

impairment of sensation over the left side of the body. With the exception of spinal fluid examination, which showed a marked rise in gamma-globulin content, all ancillary investigations were negative.

The sensory nature of the initial post-traumatic symptoms in these cases is worthy of note: signs of initial involvement of afferent pathways from the affected part have characterized other such cases in the literature.

#### Non-specific Infections

Non-specific infections have gradually replaced the epidemic fevers of the nineteenth century as putative aetiological factors in multiple sclerosis, but in fact clinically evident infection of any kind is often entirely lacking in the recent history of early cases. Although Abb and Schaltenbrand (1956) claim to have traced it in more than two-fifths of patients, the figures given by most other workers are much lower. Störtebecker's (1951) claim to have revealed a high incidence of miscellaneous antecedent infections in cases of multiple sclerosis by means of agglutination, antistreptolysin, and antistaphylococcal titres is suggestive, but as yet unconfirmed. Nor—although reliable figures are entirely lacking—has the gradual conquest of the bacterial infections during the past two decades been followed by any apparent decline in the frequency of new cases of multiple sclerosis comparable with that of which we cannot fail to be aware in the case of such frankly post-infective disorders as acute rheumatism or acute nephritis.

Again, occasional cases are impressive.

*Case 90.*—In December, 1949, a 26-year-old woman developed a severe head cold with fever and influenzal symptoms, followed within 24 hours by the sudden appearance of a partial transverse spinal-cord lesion at the mid-dorsal level. This improved rapidly after a few days, and 10 weeks later there was no residual disability. During the next seven years she had six similar episodes, each involving the spinal cord at the same level, always in winter and always immediately preceded by a frank and sometimes febrile upper respiratory infection. The three later episodes also involved the arms, and one of these was accompanied by double vision and one by pronounced left hemiparesis. Each attack lasted for less than 12 weeks, and each cleared up, leaving minimal disability. The only other episode was in the summer of 1952, when she had an attack of nystagmus and double vision lasting for two weeks, quite unrelated to clinically evident infection. Examination in 1957 revealed a mild spastic paraparesis with appropriate reflex changes. Astereognosis was found in both hands, and vibration sense was lost in the left hand and leg.

#### Allergy

Much the same reservations apply to the role of allergy, reviewed by Prigal (1956). Occasional cases are striking in which frank allergic disturbance appears to have provoked the onset or exacerbation of the disease (Compston, 1951), but statistics are unimpressive. However, anamnestic investigation of allergy is mainly limited to obtaining evidence of its more striking manifestations, such as atopy, of which evidence may be entirely lacking in other diseases which we know to arise on an allergic basis. The observations of Alexander *et al.* (1950) that multiple sclerotics show an incidence of transfusion reactions (mostly allergic) thirty times as great as that encountered in control cases is suggestive clinical evidence in favour of some instability in the machinery of immunity in these cases, while the demonstration of a frequent increase in the spinal fluid

gamma-globulin (Kabat *et al.*, 1942; Yahr *et al.*, 1954) and of an abnormal response to the intrathecal injection of tuberculin (Smith *et al.*, 1957) have been similarly interpreted. The significance of these last findings, however, remains obscure: they may represent secondary results of the vascular and meningeal changes of the disease rather than evidence of a primarily immunological disturbance.

[The conclusion of this article, together with a list of references, will appear in our next issue.]

## THE ARTIFICIAL KIDNEY

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Severe renal failure is evidenced clinically by the syndrome of uraemia. This is believed to be due to the accumulation in the body of a number of substances, only a few of which have probably been identified. The artificial kidney is a device for removing from the body some or all of these substances. Various types of machine have been used for this purpose, and their historical development has been reviewed by Merrill (1955) and by Sorrentino (1956). All of them have employed the principle of dialysis, using a semi-permeable membrane that separates a bathing solution from the patient's blood.

Dialysis with any type of artificial kidney is a complicated and time-consuming procedure, and its greatest therapeutic value has been in the treatment of patients with acute reversible renal failure.\* It has also been used for the treatment of patients with exacerbation of chronic renal failure (Parsons and McCracken, 1957) and barbiturate (Kyle, Jeghers, Walsh, Doolan, Wishinsky, and Pallotta, 1953) and other acute poisonings (Doolan, Walsh, Kyle, and Wishinsky, 1951; Danzig, 1955; Merrill and Weller, 1952). It has a limited use in maintaining life in order that diagnostic procedures can be undertaken in patients presenting with the more obscure types of renal failure. The artificial kidney also provides an opportunity of obtaining information about the uraemic state, and its potentialities as a research tool are largely unexplored.

Following the pioneer work of Kolff and Berk (1944), reports of experience with artificial kidneys have appeared chiefly from the U.S.A. (Skeggs and Leonards, 1948; Merrill, 1950; Kolff, 1957), Scandinavia (Alwall, 1947; Anthonisen, Brun, Crone, Lassen, Munck, and Thomsen, 1956; Thaysen, Gjørup, and Killmann, 1957), and the mainland of Europe (Legrain, 1953; Hamburger and Richet, 1956). Use of the apparatus in Great Britain prior to 1956 has been confined to its occasional employment between 1947 and 1949 (Bull, Joekes, and Lowe, 1958); since 1956 machines have been in use in two centres, and preliminary reports of these have been

\*The term "acute reversible renal failure" is used in preference to others, such as lower nephron nephrosis, tubular necrosis, etc.

published (Parsons and McCracken, 1957; Shackman and Milne, 1957). The present paper gives an account of 20 months' experience with the artificial kidney in Leeds.

**Description of the Machine**

We have used the Kolff rotating type of machine as modified at the Peter Bent Brigham Hospital, Boston. A full account of this has been given by Murphy, Swan, Walter, Weller, and Merrill (1952). A diagram of the essential parts is shown in Fig. 1.

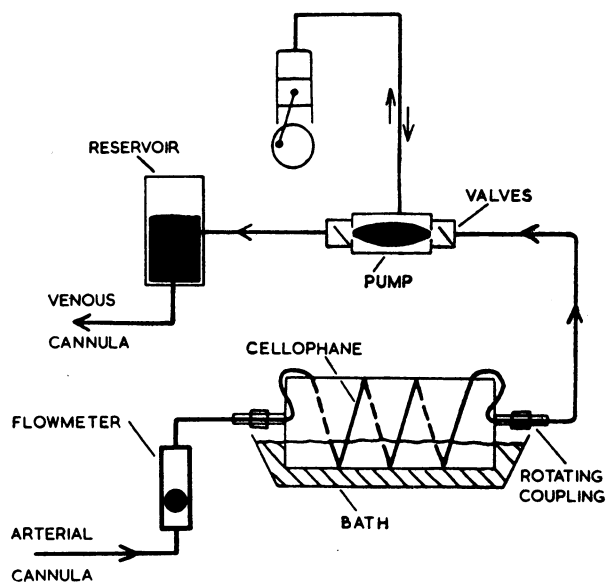


FIG. 1.—Diagram of Kolff-Brigham artificial kidney (after Merrill, 1955). Reproduced by permission of the Editor of the *British Journal of Urology*.

We have introduced certain modifications to this machine. The rate of blood flow through the dialyser has been increased from 300 ml. a minute to a maximum of 550 ml. a minute, and the dialysing surface area of the "cellophane" has been increased from 21,000 to 28,000 sq. cm. These alterations have improved the clearance rates of both urea and creatinine by approximately 40% (Parsons and McCracken, 1958a).

The composition of the bath fluid has been modified by using the acetates of calcium, magnesium, and potassium in place of chlorides (Table I). This prevents the occurrence of hyperchloraemia during the dialysis and results in a more complete correction of the plasma bicarbonate level. The acetates of calcium and magnesium have another advantage; for, unlike the chloride, they are not hygroscopic, so that they can be stored ready for use in the solid state. It has been emphasized previously that the concentration of sodium in the bath fluid should be the same as that in the patient's plasma (Parsons and McCracken, 1957). This is achieved by varying the quantity of sodium chloride added to the bath fluid.

TABLE I.—Typical Composition of Bath Fluid. The Upper Half Gives the Weight of Chemicals Added to 100 Litres, and the Lower Half the Ionic Strength

NaCl*	660 g.	Ca acetate	20 g.
NaHCO <sub>3</sub>	225 g.	Mg acetate 4H <sub>2</sub> O	10.4 g.
K acetate	34.3 g.	Glucose	400 g.
Leeds tap-water		100 litres	
Na*	140 mEq/l.	Mg	1.7 mg. per 100 ml.
K	3.6 "	Ca	6 "
HCO <sub>3</sub>	27 "	Cl*	113 mEq/l."

