# ACUTE RENAL FAILURE—ITS DIAGNOSIS AND MANAGEMENT, INCLUDING THE USE OF THE TWIN-COIL ARTIFICIAL KIDNEY

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Acute renal failure may be defined as any abrupt deterioration in renal function resulting in azotaemia and disturbance of electrolyte metabolism, usually associated with oliguria (400 ml. per 24 hours or less*). This, however, is not invariable, since instances of sudden renal failure without oliguria are encountered. This is distinct from missed oliguric renal failure, where the oliguric phase has lasted only a few hours, the patient presenting in the diuretic phase.

Its causes are many and diverse. There is virtually no field of medicine or surgery in which this condition may not be encountered; hence all clinicians should be familiar with the basic principles in the diagnosis and management of acute renal failure. The prognosis of the condition has improved vastly with the introduction of the 'conservative régime',[1,2] and there can be little doubt concerning the additional beneficial results of haemodialysis. The use of the artificial kidney should no longer be regarded as a heroic measure in a moribund patient. Today the safety and the value of haemodialysis is accepted; it is now a recognized therapeutic procedure to be considered seriously in any patient with acute renal failure. The pendulum has swung (perhaps too far) from occasional use as a desperate measure to routine daily or prophylactic dialysis.[3,4]

In Groote Schuur Hospital 55 patients with acute renal failure have been treated during the period that the Kolff disposable-coil kidney has been in operation. The advisability of earlier dialysis has become apparent, and it is therefore of paramount importance that patients be referred to experienced specialized renal-insufficiency units as soon as possible. This paper records 2 years' experience in the diagnosis and management of acute renal failure with particular reference to the use of the artificial kidney.

* This is an arbitrary level (see later).

## DIAGNOSIS

Acute renal failure is a clinical syndrome like hepatic or pulmonary failure. The majority of cases of acute renal failure are attributable to acute tubular necrosis. The variety of associated conditions and other relevant clinical details of the 55 patients are set out in Table I.

While efficient management of acute oliguric renal failure is dependent on early recognition, there are certain difficulties in the diagnosis.

