nine months at best, and the number of potential sites is limited.

The type of artificial kidney used for acute renal failure is quite unsuitable for chronic dialysis. The priming volume is large, necessitating the use of blood for each dialysis. This is not only expensive and inconvenient but leads to the production of antibodies in the patient's blood. Use is made, therefore, of a kidney which has a small priming volume and allows saline to be used. The Kiil kidney is the commonest model at present. The blood passes dialysate over flat Cellophane membranes in the grooves in two boards (Fig. 6). At the end of each dialysis blood in the artificial kidney is tipped back into the patient, and thus the transfusion requirements are low. No blood pump is needed. The whole process can be monitored automatically overnight. Small volume coil kidneys are also being investigated ("Minicoil," "Chron-a-coil"), but these have the major disadvantage that a blood pump is usually required.

Many very ill patients can be successfully treated in this way, even those with malignant hypertension. The blood-pressure can usually be controlled by restriction of salt, but in a few instances nephrectomy has been performed. At present younger adults of stable personality with family responsibilities

* Part I appeared in the issue of 1 October (p. 811).
† Senior Lecturer in Medicine, Guy's Hospital, London S.E.1.

are the main group considered for dialysis, but as the number of dialysis units increases other groups may be considered. From being just an interesting experiment, intermittent dialysis has now become an established advance in therapy in only a few years. The problem now is to find the money—and particularly the staff—to provide this service to the large group of patients who might benefit from it.

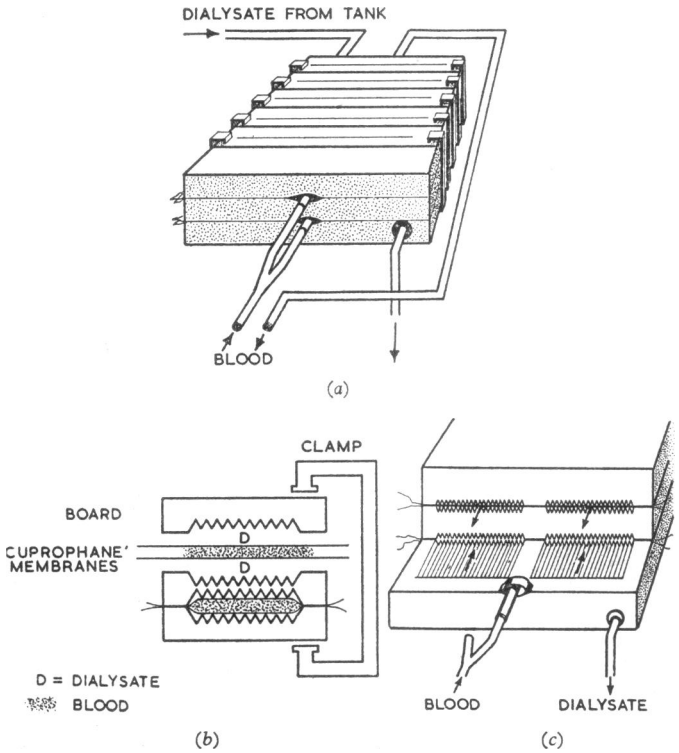

FIG. 6 (*a*).—A two-layer Kiil artificial kidney. This is a "flat plate" type of kidney, which is assembled sterile before use from the boards and membranes. These are clamped together in a stack. (*b*) The surface area is 1.2 sq. metre but it needs only 75 ml. of saline for priming the boards. Blood flows along the membrane through the kidney while the dialysate flows in the opposite direction in grooves in the kidney boards (*c*).

Development in this field has been rapid and will continue. The Kiil kidney is very clumsy, and more compact models can be expected. Home dialysis is under investigation and is promising for some patients. Chronic peritoneal dialysis is being tried at the moment, but the problem of repeated access to the peritoneum has not yet been solved.

Renal Transplantation

At present a mood of cautious optimism is reasserting itself in transplantation, which is potentially the most useful treatment for chronic renal failure. The surgical problems of transplanting the kidney, though not small, have now been solved. The problem is the body's violent rejection of any tissue recognizable as foreign. Two sources of kidneys are available.

(1) Live donors, who may be divided into close relatives (father, mother, brother, or sister), and distant relatives or non-relatives.

(2) Cadaver kidneys, removed as soon as possible after death. To these may be added the possibility of heterotransplanted kidneys from other species—for example, apes.

The patient's condition must be rendered normal by dialysis before transplantation; he may be very ill and will require a minimum of 4–6 dialyses. During and after the operation an attempt is made to suppress the rejection of the transplanted kidney. This usually takes the form of continuous immunosuppressive therapy by drugs—the ones most commonly used being azathioprine ("Imuran") and prednisolone. If rejection is likely or actual immunosuppression is reinforced with more prednisolone or actinomycin. Other methods include splenectomy and thymectomy at the time of transplantation and irradiation. It is very important to recognize the signs of clinical rejection early: perhaps the most useful is an increased excretion of white cells in the urine.

Analysis of survivors from renal transplantation, and of tissue antibodies developed in persons who have been transfused or received a graft, indicates that the major antigens by which tissue is "recognized" and rejected are small in number—probably only two or three. The major problem in transplantation is how to develop techniques by which individual donors and recipients can be "matched" with respect to their antigens to increase the chances of a successful graft. If the major antigen groups are compatible then immunosuppression can cope with the weaker antibodies.

This is illustrated by the much better survival of live-donor grafts from close relatives than grafts from others. Up to 75% of grafts from close relatives survive for one year, and 60% for two years or more after operation and will probably continue. Survival of grafts from other live donors is no better than that of cadaver grafts (40%), and hence the former type of graft is probably no longer justified in view of the sacrifice involved.

The second major problem in transplantation is the preservation of organs. At the moment transplantation of a cadaver kidney is followed by a variable period of acute renal failure before the graft begins to function. In contrast a liver-donor kidney should begin to work immediately. Techniques are needed to preserve organs in a fresh viable state for subsequent use at a time determined by the surgeon and not by the fortuitous death of a donor.

At the moment it is impossible to say what the relation between chronic dialysis and transplantation as alternative treatments will be. A small proportion of patients are unsuitable for transplantation and will probably remain so—for example, those with renal failure due to malformed urinary tracts or to severe autoimmune disease such as systemic lupus erythematosus.

Though the advances made in the treatment and palliation of terminal renal failure are impressive, it must not be overlooked that we are dealing with the end results of prolonged and often silent renal disease. The satisfaction of maintaining life in a small number of patients with renal failure should not distract us from the ultimate problems: the early diagnosis and *prevention* of juvenile pyelonephritis and the nature of glomerulonephritis in all its forms.

(*To be concluded in the next issue*)

"Obstetrics in General Practice."—This book of collected articles from the "Current Practice" section of the *B.M.J.* is available from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1. Price 30s.