\* Adjusted according to plasma level of Na.

We also dialyse the citrated blood used to prime the machine. This partly corrects the high citrate and low calcium levels in the plasma of the citrated blood before it reaches the patient's circulation (Parsons and McCracken, 1958a). This has virtually eliminated the incidence of reactions developing at the start of the dialysis.

**The Procedure**

The dialysis, which is carried out in a special room, is continued for six hours, but the whole procedure takes about nine hours. Two pints (1,140 ml.) of stored blood, less than 5 days old, are required to fill the machine prior to use, and, to prevent clotting, a total of 14,000 units of heparin is given intravenously in divided doses during the dialysis.

A trained team of four persons, consisting of medical and nursing staff, is necessary for the dialysis, and a chemical laboratory service is often required. The procedure is not unduly trying to the patient, and sedation should be avoided, if possible, as it frequently causes lowering of the blood pressure in the advanced uraemic state.

**Origin of Patients**

100 patients were referred for treatment on the artificial kidney, and 82 required dialysis. (We have excluded from this series seven patients in a terminal phase of chronic nephritis who were treated soon after receiving the machine.) The 100 patients are classified in Table II. Twenty-four of them were referred to us from Leeds and 76 came from the Midlands, Northern England, and South-west Scotland.

*Acute Renal Failure.*—(1) *Reversible*: 63 patients with acute reversible renal failure were treated—25 cases occurred as a complication of pregnancy, 25 as a result of or associated with trauma, and 13 from other causes.

TABLE II.—Classification of the 100 Treated Patients

	No. Treated	No. Dialysed
Acute renal failure:		
Reversible { Pregnancy ..	25	17
Trauma ..	25	19
Others ..	13	9
Irreversible ..	13	13
Post-renal obstruction:		
Reversible ..	9	9
Irreversible ..	4	4
Miscellaneous ..	11	11

(2) *Irreversible*: 13 patients were admitted with acute renal failure and required a dialysis. Subsequently they were found to have an irreversible disease. Five had acute glomerulosclerosis, two had necrotizing arteriolitis, two had bilateral cortical necrosis of pregnancy, one had generalized amyloid disease involving the kidneys, one had acute diffuse glomerulonephritis, one had subacute diffuse glomerulonephritis, and one had acute suppurative pyelonephritis of one kidney, the other kidney being congenitally absent. These patients are not discussed further in this communication.

*Post-renal Obstruction.*—(1) *Reversible*: Nine patients were dialysed who had post-renal obstruction and uraemia due to disorders subsequently amenable to surgery. (2) *Irreversible*: Four patients were treated with the artificial kidney. Three presented with anuria, and a retrograde pyelogram revealed a bilateral ureteric obstruction. In two of these patients a periureteric fibrosis was suspected, and the dialysis prepared the patient for a nephrostomy; but a biopsy, taken from the site of obstruction, revealed unsuspected malignant

disease. The third patient was found to have carcinomatosis at a laparotomy. The fourth patient had a recurrent carcinoma of the cervix invading the posterior wall of the bladder. These patients are not discussed further.

*Miscellaneous.*—This group concerns the remaining 11 patients who were treated with the artificial kidney. Nine had an exacerbation of chronic renal disease, and five recovered. We have treated too few of this type of patient to draw justifiable conclusions, and consider, for the time being, that each patient has to be judged separately. The remaining two patients in this group had no renal failure. One was in diabetic coma and survived. The other had a fulminating acute hepatic coma, but the dialysis made no apparent difference to the clinical condition, and he died two days later. These 11 patients are not discussed further.

### Clinical Management

The clinical management of all patients referred to the Artificial Kidney Unit has been our direct responsibility. All the patients, whether medical, surgical, obstetrical, or gynaecological, have normally been admitted to one male or one female ward. Daily records of the patients' weight, blood pressure, fluid balance, and blood chemistry are kept.

*Acute Reversible Renal Failure.*—The fluid intake was restricted to the amount necessary to achieve a daily weight loss of 300–400 g. In anuric patients this is usually achieved with a fluid intake of 400 ml. a day. Calories were limited to the amount contained in 100–200 g. of glucose, and a generous vitamin intake is given. The glucose, water, and vitamins were given by mouth, for, so far as was possible, we avoided both intragastric and intravenous therapy. Electrolyte administration was restricted to replacement of losses in urine, stool, or vomit, and the occasional use of sodium lactate as an emergency procedure in patients with severe acidosis or hyperkalaemia. Cation exchange resins were used to control hyperkalaemia only when the rise in potassium was out of proportion to the other chemical indices of uraemia. When the renal function returns to the extent of causing a fall in the blood urea nitrogen (B.U.N.), restrictions on food intake are removed, and full protein feeding is encouraged as soon as it is tolerated. Electrolyte supplements are given at this time as required, and fluid intake is determined by the volume of urine and previous fluid requirements, except in patients with frank overhydration in whom fluid intake has been curtailed until the excess water has been eliminated. Dialyses were performed when considered necessary, but this did not affect the basic therapeutic regime.

*Acute Irreversible Renal Failure.*—This group (Table II) mainly concerns patients who presented as diagnostic problems, there being no definite antecedent episode heralding the onset of renal failure. They received the same dietary management as the previous group, and dialyses were performed when thought necessary. In addition diagnostic procedures, such as bilateral retrograde pyelography, and percutaneous or open renal biopsy, were carried out. When an irreversible condition was found the dietary restrictions were relaxed and no further dialyses were performed.

*Post-renal Obstructions.*—As a major surgical procedure causes an increase in metabolic rate (Moore and Ball, 1952), we have used dialysis to correct a uraemic state prior to surgical intervention. In patients

with prostatic obstruction whose uraemic state has not been corrected by catheterization, we have used the artificial kidney early, and then waited for renal function to improve before performing a prostatectomy. This not only allows us to correct malnutrition in these patients before operation, but also prevents the occurrence of uraemia in the immediate post-operative period, when the heparinization necessary for haemodialysis might lead to excessive haemorrhage from the prostatic bed. Following the relief of a chronic post-renal obstruction many patients lose excessive amounts of sodium chloride in the urine, and ionic supplementation is required even during the immediate post-operative period (Parsons, 1954). This salt loss is usually temporary. After a dialysis there is often a reduction in urinary output in these patients, and we usually adjust the fluid intake to maintain a constant body weight. The taking of protein is encouraged, the quantity being adjusted to the degree of renal failure.

### Clinical Effects of Dialysis

The clinical improvements achieved by dialysis are usually delayed for 24 to 48 hours. The immediate responses that occur during dialysis are chiefly cardiovascular—any arrhythmias due to potassium intoxication are corrected within 15 minutes, and uraemic hypotension is usually rectified in two to four hours. When uraemic twitching and mental agitation are present they tend to be temporarily aggravated rather than improved during the period of dialysis, and in two instances thiopentone had to be administered intravenously to control convulsions. During the 48 hours following dialysis, nausea and vomiting are replaced by hunger, and normal cerebration is restored. Acidotic breathing, if present, usually disappears within 12 hours. These improvements are maintained for several days even in the presence of severe oliguria. Anaemia gradually increases in severity, and we have not observed any rise in the level of haemoglobin following a dialysis. Normal haemopoiesis is restored only when renal function has returned. Concentrated red blood cells have been used to raise the haemoglobin level when this has been necessary.

### Chemical Effect of Dialysis

The chemical response is mainly immediate and is greatly influenced by the efficiency of the machine. This is dependent on many factors, such as the initial concentration of substances in the plasma, the volume of distribution of these substances in the body, the duration of the dialysis, the properties of the dialysing membrane, the rate of blood flow through the dialyser, and the accumulation of substances in the bath. These aspects have been discussed elsewhere (Parsons and McCracken, 1958a).