TABLE I. ACUTE RENAL FAILURE—CLINICAL DETAILS OF 55 CASES

| No. | Race | Sex | Age (years) | Diagnosis | Remarks | Duration of oliguria (days) | 1st day * | Day of dialysis | Peak blood urea (mg. per 100 ml.) | Peak serum potassium (mEq./l.) | Outcome ‡ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Obstetric:** | | | | | | | | | | | |
| 1 | B | F | 40 | Accidental haemorrhage (34 weeks). Afibrinogenaemia | Persistent bleeding. 10 pints blood. Hypokalaemia during diuretic phase | 19 | 23 | 11, 17 | 452 | 7·5 | R |
| 2 | C | F | 46 | Concealed accidental haemorrhage (32 weeks) | Caesarean section—oligaemic shock. 6 pints blood | 9 | 10 | 8 | 287 | 7·1 | R |
| 3 | C | F | 21 | Concealed accidental haemorrhage (34 weeks) | Hypotension for 9 hours. 2 fits. 8 pints blood | 17 | 22 | 12, 19 | 346 | 8·4 | R |
| 4 | C | F | 30 | Concealed accidental haemorrhage (34 weeks) | Eclamptic fits. 4 pints blood | 13 | 15 | 5 | 295 | 7·1 | R |
| 5 | B | F | 42 | Concealed accidental haemorrhage (32 weeks) | 4 pints blood. High potassium from inadvertent potassium administration countered with 'CTS-3 resin'. Late urinary-tract infection | 11 | 13 | 8 | 425 | 6·8 | R |
| 6 | B | F | 50 | Spontaneous abortion (? 20 weeks) | Rapid recovery. 3 pints blood | 4 | 6 | — | 184 | 6·0 | R |
| 7 | C | F | 31 | Infected abortion (10 weeks) | *Cl. welchii* infection. Pelvic peritonitis. Severe parotitis. 3 pints blood | 15 | 20 | 10 | 560 | 10·0 | R |
| 8 | C | F | 36 | Incomplete abortion (12 weeks) | Retained placenta. Septicaemia and prolonged oliguria | 29 | 37 | 16 | 475 | 6·9 | R |
| 9 | E | F | 36 | Infected abortion (12 weeks) | Septicaemia and peritonitis. 2 pints blood. Called on 6th day to jaundiced, overhydrated, moribund, patient | 7 | — | 7 | 600 | 5·3 | D— 7 |
| 10 | C | F | 25 | Infected abortion (12 weeks) | Perforated vaginal vault with severe diarrhoea. Pelvic abscess. Septicaemia and acute endocarditis. Gross jaundice. Serum bilirubin 57 mg. per 100 ml. | 16 | 19 | 11 | 310 | 5·2 | D—19 |
| 11 | B | F | 26 | Infected abortion (12 weeks) | Pelvic peritonitis. Intravascular haemolysis. Serum bilirubin 2·2 mg. per 100 ml. 2 pints blood | 15 | 17 | 10 | 360 | 5·4 | R |
| 12 | C | F | 39 | Infected abortion (12 weeks) | *Cl. welchii* infection. Serum bilirubin 1·5 mg. per 100 ml. 2 pints blood | 13 | 17 | — | 422 | 6·0 | R |
| 13 | C | F | 19 | Infected abortion (24 weeks) | *Cl. welchii* infection. 3 pints blood | 12 | 17 | — | 560 | 6·9 | R |
| 14 | B | F | 35 | Incomplete abortion (20 weeks) | Prolonged diuretic phase—35 days. Severe persistent diarrhoea since 11th day | 4 | 5 | — | 510 | 5·5 | R |
| 15 | B | F | 23 | Infected abortion (12 weeks) | Staphylococcal septicaemia. Pulmonary abscess. 6 pints blood. Recovered from renal failure. Normal blood urea for 12 days | 5 | 6 | — | 242 | 5·5 | D—22 |
| 16 | C | F | 20 | Infected abortion (12 weeks) | Potassium remained low throughout. Persistent vomiting | 15 | 18 | — | 321 | 4·8 | R |
| 17 | C | F | 20 | Infected abortion (16 weeks) | *Cl. welchii* infection with intravascular haemolysis—bacteriogenic pan-agglutin present. 3 pints blood | 14 | 18 | 10 | 380 | 4·9 | R |
| 18 | C | F | 34 | Infected abortion (12 weeks) | Pelvic peritonitis | 25 | 27 | 6, 16 | 410 | 7·4 | R |
| 19 | C | F | 40 | Infected abortion (14 weeks) | Gross herpes febrilis. Peritonitis. Intravascular haemolysis ++ before transfusion. Serum bilirubin 26·5 mg. per 100 ml. 2 pints blood | 11 | 14 | 7, 13 | 555 | 7·4 | R |
| 20 | C | F | 25 | Incomplete abortion (8 weeks) | Mild jaundice. 3 pints blood | 18 | 23 | — | 520 | 4·9 | R |
| 21 | C | F | 28 | Infected abortion (8 weeks) | Herpes febrilis. *Cl. welchii* infection. 4 pints blood | 5 | 7 | — | 280 | 3·8 | R |
| 22 | C | F | 25 | Infected abortion (12 weeks) | Herpes febrilis. Pelvic peritonitis. Intravascular haemolysis ++. Serum bilirubin 20·8 mg. per 100 ml. | 8 | 13 | 7, 10 | 441 | 5·6 | R |
| 23 | C | F | 24 | Post-traumatic abortion (18 weeks) | Kicked in abdomen. Postabortal haemorrhage | 22 | 27 | 18 | 239 | 4·4 | R |
| 24 | B | F | 32 | Intra-uterine death—premature induction. Postpartum haemorrhage | Overhydration. Extreme oliguria. 3 pints of blood. PM: Fibrinoid necrosis of interlobular arteries. 'Failed reflow' kidney and mild proximal-tubule necrosis | 17 | — | 9 | 420 | 6·9 | D—17 |
| 25 | B | F | 40 | Postpartum eclampsia | Collapsed suddenly. PM: Renal tubular regeneration. Eclamptic lesions in liver | 4 | — | — | 148 | 6·0 | D— 5 |
| **Nephrotoxic:** | | | | | | | | | | | |
| 26 | C | M | 27 | Mercuric biniodide poisoning | Misdiagnosed elsewhere as having an 'acute abdomen'—laparotomy performed | 10 | 12 | 10 | 450 | 5·8 | R |
| 27 | C | M | 29 | Ol. chenopodium poisoning | Hepatorenal failure. Perforation and peritonitis | 5 | 7 | — | 392 | 4·0 | R |
| **Miscellaneous:** | | | | | | | | | | | |
| 28 | B | F | 67 | Extensive burns | ? Transfusion reaction. Fulminating diarrhoea since day 7—? non-specific enterocolitis | 9 | — | — | 386 | 6·2 | D—19 |
| 29 | E | F | 58 | Hepatorenal failure of unknown aetiology | Slow diuresis. ? Nephrotoxic agent. Severe bronchopneumonia | 10 | 17 | 10 | 392 | 5·7 | R |
| 30 | C | F | 68 | Mesenteric thrombosis | Infarction of bowel. Chronic pyelonephritis | 5 | — | — | 306 | 4·7 | D— 5 |
| 31 | E | M | 35 | Staphylococcal septicaemia | Acute pyelonephritis and osteomyelitis of ribs | 6 | 7 | 5 | 315 | 6·1 | R |

