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Phenylketonuria: Recommendations of an M.R.C. Conference on the detection and dietary treatment of phenylketonuria (p. 1691). Pamphlet reprints available. Leader on p. 1686.

Kidney Homotransplantation: Mr. W. J. Dempster defines four types of anuria after transplantation and discusses their prevention (p. 1697).

Immunotherapy of Cancer: Professor R. C. Nairn and colleagues report immunization of a patient against her own advanced renal cancer. They discuss therapeutic implications (p. 1702).

Hodgkin's Disease: Nearly 40% of patients with localized Hodgkin's disease, lymphosarcoma, or reticulosarcoma survive as long as the general population (p. 1704).

Pyelonephritis in Children: Report from Czechoslovakia on treatment (p. 1707).

Iron-deficiency Anaemia: Buccopharyngeal lesions and koilonychia are conspicuously absent in anaemic Kenya Africans (p. 1711).

Vitamin-B_{12} Deficiency: In South India skin hyperpigmentation is "practically diagnostic" (p. 1713).

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Ménière's Disease: Drugs used in its treatment and prevention described in "To-day's Drugs" (p. 1719).

Surgical Kidney: Professors J. McMichael and R. Shackman present a case at a postgraduate clinicopathological conference (p. 1724).

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Preventing Rheumatic Fever: "Giving penicillin V . . . may be theoretically perfect but in practice is completely unreal" (p. 1735).

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Letters on the Pool (*Supplement*, p. 319).

New Developments with Artificial Kidney

A "self-service" approach to the artificial kidney is reported by Dr. Stanley Shaldon and his colleagues in a preliminary communication at page 1716 of the *Journal* this week. They describe the case of a patient who enters hospital twice a week in the afternoon, connects himself to an artificial kidney, and after undergoing haemodialysis leaves the following morning. Two catheters have been introduced percutaneously through the same femoral vein into the inferior vena cava. They remain there and are easily accessible to the patient. The authors have trained him to connect himself to the artificial kidney. The dialyses can be performed with the help of a trained nurse, no medical attention being required. The cost of maintaining such a patient is said to be as low as £500 per year.

Haemodialysis was first used experimentally more than fifty years ago. J. J. Abel and colleagues[1] built the first artificial kidney to dialyse the blood of dogs in which nephrectomy had been performed. They used collodion as the semi-permeable membrane and hirudin as anticoagulant. But in the treatment of patients collodion would be unreliable and hirudin unsafe. It was W. J. Kolff,[2] working in a provincial hospital in Holland under the German occupation during the second world war, who had the vision to grasp the value of the newer "cellophane" membranes and the anticoagulant heparin, and he developed the first clinical artificial kidney. Blood from a heparinized patient was led through rotating couplings into a length of cellophane tubing spirally wound on a drum which rotated in a 100-litre bath of dialysing fluid.

In such a system dialysable substances come into passive equilibrium across the membrane as the blood passes along the tubing. The movement of molecules or ions out of or into the blood depends on the gradient of concentrations on either side of the membrane and the quantitative exchange varies with the rate of flow of the blood through the apparatus and the surface area of the membrane. The exchanges that occur are therefore to a large extent determined by the composition of the dialysing fluid. Any dialysable substance not bound to protein and present in the extracellular compartment of the body can be removed in a more or less predictable manner. This applies to such waste products as urea, creatinine, and uric acid. When a substance is in lower concentration in the plasma than in the cells, as is the case with potassium, its absence from the dialysing fluid leads to more complex and less predictable consequences. The presence in the dialysing fluid of sodium, bicarbonate, and chloride ions, in concentrations equal to those in normal plasma, results in correction of abnormally low concentrations in the plasma.

Since the construction of the first artificial kidney for clinical use—the rotating drum type—much has been learnt about the physiological disturbances in renal failure. In particular, the maintenance of water balance has been recognized as of major importance in the management of patients with oliguria. The single commonest cause of death in acute renal failure is overhydration. While careful conservative management of patients will prevent overhydration, once it occurs rapid removal of excess water is possible only by some form of dialysis. Water is extracted from the patient by using hypertonic dialysing solutions with a high concentration of glucose. In the rotating-drum artificial kidney the removal of water is unpredictable, and indeed the patient may take it up. Various artificial kidneys, such as the Skeggs-Leonards, Alwall, and Kolff twin-coil types, enable the removal of water to be both more certain and more rapid.