A typical chemical response obtained by the Kolff-Brigham dialyser is shown in Table III. This patient

TABLE III.—*Chemical Response to Dialysis and the Findings 48 Hours Later*

Plasma Levels	Start of Dialysis	End of 6 Hours' Dialysis	48 Hours Later
Na (mEq/l.) .. ..	133	135	144
Cl .. ..	91.5	101	100
CO <sub>2</sub> c.p. mEq/l. .. ..	14.8	27.2	23.1
K mEq/l. .. ..	6.4	4.1	5.1
P (mg./100 ml.) .. ..	15.3	2.1	10.4
B.U.N. .. ..	200	31	66
pH (arterial blood) .. ..	7.23	7.49	—

developed an acute renal failure following an abortion, and was dialysed on the 11th day. As her plasma level of sodium was 133 mEq/l. the composition of the bath was adjusted to contain 135 mEq/l., and the plasma level of sodium rose to 135 mEq/l. during the dialysis. The level of chloride, CO<sub>2</sub> combining power, potassium, and B.U.N. returned to more normal values. The plasma inorganic phosphorus level fell to 2.1 mg./100 ml., at the conclusion of the dialysis, but 48 hours later it was 10.4 mg./100 ml., a rise out of proportion to the increase in the B.U.N. (Parsons and McCracken, 1957). During the dialysis the pH in the arterial blood rose from 7.23 to 7.49. This over-correction of arterial pH during the dialysis was reported by Weller, Swan, and Merrill (1953), but we have found that it returns to normal values some hours after the dialysis. Similarly the low partial pressure of CO<sub>2</sub> in the alveolar air at the start of the dialysis remains unaltered during the procedure, but some hours after the dialysis it returns to normal values (Ramwell, Parsons, and McCracken, 1959). In anuria or severe oliguria a gradual return to the pre-existing chemical state occurs after the dialysis (Table III).

### Complications During a Dialysis

*Artificial Kidney.*—The Kolff-Brigham machine requires constant supervision during the dialysis. Mechanical faults have been few and have been limited to those parts carrying the blood. They can usually be rectified by substituting a sterilized spare component or length of P.V.C. tubing. The most frequent fault was the presence of a hole in the cellophane tube, and this can be rectified by replacing the affected area with a short length of plastic tubing as described by Merrill, Thorn, Walter, Callahan, and Smith (1950). The working blood volume of our machine is 1 to 1.5 litres, but as the potential capacity is approximately 8 litres it is essential to guard against large fluctuations of blood in the machine, as these can only occur at the expense of the corporeal circulation. In three patients the dialysis had to be terminated as the blood clotted in the machine. In the first a slow flow rate was responsible. The second patient had generalized amyloid disease and the heparin had probably been adsorbed by the amyloid deposits. The third patient had received severe traumatic injuries six days previously, but later three further dialyses were performed and no clotting occurred.

*Patient.*—Serious complications occurring in the patient are infrequent. No fatalities have been directly attributable to a dialysis, though three patients died during the procedure. Two were in advanced uraemic coma; the third had had an operation for aortic stenosis, and an acute cardiac arrest developed 30 minutes after starting the second dialysis. We have had to terminate the dialysis five times on account of complications—three for haemorrhage in post-operative wounds, one for an exacerbation of a mental disturbance, and one for the development of a small cerebrovascular accident. None of these complications proved fatal.

### Results in Acute Reversible Renal Failure

#### Pregnancy: Dialysed

Seventeen patients were treated by dialysis, and all recovered. The findings of these patients are summarized in Table IV. Twelve developed acute renal failure associated with complications occurring in late

pregnancy and five had abortions. Eight patients required a dialysis during the 5th to 7th days, six during the 8th to 10th days, and three were dialysed after the 10th day. Four required more than one dialysis.

At the time of dialysis all exhibited clinical deterioration, the commonest feature being deterioration of the mental state and nausea or vomiting. The blood chemistry at the time of the dialysis (Table IV) revealed that the B.U.N. exceeded 180 mg./100 ml. in nine patients. In only four was the plasma potassium level greater than 7 mEq/l., and in only four was the CO<sub>2</sub> combining power less than 14 mEq/l.

We measured the average daily rise in the B.U.N. in 15 patients who were observed over a sufficiently long period of severe oliguria to draw a justifiable conclusion. In two the rise was less than 15 mg./100 ml., in 12 the rise was between 15 and 30 mg., and in one it exceeded 30 mg.

The earliest fall in the B.U.N. occurred on the 12th day (Cases 42 and 57), whilst in only four was the fall delayed longer than the 25th day. The fall in the B.U.N. occurred most commonly about five days after the urine output exceeded 500 ml. per 24 hours. The average time taken before the B.U.N. started to fall in these 17 patients was 20 days. The maximum urinary output per day during recovery was not high, and averaged 2,700 ml. (range 771–5,025 ml.). Ten of these patients were discharged before the 40th day after the onset of renal failure, and the remaining seven stayed in hospital longer, either because their period of oliguria was prolonged or because complications had occurred.

#### Pregnancy: Non-dialysed

Eight patients were treated without a dialysis (Table V) and six recovered. One of the patients died 30 minutes after admission and the other died in uraemia as we failed to dialyse early enough. In this patient (Case 1 N) the B.U.N. a few hours before death was 181 mg./100 ml., and the potassium level of the plasma was 6.6 mEq/l. (a level of 9.0 mEq/l. had been lowered by means of ion-exchange resins eight days earlier).

Of the six patients who recovered, three had abortions, and three had complications occurring in late pregnancy. None of these patients developed a severe acidosis or hyperkalaemia, and the highest B.U.N. recorded was 168 mg./100 ml. (Case 3 N). The clinical condition of these patients remained good throughout the period of oliguria.

The B.U.N. fell earlier than in the previous group, the fall occurring on days 3 to 17, whilst the average maximum urinary output was similar, being 2,740 ml. per 24 hours. These patients were discharged earlier than those who were dialysed, mainly because the period of oliguria was much shorter.

#### Trauma: Dialysed

Nineteen patients who developed acute renal failure as a result of trauma or of association with trauma have been dialysed and six recovered. The findings on these patients are summarized in Table IV. Five of these patients had received accidental trauma (three survived) and 14 (three survived) had had a major surgical operation.

In the main, the first dialysis had to be performed early in the course of the illness. Nine patients were dialysed on or before the 5th day, four on the 5th to 7th days, four on the 8th and 10th days, and only two after

TABLE IV.—Findings in Patients who were Dialysed for Acute Reversible Renal Failure