| No. | Race | Sex | Age (years) | Diagnosis | Remarks | Duration of oliguria (days) | 1-l. day * | Day of dialysis | Peak blood urea (mg. per 100 ml.) | Peak serum potassium (mEq./l.) | Outcome ** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 32 | E | F | 59 | ? Periureteritis fibrosa | Intermittent oliguria lasting 2 or 3 days relieved by catheterization | — | — | — | 317 | 7·6 | R |
| 33 | B | M | 35 | Cerebral malaria | No true oliguric phase observed. No haemoglobinuria | ** | 9 | — | 378 | 5·2 | R |
| 34 | E | M | 50 | Protocoproporphyria | Profound hypotension from peripheral circulatory failure—respiratory paralysis | — | — | 12 | 269 | 6·2 | R |
| 35 | E | M | 44 | Acute beriberi | Total anuria for 6 days. Bilateral renal-cortical necrosis. Infarction of papillary muscles of heart | 9 | — | 7 | 510 | 5·7 | D— 9 |
| **Postoperative:** | | | | | | | | | | | |
| 36 | C | M | 75 | Prostatectomy | Severe postoperative haemorrhage and pyaemia. Gross overhydration. PM: Acute pyelonephritis and acute tubular necrosis | 9 | — | 8 | 400 | 6·4 | D— 9 |
| 37 | E | M | 67 | Prostatectomy | Urinary infection treated with kanamycin | ** | ** | — | 315 | 4·6 | R |
| 38 | E | F | 60 | Laparotomy (hepatic haemangioma) | Severe haemorrhage from liver haemangioma | 4 | 5 | — | 305 | 5·9 | R |
| 39 | E | F | 60 | Laparotomy (melaena) | Cerebral haemorrhage with hemiplegia on day 8 | 8 | — | — | 204 | 4·9 | D— 8 |
| 40 | C | F | 28 | Laparotomy (gastric ulcer) | Postoperative peritonitis | 4 | 8 | 4 | 248 | 8·3 | R |
| 41 | E | M | 65 | Aneurysmectomy | Popliteal embolism with gangrene. Pulmonary embolism | 7 | — | 5 | 269 | 7·2 | D— 7 |
| 42 | E | M | 76 | Aortectomy and graft | Postoperative cerebrovascular accident and myocardial infarction | 10 | — | 8 | 581 | 6·8 | D—10 |
| 43 | E | M | 21 | Excision of aortic coarctation | Hypotension during operation | 9 | 13 | — | 650 | 6·9 | R |
| 44 | E | M | 27 | VSD repair (hypothermia) | Postoperative haemorrhage | 4 | 15 | — | 437 | 4·4 | R |
| 45 | E | M | 28 | VSD repair (hypothermia) | Cardiac arrest. Myocardial infarction. Pulmonary embolism. PM: Mild tubular necrosis | 4 | — | — | 174 | 6·6 | D— 4 |
| 46 | C | F | 68 | Hysterectomy (uterine polyp) | Known diabetic | 4 | 8 | — | 133 | 5·4 | R |
| 47 | E | M | 65 | Colectomy (polyp of colon) | Pulmonary embolism | 9 | — | — | 203 | 5·8 | D— 9 |
| 48 | E | M | 65 | Choledochostomy | Cholelithiasis. Suppurative cholangitis treated with kanamycin. Died of infection after recovery from renal failure | 11 | 15 | 21 | 340 | 4·6 | D—28 |
| **Post-traumatic:** | | | | | | | | | | | |
| 49 | C | M | 29 | Multiple injuries | Intercurrent influenza. PM: Crushed chest, fracture of femur, acute tubular necrosis | 10 | — | 6 | 471 | 6·9 | D—10 |
| 50 | B | M | 45 | Multiple injuries | Complete anuria from day 2. PM: Renal cortical necrosis | 9 | — | 8 | 426 | 5·6 | D— 9 |
| 51 | B | M | 30 | Multiple injuries | 2nd dialysis during diuretic phase stopped because of severe gastro-intestinal haemorrhage | 8 | 12 | 7, 14 | 490 | 6·4 | D—15 |
| 52 | E | M | 26 | Multiple injuries | Complete anuria from day 3. Pulmonary embolism. PM: Renal cortical necrosis | 6 | — | — | 280 | 6·6 | D— 6 |
| 53 | B | M | 35 | Multiple injuries | Overhydrated and jaundiced when seen on the 4th day. Bronchopneumonia and anoxia preterminally | 6 | — | 4 | 232 | 8·5 | D— 6 |
| 54 | C | M | 30 | Multiple injuries | Severe head injury. ? Fat embolism | 5 | — | — | 255 | 5·6 | D— 5 |
| 55 | B | M | 49 | Multiple injuries | Severe oligaemic shock. 5 pints blood | 3 | 5 | — | 326 | 5·6 | R |

