Current Practice

GROWING POINTS

Renal Disease—I

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It is of course impossible in an article of this length to review all the growing points in the study of renal disease at the moment. My choice has been to discuss, first, advances in the fields of acute and chronic renal failure; and then to consider nephritis, the nephrotic syndrome, and related topics.

Recent progress has rested largely on two factors. First, technical advances, which have enabled the principle of dialysis to be applied to treating acute and chronic renal failure. Another major technical advance has been the exploitation of safe biopsy of the kidney. The second factor has been the application to clinical medicine of biochemical and physiological knowledge, particularly the former. No other branch of medicine is at the moment so dependent for its daily conduct upon applied biochemistry as the study of renal disease.

Acute Renal Failure

Immediately after the second world war over 90% of patients with acute renal failure died. Now only about one-quarter of such patients die. The mortality today reflects mainly the general condition of the patient and the precipitating causes. Renal ischaemia, trauma, hypotension, septicaemia, haemoglobin circulating free in the blood-stream, jaundice, hypoxia, and various chemicals toxic to the renal tubular cells are all known to precipitate acute renal failure, and are additive in their effect on the kidney. Young patients have a better prognosis than the aged, and obstetric patients or those with acute renal failure due mainly to nephrotoxic substances usually recover. But patients with severe trauma, hypotension, or infection—such as battle casualties and other accidents—or those with post-operative complications, still have a mortality rate of over 50%.

Recent studies of the functional disturbances in acute renal failure and the histological appearance of the kidney have shown a striking contrast: the almost complete cessation of function is associated with very few obvious changes. The glomeruli appear nearly normal, and tubular necrosis, if present, is often patchy or slight. Originally this tubular necrosis was thought to be the common or dominant lesion in acute renal failure, and now that it is known to be somewhat rare the simple descriptive term "acute renal failure" is used for this group of patients. Though the blood-flow through the kidney at the beginning of renal failure may be low, when the patient is first seen it is found to be considerable, even if there is complete anuria. Examination of the urine shows that, while tubular function is far from normal, the glomerular filtrate which is being formed is being considerably modified by the tubules. Whether the lesion in acute renal failure is glomerular, and how it comes about, are still unknown.

Diagnosis

This ignorance of the mechanism of acute renal failure has not, fortunately, hampered clinical management. The first problem is early diagnosis. The precipitating circumstances have already been discussed. In a patient with a rising blood urea acute oliguric renal failure must be distinguished from acute worsening of chronic renal failure and from oliguria due to dehydration.

The most useful single observation in distinguishing acute from chronic renal failure is to find shrunken kidneys on a straight abdominal x-ray film; this also helps to exclude obstruction of the urinary tract as a cause of the oliguria. In dehydration, when the urine is maximally concentrated, the adult cannot excrete the normal products of the breakdown of protein if the urine volume is less than about 30 ml. per hour (730 ml. per day). Accurate, frequent measurements of urinary volume are essential. The fact that the urine volume exceeds 30 ml. per hour may not mean that the kidneys are normal, since oliguria is not always present in renal failure. Indeed, if the urine is dilute renal failure may be present with a urinary volume of 60 ml. per hour or more.

Another guide is to measure the quality of the urine. The best readily available measure is the urinary urea concentration, which is normally at least 1,500 mg./100 ml. in dehydration. Intravenous mannitol is another useful test, since it will produce an immediate diuresis in any oliguric state except that due to established acute renal failure.

Another period when measuring the urinary urea concentration is important is during the prolonged intense diuretic phase which follows the initial oliguric phase of acute renal failure. Patients need very careful management during the early stages of this diuretic phase, because the glomerular filtration rate is still very low. They may die even though their kidneys appear to have "opened up."

Conservative Management

This still depends upon matching fluid intake with fluid output to avoid overhydration during the oliguric phase and dehydration during the diuretic phase. The second principle is to keep the production of urea, acid, and free potassium to a minimum by giving the patient a high-calorie diet containing little or no protein. This is usually done by feeding carbohydrate alone—such as pure glucose. Fat has proved troublesome for patients to take, and in spite of its higher calorific value is little used now. If the patient is too ill to eat, very strong (30%) glucose solutions can be infused for long periods into peripheral veins. This has been made possible by the use of small quantities of heparin and hydrocortisone in the solution; these act locally and postpone the thrombosis caused by the concentrated glucose solution, which acts as an irritant. In this way the

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insertion of a catheter into the vena cava may be avoided—a great advantage, since the end may be the site of septic thrombi and lead to pulmonary embolism and infarction.