Cause	Case No.	Age and Sex	Day Transfer to Kidney Unit	1st Dialysis after Admission Days	No. of Dialyses	Plasma Levels at First Dialysis			Average Daily Rise of B.U.N. mg./100 ml.	Day Urine Output Exceeded 500 ml./24 Hours	Day 1st Fall in B.U.N.	Maximum Urine Output ml./24 Hours	Outcome
						K mEq/l.	CO <sub>2</sub> c.p. mEq/l.	B.U.N. mg./100 ml.					
<i>Pregnancy Group</i>													
Abortion .. .. .	9	39 F	5	2	1	5.1	15.2	120	17.5	13	20	2,800	Discharged 37th day
Accidental haemorrhage ..	12	39 F	8	<1	3	8.8	13.5	216	22.6	19	35	3,000	Discharged 59th day
Abortion .. .. .	18	31 F	6	2	2	5.5	10.5	118	12.8	26	31	2,930	Discharged 50th day
Haemorrhage; placenta praevia	28	29 F	4	3	1	5.7	15.4	216	36	9	14	3,120	Discharged 45th day
Pre-eclampsia .. .. .	31	25 F	20	<1	1	2.8	19.1	320	—	> 500 on admission	27	3,600	Discharged 41st day
Abortion .. .. .	33	33 F	2	7	1	4.8	14.8	178	15	11	17	2,760	Discharged 36th day
" .. .. .	35	24 F	7	4	1	6.6	14.8	200	13.5	13	19	2,345	Discharged 25th day
Toxaemia of pregnancy ..	36	31 F	2	3	3	6.8	16.1	146	16.3	38	42	771	Discharged 68th day
Eclampsia .. .. .	42	26 F	6	<1	1	8.4	14.8	176	15	8	12	2,910	Discharged 23rd day
Accidental haemorrhage ..	43	35 F	7	<1	2	6.4	14.8	250	27.5	13	18	2,520	Discharged 25th day
Abortion with hysterectomy	54	27 F	6	<1	1	4.5	15.5	188	19.5	13	14	3,000	Discharged 40th day
Accidental haemorrhage ..	55	21 F	8	<1	1	5.9	13.6	174	20	15	16	2,145	Discharged 29th day
Toxaemia of pregnancy ..	57	27 F	3	3	1	7.1	15.2	190	15	6	12	5,025	Discharged 20th day
Accidental haemorrhage ..	67	39 F	6	2	1	6.0	16.4	204	20	17	19	2,525	Discharged 36th day
Toxaemia of pregnancy ..	76	32 F	13	2	1	5.8	9.6	144	—	20	24	1,890	Discharged 47th day
Placenta praevia; hysterotomy	80	39 F	2	4	1	6.0	18.5	192	22	7	15	2,160	Discharged 28th day
Placenta praevia and accreta; hysterectomy	91	30 F	4	4	1	8.4	15.5	178	16	12	13	2,460	Discharged 21st day
<i>Trauma Group</i>													
Multiple injuries .. .. .	1	25 M	5	4	1	6.0	13.1	342	—	—	—	—	Died 9th day
Cysto-ileoplasty .. .. .	19	44 M	5	<1	1	5.6	14.8	176	—	Incontinent <7	—	Approx. 2,000	Died 19th day
Cystectomy; uretero-sigmoidostomy	20	59 M	7	<1	2	7.8	13.5	282	55	—	—	1,605	Died 20th day
Hysterectomy; haemorrhage	22	40 F	5	<1	4	5.7	12.2	208	78.5	24	—	780	Died 26th day
Per-urethral prostatectomy	24	67 M	3	6	2	7.5	8.8	202	32	—	—	300	Died 17th day
Aortic valvuloplasty ..	40	58 M	5	2	2	7.6	19.1	204	30	—	—	—	Died 13th day
Wertheim's hysterectomy	41	44 F	5	5	1	3.9	19.1	184	—	> 500 on admission	12	3,180	Discharged 78th day
Secondary haemorrhage; appendicectomy	45	32 M	4	<1	3	7.8	25.1	312	46	—	—	—	Died 10th day
Multiple injuries .. .. .	46	29 M	5	<1	4	8.6	13.1	256	43	20	27	11,940	Discharged 80th day
Aortic graft .. .. .	49	64 M	3	1	1	7.2	25.1	172	26	9	10	53rd day 1,760	Discharged 28th day
Partial gastrectomy ..	50	55 M	9	<1	1	6.1	24.2	212	—	—	—	—	Died 12th day
Parathyroidectomy; acute pancreatitis	53	57 F	7	<1	1	3.4	9.6	180	—	—	—	—	Died 8th day
Per-urethral prostatectomy	61	51 M	11	<1	7	6.1	11.3	225	50	32	—	1,200	Died 36th day
Multiple injuries .. .. .	69	30 M	11	<1	1	7.4	—	272	>30	Incontinent 9	17	34th day 9,835	Discharged 27th day
Partial gastrectomy; incompatible blood transfusion	73	48 F	3	<1	1	4.9	26.4	138	20	—	18	3,800	Discharged 24th day
Burns .. .. .	79	24 M	4	2	2	6.7	21.1	236	40	—	—	—	Died 12th day
Acute dehydration; nephrectomy	81	58 F	5	<1	1	7.4	Specimen lost	Specimen lost	—	—	—	—	Died 6th day
Multiple injuries .. .. .	82	44 M	5	<1	3	6.8	11.3	232	42	19	25	3,660	Discharged 44th day
Laparotomy; staphylococcal enteritis	85	52 M	4	<1	1	4.7	16.4	206	40	—	—	—	Died 6th day
<i>Others</i>													
Hepato-renal syndrome ..	14	23 M	8	<1	1	8.2	13.5	208	17.8	—	—	—	Died 9th day
" .. .. .	26	57 M	2	<1	1	5.1	13.1	216	34	5	11	3,300	Died 15th day
Mercury poisoning ..	29	26 M	5	1	1	7.1	12.2	292	40	9	19	4,900	Discharged 34th day
Hepato-renal syndrome ..	37	65 M	8	2	1	4.0	30.2	228	—	11	13	3,960	Discharged 67th day
Aortogram .. .. .	44	62 F	8	<1	1	4.5	22.0	242	—	—	—	—	Died 19th day
Diabetic coma .. .. .	47	13 F	4	<1	1	2.6	7.9	92	17	6	16	4,040	Discharged 36th day
Pyloric stenosis .. .. .	48	44 M	3	5	1	4.3	17.5	250	21.5	12	15	2,774	Discharged 33rd day
Hepato-renal syndrome ..	51	47 M	8	<1	2	9.0	13.0	222	33	—	—	—	Died 14th day
Aortogram .. .. .	70	33 M	5	3	1	5.0	16.8	160	22	12	15	3,375	Discharged 24th day

the 10th day. Thirteen patients had to be dialysed within 24 hours of admission to the kidney unit, and in seven of these a dialysis had to be performed as an emergency on admission. Nine patients required more than one dialysis, and the greatest number performed on one patient was 7 (Case 61).

The blood chemical findings on these patients are important. At the time of the first dialysis only one (Case 73) had a B.U.N. of less than 170 mg./100 ml., whilst in the seven patients who were dialysed as soon as possible after admission six had a B.U.N. greater than 200 mg./100 ml.

In eight patients the potassium level at the time of the first dialysis exceeded 7 mEq/l., and the CO<sub>2</sub> combining power was below 14 mEq/l. in eight patients.

These chemical findings must be considered in conjunction with the clinical state of the patients. In all these patients the clinical deterioration was more rapid than in the other two groups of patients with acute reversible renal failure. In particular we would single out mental deterioration as the most constant finding. Gastric disturbance, such as nausea and vomiting, was also frequent, but an acidotic type of respiration was infrequent, whilst uraemic hypotension was present in only five patients at the start of the first dialysis and bore no specific relationship to the degree of uraemia, except in one patient who had hyperkalaemia.

It was possible to assess the average daily rise in the B.U.N. in 13 of these patients, and in 11 it was 30 mg./100 ml. or over (average rise 46 mg.). This rise, indicating the degree of protein katabolism, was much higher than in the pregnancy group, and accounts in

part for the greater number of dialyses that were required for these patients in the traumatic group. The average time taken for the B.U.N. to start falling was 18 days, which was slightly less than in the pregnancy group.

The maximum urinary volume per 24 hours in the patients who recovered varied from 1,760 to 11,940 ml., and appeared to be higher than in the pregnancy group. The patient who passed the largest volume of urine, 11,940 ml. per 24 hours, was given "pitressin," but no reduction of urine volume was noted.

Those patients who recovered had a protracted stay in hospital before discharge, but this was necessary for treatment of their initial lesion rather than their renal function.

**Deaths.**—Thirteen patients died. In five renal function was recovering, death occurring after the 16th day either from complications of the primary lesion or from sepsis. In the remaining eight patients death occurred earlier than the 14th day before there was evidence of the return of renal function. Only one patient (Case 1) died in uraemia: death occurred in a convulsion during the dialysis. In the remainder the uraemia had been kept under control by dialyses. Eight patients died from sepsis, one from acute pancreatitis, and another, who had had a valvulotomy for an aortic stenosis, developed an acute cardiac arrest during his second dialysis. Two patients died from overhydration, and both had received massive intravenous therapy before they were transferred to our care.

**Trauma: Non-dialysed**

Six patients in this group were not dialysed (Table V). Five of these died in uraemia before a dialysis could be

TABLE V.—Findings in Patients who were not Dialysed for Acute Reversible Renal Failure

Case No.	Cause	Age and Sex	Day Transfer to Kidney Unit	Plasma Levels			Average Daily Rise B.U.N. mg./100 ml.	Day Urine Output Exceeded 500 ml./24 Hours	Day 1st Fall in B.U.N.	Maximum Urine Output ml./24 Hours	Outcome
				Highest K mEq/l.	Highest B.U.N. mg./100 ml.	Lowest CO <sub>2</sub> c.p. mEq/l.					
<i>Pregnancy Group</i>											
1 N	Accidental haemorrhage	26 F	5	9.0	181	15.5	21	—	—	240	Died 13th day
3 N	" "	29 F	3	6.1	168	15.0	8	8	17	2,900	Discharged 29th day
4 N	Placenta praevia; caesarean section	24 F	1	4.1	145	15.5	—	3	5	24th day 3,810	Discharged 17th day
5 N	Hypotension; forceps delivery	27 F	7	Not forwarded		—	—	—	—	6th day —	Died 30 min. after admission
11 N	Abortion .. ..	21 F	3	4.1	138	23.2	—	Over 500 ml. on admission		2,010	Discharged 16th day
13 N	Post-partum haemorrhage; ? incompatible blood transfusion	26 F	7	4.1	91.5	22.4	—	" "	7	13th day 2,490	Discharged 15th day
14 N	Abortion .. ..	26 F	10	6.6	150	16.4	13	11	11	2,788	Discharged 31st day
15 N	" .. ..	21 F	1	4.3	137	15.8	—	2	3	14th day 2,480	Discharged 11th day
<i>Trauma Group</i>											
6 N	Cholecystectomy ..	75 F	7	Not forwarded		—	—	—	—	—	Died 12 hr. after admission
7 N	Partial gastrectomy ..	69 M	4	8.7*	220	15.0	—	—	—	—	Died 30 min. after admission
9 N	Suture of burst abdomen	52 F	2	4.6	114	20.2	—	3	5	2,330	Discharged 11th day
12 N	Multiple injuries ..	28 M	6	9.4*	183	—	—	—	—	9th day —	Died 1 hr. after admission
16 N	" .. ..	19 M	5	8.1	158	23.4	—	—	—	—	Died 3 hr. after admission
17 N	Haematemesis; partial gastrectomy	49 M	7	5.8*	202	—	—	—	—	—	Died 2 hr. after admission
<i>Others</i>											
2 N	Haemophilia; blood transfusion reaction	28 M	5	7.5	275	15.5	—	7	10	4,970	Discharged 21st day
8 N	Ulcerative colitis; blood transfusion reaction	44 F	3	6.4	168	18.0	—	10	13	4,546	Discharged 30th day
10 N	Intravascular haemolysis	22/12 M	3	5.1	298	12.6	12	Incontinent		17th day	Discharged 42nd day
18 N	Pneumonia .. ..	68 F	5	5.4	211	15.5	24	6	10	1,624	Discharged 64th day

\* This and the other blood chemical findings were sent with the patient.

attempted—four within three hours of admission; the other was admitted when the artificial kidney was in use, and died 12 hours later. (A further patient, not included in this series, died in an ambulance before reaching this hospital.) These cases are recorded to emphasize the importance of referring this traumatic group of patients to an artificial kidney unit early, for all five patients died seven days or less after the onset of renal failure.