B = Bantu, C = Coloured, E = European, M = male, F = female, PM = postmortem findings, VSD = ventricular septal defect.

Under 'remarks', the amount of blood transfused initially is recorded in pints.

* '1-l. day' = day on which urine volume reached 1 litre.

** R = recovery, D = death, followed by the day of death.

Trauma, shock, blood loss, salt and water depletion — these and many other pre-renal factors lead to oliguria and azotaemia. This condition, which is here termed acute renal circulatory insufficiency, may be difficult to differentiate from acute renal failure caused by acute tubular necrosis. Apart from clinical assessment of dehydration and the observation of alterations in the specific gravity (SG) of the serum, and in haemoglobin and haematocrit values, this distinction is made in the first instance by directing attention to the urine and not to the serum chemistry.

*The Importance of Investigation of Urine*

Careful urine collection is essential — inaccurate measurements, failure to chart urine, urine mixed with bowel action, wetting the bed, and blocked catheters, are all likely to lead to a false assessment. The definition of oliguria has been a contentious subject, and upper limits have been arbitrarily set at 300 ml.,[2] 400 ml.,[6] 500 ml.,[6,7] 760 ml.,[8] and even 1,000 ml.[9] We accept 400 ml. as the upper limit, since, in our experience, once the urine volume reaches this figure a progressive stepwise increase follows, so that the '1-litre day' is reached 4 - 5 days later. While the presence of proteinuria and abnormal formed elements in the urinary sediment point to a primary renal condition, the measurement of the SG and analysis of the composition of the urine is of real assistance in diagnosis.

The measurement of the SG of the small amounts of urine available is often difficult, and should be carried out by the doctor and not by the nursing staff. While a high SG (> 1018) favours a pre-renal cause, a low SG (usually about 1010) does not necessarily mean renal failure. Physiological oliguria can be demonstrated to occur with a low or a high urine concentration,[5] depending on solute and water intake. Oliguria with a low SG may be encountered when sodium and urea excretion is low, as in renal circulatory insufficiency, and, postoperatively, following pre-operative restriction of protein and salt intake. Nevertheless, SG measurement when properly done is useful, and while it is not as refined as the estimation of urine osmolarity, it has the advantage of simplicity.