When conservative management fails to prevent a rise in the levels of urea, acid, and potassium in the plasma, or when the patient's state is found to be grave when he is first seen, dialysis is now standard treatment. Rather than waiting for the patient to worsen, or to become seriously ill, the tendency is to resort to dialysis at an early stage, when the level of blood urea is comparatively low (about 100 mg./100 ml. in children, and 200 mg./100 ml. in adults). Early dialysis is particularly important if the blood urea is rising rapidly—for example, 60 mg./100 ml./day or more—the so-called “hyper-catabolic” renal failure. Once dialysis has been begun it is usually carried out daily or continuously to keep the blood chemistry near normal limits. The patient is well, is allowed a relatively normal diet and fluid intake (the excess urea or water being removed by the dialysis), and is free of the more dangerous complications of renal failure—namely, infection and bleeding. It is often necessary to continue dialysis for three or four weeks.

Principles of Dialysis

Dialysis involves the exchange of solute, such as Na ions, K ions, glucose, or urea, across a membrane. The membrane may be a natural one, perfused *in situ* by blood, as in peritoneal dialysis; or a man-made one (cellophane), in which case the blood must be circulated outside the body to perfuse the membrane. The cellophane membrane does not permit either cells or protein to leak from the blood, or bacteria to enter. The peritoneum, on the other hand, is less selective, and so protein may be lost and bacteria enter through this route.

In renal failure the body poisons its own internal environment with products of catabolism, particularly of protein catabolism. The problem is to return the composition of the body fluids (represented here by the blood) towards their normal state. The main troubles in renal failure are an excess of urea, acid (H ions), and potassium, all of which can be measured easily, and many other products of metabolism about which we know little. If blood is separated by a membrane through which all these substances can diffuse, from a solution containing none of them but otherwise having the ideal composition of extracellular fluid, then there will be a net transfer of all these products of catabolism down the concentration gradient out of the body.

The rate of transfer depends mainly on: (1) the difference between the concentrations on either side of the membrane; (2) the area of the membrane; and (3) the blood-flow. Ideal conditions are therefore a large flow of blood in a very thin film over a membrane of very large area, with fresh solution provided continuously on the other side.

The area of the artificial kidney membrane can be varied at will; the problem is to keep it at a feasible size while the blood is presented at a high flow rate in a very thin film. With peritoneal dialysis neither the blood-flow nor the area of membrane can be altered. All that can be done is to provide fresh solution as fast as possible. If this solution is changed rapidly, and contains a great deal more glucose than can be absorbed by the patient, water will transfer from the blood faster than it enters because of the osmotic pressure of the glucose. In this way water may be removed from the patient's body.

Peritoneal Dialysis

Peritoneal dialysis was first performed in animals in 1877. Few people were interested in the technique, however, because it proved difficult to enter the peritoneum without infection, while the materials available were not suitable and were difficult

to sterilize. The recent development of sterile polyvinyl chloride tubing, non-irritant nylon catheters for introduction into the peritoneal cavity, and commercially available cheap fluids have now made the technique practicable. Thus today peritoneal dialysis is extraordinarily easy to perform.

The patient requires no preparation except that his bladder should be emptied beforehand. Local anaesthetic is injected into the abdominal wall down to the peritoneum, and the catheter (Fig. 1) is inserted through a nick in the skin. The best site is in the midline, because it is avascular and subcutaneous fluid tracking is limited, but any site is possible. An inflow tube is then set up (Fig. 2, a, b). A litre of fluid warmed to 40° C. is run into the peritoneal cavity, and then allowed to drain. It is not necessary to leave the fluid in to equilibrate, the limiting factor being how many litres per hour (usually 2 or 3) can be run in and withdrawn. Dialysis is continued until the blood chemistry approaches normal. Usually this takes about 36 hours, but with very high levels of urea in the blood a longer period may be required. Thereafter, dialysis is carried out intermittently, the catheter is left *in situ* (Fig 2a), and the patient is encouraged to be up and about and to eat and drink fairly normally. Food intake is important, since protein is lost from the peritoneum.