The one patient who survived developed an acute renal failure following the suture of a burst abdomen.

#### Others: Dialysed

Thirteen patients with acute reversible renal failure who were admitted to the unit did not fall into the previous two groups. The renal lesion was precipitated by various factors.

Nine of these patients had to be dialysed and five recovered. The findings are summarized in Table IV. All were admitted eight days or less after the onset of renal failure, and all were dialysed on or before the 10th day. Five required a dialysis within 24 hours of admission. At the time of the first dialysis seven had a B.U.N. in excess of 200 mg./100 ml. Case 47 had diabetes, and although the blood-sugar level had been controlled with insulin she was admitted in uraemic coma with a CO<sub>2</sub> combining power of 7.9 mEq/l. in spite of a B.U.N. of only 92 mg./100 ml. The remaining patient, who had a B.U.N. less than 200 mg./100 ml. (Case 70), was dialysed for uraemic convulsions, which developed quite unexpectedly.

In those patients who survived, the B.U.N. started to fall between the 13th and 19th days—that is, earlier than in the pregnancy and traumatic group. The maximum 24-hour urinary output averaged 3,800 ml., about 1,000 ml. more than the average for the pregnancy group.

**Deaths.**—Four patients died—two from sepsis (in one of these renal function had recovered), one from a perforated duodenal ulcer, and one was admitted and died in pulmonary oedema from overhydration.

#### Others: Non-dialysed

The remaining four patients in this group did not require a dialysis, and all recovered. The findings are summarized in Table V. Case 2 N was a haemophiliac, and although the B.U.N. rose to 275 mg./100 ml. and the plasma potassium level reached 7.5 mEq/l., the clinical condition remained good. The B.U.N. in the child (Case 10 N) reached a maximum of 298 mg./100 ml., but the clinical condition was satisfactory. He, however, became drowsy and vomited frequently during the early part of the recovery phase.

#### Results in Reversible Post-renal Obstruction

The findings in the nine patients who had reversible post-renal obstruction and uraemia are summarized in Table VI.

Seven had prostatic obstruction with retention of urine. The degree of uraemia according to the blood chemical findings was not severe except in one patient (Case 65) who had a B.U.N. of 198 mg./100 ml., and a plasma potassium level of 7 mEq/l., which was lowered by means of cation exchange resins prior to the dialysis. All these patients had severe clinical symptoms,

consisting in some of nausea and vomiting and in others of gross mental retardation. After dialysis all were improved clinically; the most striking improvement occurred in their mental state, and all became co-operative and interested in their surroundings. In three of these patients prostatectomy was performed seven days or less after the dialysis, but in the other four

TABLE VI.—Findings in Patients who were Dialysed for Reversible Post-renal Obstruction

Cause	Case No.	Age and Sex	No. of Dialyses	Plasma Levels at 1st Dialysis			Operation Days after Dialysis	Outcome
				K mEq/l.	CO <sub>2</sub> c.p. mEq/l.	B.U.N. mg./100 ml.		
Prostatic obstruction	15	69 M	1	6.2	20.8	62	7	Discharged
"	16	78 M	1	4.75	22.5	59.5	12	"
Ureteric obstruction	27	37 F	2	4.95	14.8	292	2	"
Carcinoma bladder	38	60 M	1	6.4	25.1	164	2	Died after cystectomy
Prostatic obstruction	56	63 M	1	3.1	23.2	101	17	Discharged
"	65	76 M	1	4.0	10.4	198	28	"
Prostatic obstruction. Chronic nephritis	77	55 M	1	4.4	20.6	65	3	"
Prostatic obstruction	86	68 M	1	5.1	24.5	104	2	"
"	89	34 M	3	4.0	13.1	168	26	"

prostatectomy had to be delayed until renal function had improved, and in Case 89 two further dialyses were required, the first having been performed as an emergency to control uraemic convulsions.

The remaining two patients had an obstruction at the ureterovesical junction. One is described below. The second had a carcinoma of the bladder involving both ureteric orifices; a dialysis corrected the uraemic state, and a nephrostomy was successfully carried out, but he died after a total cystectomy.

#### Infection

Early in this series we encountered a high incidence of infection which caused the death of several patients. The organism chiefly responsible was tetracycline-resistant *Staphylococcus aureus*. This finding led us to examine more closely the bacterial flora of the noses and faeces of those patients admitted with acute reversible renal failure. Of 24 patients so investigated, 15, at the time of their transfer to our unit, were harbouring a tetracycline-resistant strain of staphylococcus, in four a penicillin-sensitive strain was isolated, and in five no staphylococci were found. During the patients' stay in our wards reverse barrier nursing was carried out, and the blankets were subjected to frequent chemical sterilization. In four of the nine patients who were not carrying an antibiotic-resistant staphylococcus on admission, the organism was subsequently isolated during their stay in our hospital. One remained free from this organism, whilst inadequate records were available in four.

The incidence of an erythromycin-resistant strain of staphylococcus was significant. Three patients were admitted harbouring this organism, and it occurred in a further five during their stay in our unit (three of these were treated with erythromycin when staphylococcal enteritis occurred).

Seven patients developed severe staphylococcal enteritis, and were treated with erythromycin at the onset of symptoms and recovered. This was in sharp contrast to those who were not treated at the onset of symptoms but in whom we awaited the result of bacteriological examination of the stools (see Case 22 below). It seems to us that it is dangerous to delay treatment when severe diarrhoea develops in acute renal failure, and at the moment we are guided by the staphylococcal sensitivity patterns obtained from the nose and faeces when routine investigations are made. It should be noted that we have not encountered diarrhoea in these patients except when staphylococcal enterocolitis has developed.

For the past 16 months we have refrained from using any antibiotics prophylactically. We believe that this has reduced the incidence of staphylococcal enteritis, and there has been no increase in other types of infection.

**Representative Case Reports**

**Case 43**

A woman aged 35 developed pre-eclampsia, and a concealed accidental haemorrhage precipitated anuria. Delivery of a stillborn child was associated with periods of hypotension (80/50), treated with blood transfusions. Two days later slight jaundice was present. The dietary regime was instituted on the second day of anuria, and she was transferred to Leeds on the seventh day. At this time there was moderate oedema with vomiting, but her mental state appeared normal. Blood chemistry showed severe uraemia, and the first dialysis was performed on the eighth day, with a good chemical and clinical response (Fig. 2). On the 11th day she suddenly became mentally deranged and refused all treatment. The second dialysis was performed on the 12th day with the aid of light anaesthesia, and the mental state returned to normal within 24 hours. A further transient mental derangement occurred on the 19th day, but renal function was now returning. During the oliguric phase there was moderate diarrhoea and a tetracycline-resistant staphylococcus was isolated from the faeces, but the condition cleared spontaneously.

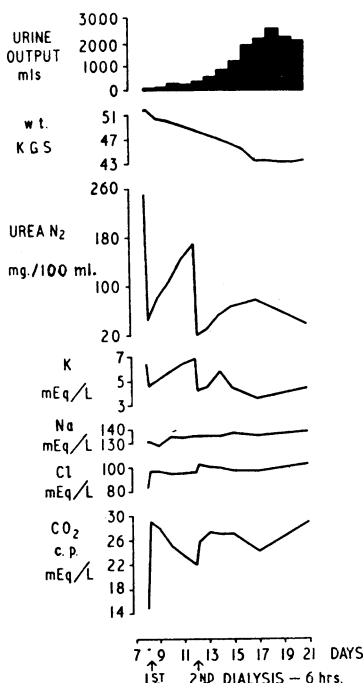


FIG. 2.—Case 43. Chemical findings in a patient who developed acute reversible renal failure following an accidental haemorrhage.