Urine-urea concentration is especially useful when very small amounts of urine are available. It may be high in the first instance, but with the evolution of tubular necrosis the concentration falls towards plasma levels — urea concentration is usually below 1·5 G. per 100 ml. (510 - 1029 mg. per 100 ml. in this series). A blood-urea concentration above 100 mg.

per 100 ml. and a urine concentration under 2 G. per 100 ml. has been held to favour acute renal failure, provided chronic renal disease can be excluded.[10]

The electrolyte pattern of the urine is variable; sodium concentrations have ranged from 43 - 102 mEq./l., chloride from 19 - 64 and potassium from 16 - 50. In general, in acute tubular necrosis urine-sodium concentration is almost invariably 'high' (> 35 mEq./l.), but may be low in certain cases — commonly following burns,[11] sometimes after trauma[12] and transfusion reactions,[13] and after pre-operative restriction of salt. Thus, while a low sodium concentration may sometimes occur in acute tubular necrosis, in general a high urinary-sodium concentration and a low urea favour this diagnosis. On the other hand, a low sodium and a high urea concentration favour acute renal circulatory insufficiency. This is also the pattern seen in acute glomerulonephritis.

Having made the diagnosis of acute renal failure, questions of aetiology and reversibility must be considered.

## AETIOLOGICAL CONSIDERATIONS

Acute renal failure rarely occurs without apparent cause and, indeed, there is frequently evidence of more than one precipitating factor.

Careful questioning is important (ingestion of drugs and poisons, attempted abortion, previous state of shock, etc.). An inadequate history is frequently the result of ignorance or evasiveness on the part of the patient and, sometimes, the uraemic mental state precludes questioning. Interrogation of the relatives or friends may assist, but enquiries may be fruitless, particularly in cases of criminal abortion. Over 70

TABLE II. CAUSES OF ACUTE RENAL FAILURE

*Intrinsic Renal Failure*

1. *Acute tubular necrosis:*
   - Group I: Obstetric; nephrotoxic; intravascular haemolysis; and miscellaneous, especially 'hepatorenal' syndrome and infections
   - Group II: Postoperative; and post-traumatic, including 'crush syndrome'
2. *Bilateral cortical necrosis*
3. *Vascular obstruction:*
   Bilateral renal emboli
   Bilateral thrombosis of renal artery and vein
4. *'Hypersensitivity states':*
   Acute diffuse glomerulonephritis
   Polyarteritis nodosa
   Systemic lupus erythematosus
   Other hypersensitivity states, e.g. to penicillin
5. *Acute pyelonephritis:*
   Renal medullary necrosis
6. *Acute renal failure superimposed on chronic renal disease*

*Extrinsic Renal Failure*

1. *Prerenal (acute circulatory insufficiency):*
   Hypotension
   Haemorrhage
   Water and electrolyte imbalance
   Burns
2. *Post-renal:*
   - *Intrarenal:* Sulphonamide crystalluria; and precipitation of uric-acid crystals following treatment with nitrogen mustard, etc.
   - *Extrarenal:* Ureteric and urethral obstruction.

causes[13] have been recorded and Table II summarizes these.

Glomerulonephritis may cause acute oliguric renal failure. As a rule, however, the history of a preceding streptococcal infection in a young subject, and the association of facial oedema and hypertension with proteinuria and haematuria suggest the diagnosis. It should be realized that, while an elevation of systolic blood pressure is common, diastolic hypertension and retinopathy are not usual features of acute renal failure from tubular necrosis. Hypertension may be present with gross sodium and water overload, and has been seen most frequently in post-traumatic cases. Furthermore, oedema usually occurs only if overhydration is present or as a result of the underlying state, e.g. congestive heart failure. Periorbital oedema, except in cases following carbon tetrachloride and chloroform intoxication,[5] is not a usual feature of the condition.