By using strong glucose solution (6 g./100 ml.) up to 1,700 ml. of fluid can be drained from the peritoneal cavity for every litre run in. Hence it is possible to control the patient's fluid balance even in the presence of anuria. Two to three weeks' daily dialysis is often necessary, and should be continued well into the diuretic phase. During the diuretic phase, also, the intake of fluid can be supplemented by the intraperitoneal route. If the patient finds it difficult to drink the very large volumes

FIG. 1.—Peritoneal dialysis: the catheter used (McGaw “Trocath”). For insertion the nylon catheter (ii) is mounted on the metal stylet (i). Just visible are the multiple perforations at the peritoneal (curved) end of the catheter. The stylet is removed and the catheter connected to the fluid supply by the connexion tubing (iii).

(up to 7 litres/day) that may be necessary in this phase the use of fluid which contains no glucose for dialysis will enable water to be transferred to the patient. Bacterial contamination of the peritoneum is common after a week or so, but is normally easy to deal with. Clinical peritonitis is rare.

Haemodialysis

As with peritoneal dialysis, the principles of haemodialysis were known for a long time before advances in materials made the technique clinically useful. The story of Kolff's first application of haemodialysis during the German occupation of Holland is well known, and since then polyvinyl chloride tubing and modern sterilizing techniques have brought easily prepared disposable kidneys into use.

Access to the circulation is usually obtained by taking blood from the radial artery and returning it to the basilic vein. For a single haemodialysis this can be done through simple cannulae introduced into the vessels; these simple cannulae can be kept open for several weeks, but most doctors who perform haemodialysis for acute renal failure usually employ some form of arteriovenous shunt to permit the frequent or daily dialysis which is now customary.

The blood is then passed over a membrane of large area round which the dialysing solution is being pumped. The solution need not be sterile, since the membrane does not permit the passage of even small protein molecules. The commonest "kidney" in use is the Kolff disposable twin-coil model, which employs cellophane coiled on a fibreglass net base to give the maximum surface area (Fig. 3). The coil and tubing are discarded after use. The blood dialyses against the bath fluid and is then returned to the body via the venous cannula. With this "kidney" a pump is required on the tubing coming from

the artery to ensure a good blood-flow. One big disadvantage of the Kolff kidney is the need for 2-3 pints (1-1½ l.) of fresh blood to prime the circuit outside the body, and this blood must of course be cross-matched. Because of this, "kidneys" with a smaller priming volume (which can therefore be filled with saline only) have been used for acute renal failure, but their lower efficiency means that dialysis must be performed for long periods (12-14 hours rather than 5-6 hours) or even continuously.

(a)

(b)

FIG. 2.—The patient (a) had her abdomen opened twice only four days before dialysis was begun. She was dialysed daily for 24 days, using the single catheter placed just right of the midline. The end of the peritoneal catheter and the connecting tube are visible. (b) Shows the very simple connexions of the catheter; it can be disconnected at A between dialyses, but this encourages infection. The inflow and outflow tubing is occluded alternately during dialysis.

FIG. 3.—The Kolff-Travenol "twin coil" kidney. This has a membrane surface area of 1.9 sq. metres and needs 1,000-1,500 ml. of blood for priming. The coil has been opened out to show the layers of its structure—cellophane tubing and nylon net backing.

As discussed above, substances can be transferred into the blood as well as being withdrawn from it by dialysis. It is usual to transfer large quantities of glucose into the patient, because retention of urea by the brain may lead to cerebral oedema if the blood urea is dropped sharply over 4-6 hours. The patient can be dehydrated if required if the pressure within the coil is raised, the net transfer of water being into the bath under these conditions.

Choice of Dialysis in Acute Renal Failure

Peritoneal dialysis can do everything that haemodialysis can do, with the advantages of less trauma, simplicity, speed of setting up, and absence of damage to the blood-vessels. It can be done even in the presence of peritonitis (which it improves) and two or three days after abdominal surgery (Fig. 2). Is there any place left for haemodialysis in the treatment of acute renal failure? The answer is yes, but in only a small number of selected cases. Some patients have dense adhesions from previous peritonitis, but more commonly the state of the abdomen after abdominal surgery may be such that it cannot be used—for example, burst abdomen or fistulae. Here haemodialysis is essential. The role of peritoneal dialysis in the "hypercatabolic" type of renal failure is still being explored, but in three years at Guy's Hospital only one patient has been seen who could not be controlled with intensive peritoneal dialysis alone. Good conservative management and peritoneal dialysis now enable almost any hospital without special facilities to cope with the vast majority of its patients with acute renal failure.

(To be continued in the next issue)

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