Dialysis is now commonly applied in the treatment of acute reversible renal failure and is an essential in any specialized centre.[3,4] In the treatment of chronic renal failure it is more debatable, though an occasional patient with a sudden deterioration of renal function may be improved considerably for some weeks or months by one or two dialyses.[5] In the majority of patients with severe renal damage dialysis will result in only temporary improvement.

B. H. Scribner and his colleagues in Seattle[6,7] introduced the use of permanent indwelling arteriovenous cannulae, allowing patients to be repeatedly connected to an artificial kidney. Such an approach was intended for patients in whom irreversible damage to the kidneys left insufficient renal function to maintain life. Once several dialyses over a relatively short period had corrected the disturbances of blood biochemistry the patient could be discharged with the arteriovenous cannula in position to live a normal life, returning about once a week to hospital to be connected to an artificial kidney for periods up to 24 hours. A very small number of patients throughout the world have been kept alive by this technique. The psychological consequences for the patient of being entirely dependent on artificial means of being kept alive are an exceedingly important consideration.

It is too early yet to be certain about the possibilities of the latest developments with this method of treatment. Difficulties such as control of anticoagulation in the coil during a prolonged dialysis may arise, and the danger of infection has to be combated. Damage to the dialysing membrane with repeated use of the coil may not yet be fully assessed. It is, however, a progressive approach to the treatment of severe irreversible renal failure in which the intelligent patient is trained to undertake some of the technical aspects of his own care.

1 Abel, J. J., Rowntree, L. G., and Turner, B. B., *J. Pharmacol. exp. Ther.*, 1914, **5**, 275.
2 Kolff, W. J., and Berk, H. T. J., *Acta med. scand.*, 1944, **117**, 121.
3 See *Brit. med. J.*, 1959, **1**, 772.
4 Ibid., 1960, **2**, 1507.
5 Keleman, W. A., and Kolff, W. J., *Arch. int. Med.*, 1960, **106**, 608.
6 Scribner, B. H., Hegstrom, R. M., and Buri, R., First International Congress of Nephrology, Karger, Basel. New York, 1961.
7 See *Brit. med. J.*, 1963, **1**, 1101.

TREATMENT OF PHENYLKETONURIA

Phenylketonuria, originally discovered by the Norwegian chemist A. Fölling,[1] is one of the large number of inborn errors of human metabolism. It is rare, occurring perhaps in one in 20,000 of the British population. More precise knowledge of general and regional incidence will result from the surveys now being undertaken by most local authorities. While the intelligence of most of the affected patients has been grossly impaired, occasionally an untreated individual has been normal in this respect. Patients with phenylketonuria do not look very different from the ordinary population and the disease can be reliably detected only by means of chemical tests.

The disorder affects the entire metabolism, and organs other than the brain may show evidence of the abnormality. For example, patients tend to be fairer than their siblings and are liable to dermatitis. But the main effect is on the brain. In chronic, untreated cases severe loss of myelin may occur.[2] It is not known for certain over what period in life damage to the brain occurs, though it is reasonable to assume that at birth the infant's brain is functionally and structurally normal. The disease is transmitted in a recessive manner. Like most hereditary metabolic errors phenylketonuria is an enzyme defect. Phenylalanine hydroxylase is either lacking or functionless in the liver.[3] Phenylalanine, an essential amino-acid, is therefore not converted to tyrosine, the level of phenylalanine in the blood becomes high, and there are secondary disturbances of many metabolic processes, some of which are essential to normal function of the brain.

From being something of an obscure curiosity the disease became a focus of attention when a hopeful method of treatment was devised.[4-7] The rationale of the treatment is simple: the quantity of phenylalanine given in the diet is restricted to the bare minimum compatible with wellbeing. For experimental purposes an artificial mixture of amino-acids could be used, but in clinical practice this would be exceedingly expensive, and for general use there are now on the market a number of preparations of