With underlying chronic renal disease, it may be difficult to differentiate a superimposed acute episode from acute renal failure *de novo*. Although the history may be helpful, radiological evaluation of the size of the kidneys is mandatory. The small kidneys of chronic renal disease may be demonstrated — this is in contrast to the normal-sized or slightly enlarged kidneys of acute tubular necrosis.

Our cases of acute renal failure have been drawn from the 3 main racial groups of the Cape Peninsula. There were 24 Coloured, 17 White and 14 Bantu patients. The important clinical details are recorded in Table I. These cases of acute renal failure have been subdivided into 2 groups; 64% in group I and 36% in group II.

Group I includes obstetric and nephrotoxic causes and miscellaneous causes such as infections, intravascular haemolysis and hepatorenal failure of uncertain origin. Group II is limited to postoperative and post-traumatic cases where there is rapid and extensive tissue destruction, often with infection and characterized by rapidly progressive uraemia. This differentiation is important, since the prognosis is very different in the 2 groups.

Apart from the cases attributable to acute tubular necrosis there was 1 patient with suspected peri-ureteric fibrosis in which, however, acute tubular necrosis could not be excluded; 2 with severe acute pyelonephritis, one of whom had proximal tubular necrosis as well; 3 patients with renal cortical necrosis; and 1 with 'failed reflow' kidney.[14] In assessing the mortality of acute renal failure the last 2 conditions mentioned are frequently excluded on the grounds that they are irreversible. This is not justifiable, since these conditions occur in the same clinical setting and, furthermore, they frequently cannot be distinguished during the oliguric phase. Two patients with non-oliguric acute renal failure are included because this is a variant of acute tubular necrosis.

*Clinical Settings*

The clinical settings are conveniently grouped as follows: (1) obstetric; (2) medical; (3) postoperative, and (4) post-traumatic.

The majority of the 25 obstetric cases followed infected abortions, many of which, it is believed, were induced. No less than 23 of the 27 patients of Russell *et al.*[15] who had abortions in the first trimester were criminally induced. Apart from mechanical interference, commonly soap and water, concentrated chloroxylenol ('dettol') or unknown corrosives are introduced into the uterus. The relationship between *Cl. welchii* infection and acute renal failure[16] has been stressed. In 5 cases (cases 7, 12, 13, 17 and 21) *Cl. welchii* infection was proved. In 4 further cases (cases 11, 19, 20 and 22) it was strongly suspected on clinical grounds. In some of these, intravascular haemolysis was severe.

Nephrotoxic cases numbered 2 only, but in 2 other cases (37 and 48) kanamycin was a likely contributory cause. Of the miscellaneous group of 8 cases, 3 unusual instances should be noted, viz. cerebral malaria (without haemoglobinuria), protocoproporphyria, and fulminating beriberi. In contradistinction to several other reports, mis-matched transfusions do not feature in this series. In only 2 cases was that possibility considered, and in only 1 could it not be excluded. The postoperative cases include several with major arterial surgery, and 2 cardiac cases in which hypothermia was employed. The traumatic cases resulted from 6 motor accidents and 1 train accident. The injuries were severe and multiple, involving fractures of long bones, crushing of the thorax and multiple visceral injuries. Hypotension was the major precipitating factor in most of these cases.

## REVERSIBILITY OF THE RENAL LESION

Acute renal failure from tubular necrosis is reversible. The truly irreversible conditions are: extensive bilateral renal cortical necrosis, rare cases of glomerulonephritis and of severe pyelonephritis with renal medullary necrosis, and vascular obstruction to both kidneys. Renal cortical necrosis may be suspected from the history — it usually follows concealed

accidental haemorrhage, but other causes have been recognized.[17] Two of our cases were post-traumatic (cases 50 and 52), and one followed acute fulminating beriberi (case 35). Complete anuria, macroscopic haematuria, especially in the first few days of severe oliguria, and prolongation of profound oliguria beyond 3 weeks, are features favouring the diagnosis of bilateral cortical necrosis. In cases of doubt and when anuria continues past the 3rd week, renal biopsy may help, but this may be hazardous because of the bleeding tendency of the uraemic state. We have, therefore, been reluctant to use this procedure. Furthermore, biopsy need not necessarily assist in assessing the extent of the necrosis. Although the study of routine biopsy samples is of considerable academic interest, it is of little or no practical assistance.