**Case 18**

A woman aged 31 had an evacuation of the uterus for an inevitable abortion. At the time the uterus was irrigated profound shock occurred; the B.P. fell to 70/55, and this was restored with 1 pint (570 ml.) of dextran and 1 pint of blood. Anuria was present after the operation. Jaundice occurred 24 hours later. She was not treated by a strict dietary regime, and six days later was transferred to Leeds. The following day she began to vomit, and the first dialysis was

performed on the eighth day of anuria (Fig. 3), the CO<sub>2</sub> c.p. being 10.5 mEq/l., and the B.U.N. 118 mg./100 ml. The dialysis had to be terminated after four and a half hours, as a technical fault developed in the machine. After the dialysis she took glucose, water, and vitamins orally, but by the 16th day the clinical condition had deteriorated, the CO<sub>2</sub> c.p. had fallen to 11.3 mEq/l., and a second dialysis, lasting six hours, was carried out. Another good clinical response was obtained. The urine volume started to increase

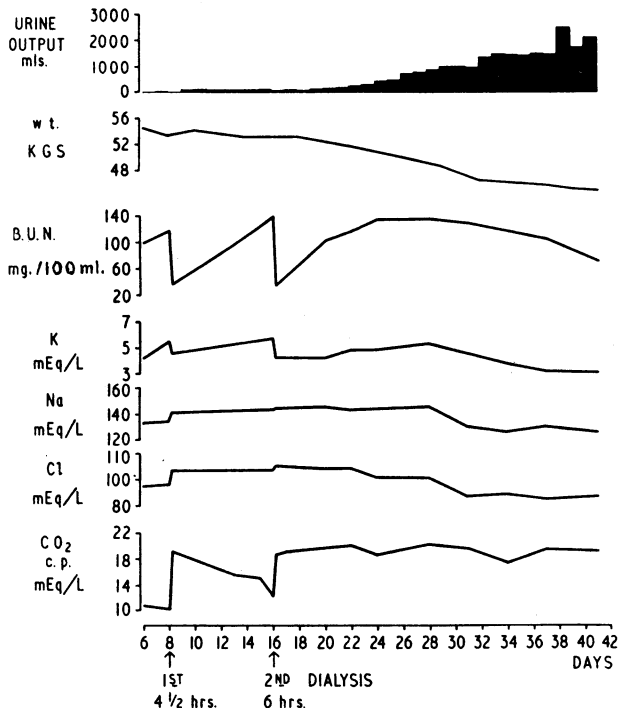


FIG. 3.—Case 18. Chemical findings in a patient who developed acute reversible renal failure following an abortion.

after the 24th day, and the B.U.N. began to fall on the 31st day. On the 30th day nausea returned, and as she was unable to take the requisite quantity of fluid orally some was given subcutaneously.

On the 35th day she started to vomit more copiously, and in order to administer food it was necessary to give milk by intragastric drip and suppress the vomiting with chlorpromazine. Three days later the vomiting ceased and she then made an uninterrupted recovery. The maximum urine output during the recovery phase was 2,930 ml.

After the second dialysis diarrhoea occurred and a tetracycline-resistant staphylococcus was isolated from the faeces. The diarrhoea cleared spontaneously.

**Case 46**

In a motor-cycle accident a man aged 29 received a fracture-dislocation of the right hip with injury to the sciatic nerve, multiple fractures of the pelvis, a fractured vault of skull, and concussion. The B.P. was reported as unrecordable for six hours after injury, and he was given 6 pints (3.4 litres) of blood. Anuria was present from the time of injury and the dietary regime was instituted on the third day. He was transferred to Leeds on the fifth day because of rapid clinical deterioration. The recent head injury accounted for a semi-stuporous state. He was of excellent physique. Slight jaundice was present. The blood chemical findings showed severe uraemia (Fig. 4), and the first dialysis was necessary immediately. Ion-exchange resins were used subsequently to control the plasma level of potassium, which was rising disproportionately. Because of the head injury, the mental state was unreliable as a guide for clinical assessment of uraemia. A B.U.N. level in excess of 200 mg./100 ml. was used as the main guide for further dialyses,



and these were necessary on the 10th, 14th, and 18th days. Urine output started to increase on the 20th day, but a fall in the B.U.N. did not occur until the 27th day. A full diet was started at this time. Urine output rose to approximately 12 l. a day, which was unaffected by administration of pitressin, but it subsequently fell to 5-6 l. a day.

His mental state returned to normal about the 36th day. His katabolism was very high, and during the period of renal failure his subcutaneous fat and his musculature wasted dramatically. During the recovery phase his appetite

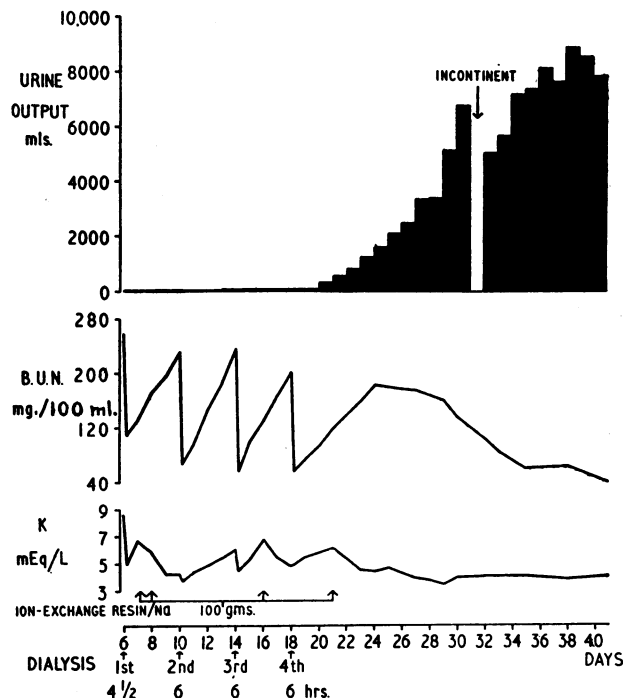


FIG. 4.—Case 46. Chemical findings in a patient who developed acute reversible renal failure following multiple injuries.

became voracious, and he had apparently replaced most of his lost tissues by 14 weeks after injury. He subsequently responded well to orthopaedic treatment of his residual disabilities.

#### Case 22

A woman aged 40 developed a severe intra-abdominal haemorrhage 24 hours after a hysterectomy for fibroids. A laparotomy was performed, but further haemorrhage resulted in periods of hypotension. Anuria developed at the time of the first haemorrhage, and the dietary regime was instituted from the second day. On the fifth day ureteric catheterization showed that there was no urinary obstruction, and she was transferred to Leeds the same day.

On admission she was drowsy, responding only to simple questions. There was acidotic breathing, pitting oedema of the sacrum and lower limbs, basal crepitations, and slight jaundice. Blood chemical findings included a B.U.N. of 208 mg./100 ml., and a  $\text{CO}_2$  c.p. of 12.2 mEq/l. (Fig. 5). Dialyses were necessary immediately on admission and again on the 8th and 13th days. Oxytetracycline, 400 mg., was given prophylactically after each dialysis. After the third dialysis her clinical condition improved considerably, but on the 18th day severe diarrhoea developed and general clinical deterioration with circulatory failure followed. A fourth dialysis was performed on the 19th day, and, after bacteriological reports had shown the faeces to contain a tetracycline-resistant staphylococcus, erythromycin was begun on the 22nd day. Clinical deterioration continued, and the patient died on the 26th day, although by this time the urinary output had reached 718 ml. a day.