Apart from renal cortical necrosis, complete anuria may also occur in acute diffuse glomerulonephritis and in a post-renal obstructive lesion — the most frequent cause of complete anuria. In post-renal obstructive lesions the clinical features, cystoscopy, ureteric catheterization and retrograde pyelography usually establish the diagnosis, but peri-ureteric fibrosis is a source of difficulty. Ormond[19] has recently emphasized the importance of severe low backache, and abdominal and flank pain, which often precede the onset of oliguria or, more usually, anuria. The picture is further complicated by symptoms of uraemia and of secondary infection. Pyuria was present in 24 of 34 patients.[19] The presence of oliguria or anuria with no recognizable cause of obstruction is suggestive, especially when urine flow is re-established following ureteric catheterization. The importance of intravenous urography in demonstrating widening of the upper ureter and pelvis, in contrast to narrowing of the mid-ureter with medial deviation, has been stressed.[18]

## COURSE AND MANAGEMENT

The course and management demand consideration together since mismanagement can materially alter the course and produce disastrous results. In order to gauge the course during the oliguric and early diuretic phases, daily estimation of the concentrations of blood urea or serum creatinine and serum electrolytes is essential, in addition to meticulous measurement of fluid intake and output and regular weighing, where possible. The daily urine volume and the blood-urea or serum-creatinine estimations provide the main yardsticks in assessing progress.

The mean duration of the oliguria in 35 'recovered' patients was 11·1 days (±6·5) and varied between 4 and 29 days. Findings similar to these have been reported by others.[20,21] While the division into early and late diuretic phases has been defined as the point at which the first sustained downward trend in the blood-urea level occurs,[21] we have preferred to note the '1-litre day'. The mean duration for the period, onset to '1-litre day', was 14·6 days (±7·4) and varied between 5 and 37 days. In general, with the start of the diuretic phase, a stepwise increase in urine output occurred until the '1-litre day' was reached 4 - 5 days later. Unlike the findings 10 years ago, when basic fluid intake was 750 - 1,000 ml. per 24 hours, the urine volumes rarely exceeded 3 litres in the diuretic phase.

With the onset of oliguria the blood-urea and serum-creatinine concentrations rose rapidly. At the same time the fall in serum bicarbonate was profound, frequently to levels in the vicinity of 10 mEq./l. Hpyocalcaemia occurred concurrently with a marked rise in serum inorganic phosphate, often to levels of 10 mg. per 100 ml. or more. Hyperkalaemia (potassium — 6 mEq./l. and above) occurred in 28 patients (> 7 mEq./l. in 11, and > 8 mEq./l. in 4 patients). Where sufficient data were available, the mean daily rise in blood urea during the oliguric phase was calculated. In group I the rise in both dialysed and undialysed patients was 35 mg. per 100 ml. In group II the rise was considerably greater — 48 mg. per 100 ml. The clinical course of our recovered patients in group I has, in general, resembled that described by Loughridge *et al.*[21] — despite the frequency of severe infection in the obstetric cases.

Notwithstanding wide publicity concerning the importance of a restricted fluid intake, 6 patients (5 of whom died) were overhydrated when first seen by us (cases 3, 9, 24, 36, 48, and 53).

The management of acute renal failure has been well reviewed,[22] but in order to assess our results it is necessary to consider our practice, including the use of haemodialysis.

Careful explanation of the management to the patient is important. Initially the patient may feel perfectly well and resent the restrictions of food and fluid imposed on him. Most of our patients were drawn from the underprivileged section of the community. The intelligent, well-informed patient usually has little difficulty in understanding the purpose of the restrictions, but considerable tact and patience are necessary to overcome the ignorance and fear of some patients. Explanation to these patients in their own language through an interpreter, where necessary, is essential.

We have avoided the use of indwelling urethral catheters, except in patients with local complicating pathology. Only if necessary is the patient catheterized initially to obtain a urine specimen for diagnosis. Early mobilization of bed patients (and physiotherapy for those confined to bed), and isolation with barrier nursing is important in preventing infection — a prime cause of death in acute renal failure.