Necropsy showed the mucosa of the proximal three-quarters of the large intestine to be studded with

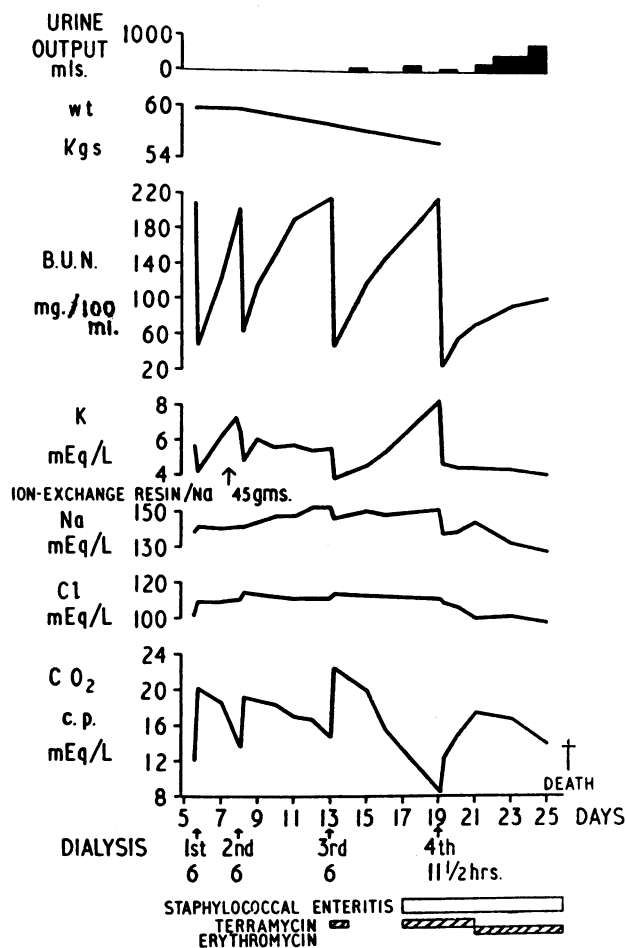


FIG. 5.—Case 22. Chemical findings in a patient who developed acute reversible renal failure following an intra-abdominal haemorrhage.

innumerable ulcers. In the lungs there were minute pyaemic abscesses, and the brain contained a single abscess about  $\frac{3}{4}$  in. (2 cm.) in diameter. *Staph. aureus* was cultured from these affected areas. Histological examination of the kidneys showed a recovering tubular necrosis.

#### Case 27

A woman aged 37 had a left tuberculous pyonephrosis with an impassable stricture of the left ureter 3 cm. from the ureteric orifice. There was a right ureterocele (which had been treated by diathermy) and a right hydronephrosis and hydroureter. The uraemia was treated by dialysis. Later she developed severe hypertensive attacks while being treated in the sanatorium, and it was decided to remove the left kidney and ureter in the hope that the hypertension would decrease and that the function of the right kidney might improve. As the blood chemical findings suggested that a severe degree of uraemia might ensue after the operation, a pre-operative

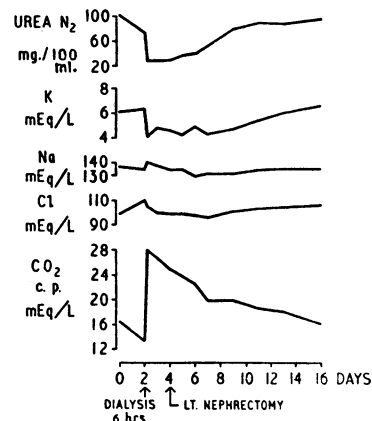


FIG. 6.—Case 27. Chemical findings in a patient who had a pre-operative dialysis for chronic renal disease.

dialysis was performed (Fig. 6) and the uraemic state was corrected. The clinical condition of the patient improved also. 48 hours later a left nephro-ureterectomy was performed. The post-operative period was entirely uneventful even though the blood chemical levels gradually returned to the levels existing prior to the dialysis. Sodium and chloride supplementation was required in the immediate post-operative period as she had a salt-losing nephritis.

After the nephrectomy the hypertension disappeared though no further improvement in the function of the right kidney was noted. Two months after her discharge we were informed that she had developed a right pyelonephritis, and had died.

### Discussion

Although haemodialysis is a safe procedure it has a restricted use in the treatment of patients with renal failure. We have found it of most value in the treatment of acute reversible renal lesions, and reversible post-renal obstruction presenting with uraemia.

#### Indications for Performing a Dialysis

The main purpose of dialysis is to decrease the mortality in patients with the reversible types of renal failure and to make the clinical management easier. In keeping with these principles we have accepted as indications for dialysis, firstly, clinical changes which may presage deterioration, and, secondly, those changes in the blood chemistry that are generally accepted as constituting a hazard to life. We have found that the clinical changes are more important than the chemical ones.

In the first category we have placed early mental changes, such as mental retardation or developing uncooperation, and persistent nausea and vomiting. We advocate dialysing before the onset of convulsions, semicoma, severe mental confusion, or uraemic hypotension. In our series the earliest mental change has been regarded as serious, and if deterioration progresses then a dialysis must be performed as soon as possible, if necessary throughout the night.

In the second category we advocate dialysis if the  $\text{CO}_2$  combining power falls below 13 mEq/l. or the plasma potassium level exceeds 7 mEq/l. The use of ion-exchange resins should be reserved for those instances where the potassium level is rising out of proportion to the other indices of uraemia.

The level of the blood urea is important, not because urea has any toxic properties, but because the level acts as an indicator of the breakdown of protein. We have been impressed from the beginning by the regularity of one or more of the clinical indications for dialyses arising at about the same time that the B.U.N. reaches 180–200 mg./100 ml. (blood urea 385–428 mg./100 ml.). We have witnessed relatively sudden deterioration and death in these circumstances, and, having satisfied ourselves that a dialysis is a safe procedure and that nothing is to be gained by waiting until the last possible moment, we have now added a B.U.N. of 180–200 mg./100 ml. as an indication for dialysis. It is emphasized that these three chemical indications need not be present at the same time, and we consider each as an indication in its own right.

These indications should still be applied whether the patient is anuric or entering the recovery phase. Even if the urine output is increasing but the clinical and chemical assessments show that the uraemia is becoming

more pronounced, it is far safer to dialyse. Whether or not the patient would have survived without a dialysis in such circumstances is quite academic, for the rapid improvement that occurs makes the ultimate recovery more certain.

Special mention is required for those patients presenting with a post-renal obstruction causing uraemia, for the renal function usually recovers sufficiently to allow the patients to live a useful life, once the uraemia has been relieved by surgical procedures. The clinical condition of these patients has often deteriorated more than the examination of the blood chemistry would suggest, and the decision to dialyse has been made more on clinical assessment. When the obstruction occurs in the upper renal tract dialysis should be followed within 48 hours by surgical relief of the obstruction. When the prostate gland causes obstruction it is safer to treat the patient initially with an indwelling catheter and correct the uraemia by dialysis. Operation should be delayed until renal function has partially recovered, a further dialysis being performed immediately before operation when indicated. Particular attention must be given to the care of the patient with an indwelling catheter so that ascending infection is prevented (Pyrah, Goldie, Parsons, and Raper, 1955; Gibbon, 1958). This is vital, as prolonged catheter drainage may be required before the patient is fit to withstand a prostatectomy.

#### Metabolic Response

Some workers have been impressed by the variation in mortality of patients with acute renal failure according to the primary disease (Teschan, Post, Smith, Abernathy, Davis, Gray, Howard, Johnson, Klopp, Mundy, O'Meara, and Rush, 1955; Taylor, 1957). It is generally agreed that those cases complicating trauma (such as war injuries, road accidents, or major surgical procedures) have a less favourable prognosis than cases in which renal failure is the main feature (such as transfusion reactions or hypotension complicating an abortion). Other workers, dealing mainly with non-traumatic cases, have emphasized the good results that can be obtained with a dietary regime alone when the period of oliguria has been less than say 10–14 days (Bull, Joekes, and Lowe, 1949).

In assessing our cases we have been impressed by an association between the severity of the illness and the metabolic response of the patient as measured by the speed at which uraemia develops, for which the daily rise of the B.U.N. is the best available laboratory index. The urea production which occurs in normal persons, or in patients with uncomplicated renal failure, whilst taking the dietary regime would correspond to a daily rise of the B.U.N. of less than 10 mg./100 ml. a day if anuria was present (Gamble, 1947; Parsons and McCracken, 1957). We have, wherever possible, classified our cases as mild, moderate, or severe according to the rate of rise of the B.U.N. a day whilst anuric and receiving the standard dietary regime.

The mild group (Table VII), where the rise is less than 15 mg./100 ml. a day, can for the most part be managed without the need for dialysis, and perhaps the majority of patients in this category have been managed successfully in their own hospitals. The two patients who were dialysed had either inadequate treatment or an unduly protracted oliguric phase. Those patients that came into the moderate group (B.U.N. rise 15–30 mg./100 ml. a day) and the severe group (B.U.N. rise greater

than 30 mg./100 ml. a day) had evident causes of an increased metabolic breakdown. A study of our cases shows that the majority of anurias associated with the complications of late pregnancy have fallen into the moderate group (Parsons and McCracken, 1958b), whilst the majority of cases following major surgery or trauma have fallen into the severe group (11 out of the 15 patients, Table VII). Whilst the primary condition

is more important than the return of urine volume to any particular figure.

We have found that the maximum daily volume of urine during the late recovery phase is usually about 3-4 l., except when overhydration has occurred, and then it is correspondingly higher. We would agree with Merrill (1955) that ionic supplementation is usually unnecessary in this phase when the patient is eating a normal diet.

TABLE VII.—Average Rise of B.U.N. in Patients With Acute Reversible Renal Failure

Group	Average Daily Rise B.U.N. mg. 100 ml.	No. of Patients	No. Dialysed	No. Recovered
Mild	< 15	5	2	5
Moderate	15-30	20	18	18
Severe	> 30	15	15	5

which precipitated the acute renal failure seems largely to determine the degree of metabolic response, complications can increase the response. For instance, one patient initially fell into the mild group, but the occurrence of a staphylococcal enteritis rapidly increased the metabolic response, so that the B.U.N. rose at a greater rate than 30 mg./100 ml. a day.

The importance of assessing the severity of the metabolic breakdown is stressed for several reasons. (1) The moderate and severe groups will probably require dialysis for survival. (2) Cases in the severe group will require dialysis so soon after diagnosis that no time must be lost in transferring them to an artificial kidney unit. (3) Cases in the severe group have a high mortality, and all the complications in addition to the uraemia must be treated adequately. (4) It affords some basis for comparison of results in different series.

**Reduction of the Metabolic Response by Hormones.**—Although testosterone has been used to reduce the metabolic response in patients with acute renal failure the evidence is not conclusive (Merrill, 1955). We have described elsewhere (McCracken and Parsons, 1958) that the synthetic anabolic steroid norethandrolone ("nilevar"; 17-ethyl-19-nortestosterone) reduces protein katabolism by approximately 70% in patients who have developed acute renal failure as a complication of pregnancy. Norethandrolone has been used in other conditions, but no significant reduction of protein katabolism was observed. We would now advocate giving norethandrolone (30 mg. a day) to all patients with acute reversible renal failure occurring as a complication of pregnancy, as it might largely eliminate the need for dialysis (Parsons, 1959).

#### Recovery Phase of Acute Reversible Renal Failure

The period of oliguria has usually been expressed in terms of urine volume per 24 hours. This has little practical value. For instance, in mild cases we have observed correction of the uraemic state when the urine volume has been as low as 700 ml. a day, whilst in the severe case uraemia may be increasing when the urine output is 1,200 ml. a day. The correction of the uraemic state in these patients is dependent on the rate of katabolism of protein as well as the degree of renal function. It should be remembered that the patient will continue to deteriorate until the B.U.N. starts to fall as a result of returning renal function. This event

#### Optimum Time for Transfer

Many of the patients with acute renal failure have been referred to us with advanced clinical deterioration due to uraemia. This has occurred most frequently in the traumatic group, where the high metabolic rate produces uraemic manifestations early in the course of the illness. Of the 19 patients in the traumatic group, 13 required dialysis seven days or less after the onset of anuria, and nine of these on or before the fifth day. Many of these patients had to be dialysed as an emergency on admission, for, according to our criteria, they had been allowed to progress too far before transfer. It is therefore imperative that these patients should be transferred earlier, and if possible 48 hours before the optimum time for dialysis, for if this has passed the chances of survival are lessened. Daily observations of the rise of the blood urea give a reliable index of the rate of progress towards the uraemic state, and will forecast the day the B.U.N. reaches 180-200 mg./100 ml.

Patients in the moderate group usually require a dialysis between the 6th and 10th days after the onset of anuria, and again transfer should be arranged early.

When a patient develops an acute reversible renal failure we advocate that the nearest artificial kidney unit should be informed so that when the need for transfer becomes apparent it can be arranged early. This should save the distressing sight of seeing some patients die within a few minutes or hours of admission, and should save the artificial kidney team from having to use the machine throughout the night.

#### Infection

Uraemic patients are very susceptible to infection and, in particular, to staphylococcal enterocolitis. It should be noted that we have not encountered diarrhoea in these patients except when staphylococcal enterocolitis has developed. Bull (1955) advocated the routine administration of penicillin to patients with acute renal failure, but to-day the high incidence of antibiotic-resistant strains of staphylococci demands a reassessment. Our experience suggests that it is unwise to administer broad-spectrum antibiotics prophylactically, as these have undoubtedly precipitated staphylococcal infections in some of our patients. We have tried to minimize infections by reverse barrier nursing and by frequent sterilization of blankets, and have used antibiotics only to treat known infections. The situation, however, must not be viewed with complacency, because staphylococci resistant to erythromycin are now being encountered.

It is important to emphasize that these infections are not due to or associated with the artificial kidney. They occur with the same incidence in patients not treated by dialysis. In some patients infections arose before the dialysis, and it has occurred in uraemic patients who have never received antibiotics. Because these infections

were regarded as terminal events they have not hitherto had the same importance attached to them, but they are of the utmost importance now that the uraemia can be controlled by dialysis.

#### Demand for Artificial Kidneys

The number of patients who require dialysis are relatively few. For optimum efficiency we would agree with Merrill (1955) that an artificial kidney must be in fairly constant use so that the unit can be maintained at optimum efficiency. It would seem unrealistic, therefore, to have too many of these machines in the country. This is important, for the cost of staffing and maintaining an artificial kidney is considerable. In support of this, we have found that these patients can be transported over long distances (many have travelled over 200 miles—320 km.) with safety, provided that the transfer is arranged early.

There are many types of artificial kidney available. Some of these machines can also remove water from the patient by ultrafiltration (Alwall, Skeggs-Leonards, and Kolff disposable pack), but unfortunately their dialysing surface area, and hence efficiency, is less than the modified Kolff-Brigham model used in this series. Among patients with acute reversible renal failure we have had 15 with a severe metabolic response but only three in whom overhydration was a problem. We regard maximum efficiency of dialysis as more important than the ability to remove water, and therefore prefer the modified Kolff-Brigham machine, as the uraemia can be more effectively treated and controlled.

#### Summary

A total of 100 patients referred to the artificial kidney unit are reviewed. Of these, 82 were dialysed with an improved Kolff-Brigham artificial kidney. Complications occurring during the dialysis were few and not serious.

Acute reversible renal failure occurred in 63 patients, and 45 were dialysed. The basic treatment was a dietary regime (400 ml. of water and 100 g. of glucose daily, with vitamins). The most consistent indication for dialysis was clinical deterioration, particularly early mental changes, nausea, and vomiting. The biochemical indications were a B.U.N. 180–200 mg./100 ml., K 7 mEq/l., and CO<sub>2</sub> c.p. 13 mEq/l. The metabolic response, estimated by the daily rise of the B.U.N., was remarkably constant in any one patient, and a classification into mild (rise <15/mg./100 ml. a day), moderate (rise 15–30 mg./100 ml. a day), and severe (rise >30 mg./100 ml. a day) is suggested. The mild group were frequently managed successfully without dialysis, whilst the moderate group (mainly complications of late pregnancy) usually required a dialysis between the 6th and 10th days. The severe group (mainly trauma, accidental or surgical) often required a dialysis as early as the fourth or fifth day. In the severe group the incidence of complications, particularly sepsis, was high and the mortality greater. Many of these patients were referred too late; earlier transfer might improve the prognosis.

The metabolic response in the pregnancy patients was reduced by 70% when 30 mg. of norethandrolone ("nilevar") was given daily. Administration of this steroid might largely eliminate the need for dialysis. A similar action has not been observed in other conditions.

Nine uraemic patients with reversible post-renal obstruction have been dialysed. Obstructions in the upper renal tract have been relieved surgically following a dialysis. Obstructions caused by the prostate gland were relieved by an indwelling catheter, and a dialysis was performed, operation being delayed until renal function improved.

In chronic renal failure too few patients have been treated for justifiable conclusions to be drawn. In those patients with acute renal failure of obscure origin dialysis has been used so as to maintain life while diagnostic procedures were being undertaken. If an irreversible condition was found no further dialyses were performed.

The artificial kidney was bought and is being maintained by the Board of Governors of the United Leeds Hospitals. They also defrayed part of the expenses of this investigation. We thank all the consultants who referred patients to the unit. We are grateful to Professor L. N. Pyrah, Mr. F. P. Raper, and Professor R. E. Tunbridge for advice and for help with some of the diagnostic procedures. During the past six months Drs. O. Ciniewicz and C. R. Blagg have given much help in the routine management of the patients. We thank Sisters M. Thwaites, M. Sharpe, and F. N. Ellis, who nursed these patients; Dr. C. K. Anderson for the pathological findings; the staff of the department of bacteriology for the bacteriological findings; Mr. J. Hainsworth for the figures; and Mrs. S. M. Hobson, Miss M. Nicholson, and Mrs. J. McNeill for the biochemical data.

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