### *The 'Conservative' Régime*

Restriction of the fluid intake and the use of an electrolyte-free carbohydrate solution is the basis of therapy.

Following admission to hospital, assessment of the state of water and electrolyte balance, although often difficult, must be made before the maintenance programme is instituted — overhydration is likely to be present. After judicious correction of any major losses, daily maintenance fluids are set at 400 - 500 ml. per day. In the absence of any great variation in the breathing, temperature or humidity, this allows for adjustment to insensible respiration at a rate of 0·5 ml. per kilo. per hour and for water of oxidation on a protein-sparing régime. Additional basic fluids to cover the losses during fever [+ 200 ml. (?) for every degree over 100°F.] or the very hot weather of the local summer are difficult to estimate, and we have exceptionally set the intake at 750 or even 1,000 ml. per 24 hours. A record of the *daily weight* provides the best guide. With appropriate fluid intake the patient should lose 250 - 500 G. per day.

Replacement fluids consist of an amount equal to the previous day's urine output plus any gastro-intestinal aspirate or loss from vomiting and/or diarrhoea. Owing to the poor gastro-intestinal tolerance of these patients, we have abandoned the use of oral fat emulsions as a means of decreasing protein metabolism. Nor do we believe tube feeding offers any advantage. An amount of 100 G. glu-

cose a day provides a near-maximal protein-sparing effect.[22] We have found oral lactose more palatable than glucose, and most patients tolerate a 15 - 20% concentration well with minimal diarrhoea. Where intravenous administration is necessary, we have avoided indwelling venous cannulae because of the very real danger, particularly in uraemic patients, of suppurative thrombophlebitis following infection with a resistant staphylococcus. We have abandoned the intracaval use of concentrated glucose (40%) in view of the great hazard of thrombosis.[10] A 10 - 15% invert-sugar or glucose solution, sometimes combined with ethyl alcohol, is used. The alcohol provides 6 calories per ml. and should not be infused faster than 15 ml. per hour. The rate of infusion of the glucose and alcohol mixture can be calculated from this basic information.

During the oliguric phase the use of glucose or lactose only is often essential, but in practice many patients with normal or slightly raised serum potassium are given the following: small helpings of apple charlotte, ice cream, custard, maize-flour puddings and potassium-free carbonated sweet drinks — ginger beer has been a great standby. Glucose sweets are allowed *ad lib*. Small slivers of crisp toast with occasional cups of black tea add variety and help to maintain the morale of many patients. Any bread and butter used is salt-free, and fruit juices and high-potassium foods are forbidden. Allowance is made for the fluid content of the food. When, however, nausea or vomiting occurs, the intravenous route is used — preferably with a fine needle in a peripheral vein.

Electrolytes are withheld during the oliguric phase except for replacement of gross losses. Gastric and intestinal losses are conveniently replaced by 0·5-N saline or fluid containing an anionic pattern similar to that of plasma with regard to choride and bicarbonate ions. Like some, we usually replace urine volume by water only, but others add electrolytes, depending on the urinary losses. Usually no attempt is made to correct hyponatraemia, since excessive amounts of cation need to be infused. Only occasionally is correction of acidosis with M/6 sodium lactate necessary. Calcium gluconate may be used to combat hypocalcaemia. Appropriate electrolyte replacement in the diuretic phase is required when sodium and potassium losses are considerable, but no good purpose is served by forcing electrolytes at this stage, since the restoration of tubular function is usually rapid. During the diuretic phase there is a rapid fall in blood urea, and once levels of about 150 mg. per 100 ml. are reached at 20 G. protein diet is instituted.

Hyperkalaemia must be viewed in relation to the course of acute renal failure. In addition to the daily (or twice daily) estimation of potassium, ECG monitoring for evidence of hyperkalaemia is necessary. Hypocalcaemia and hyponatraemia potentiate the effect of a high serum potassium and should be corrected when gross. In group II cases, and when there is much infection with rapid tissue destruction, the serum potassium may rise sharply, out of proportion to the other biochemical indices, and is often at dangerous levels before the end of the first week. These levels may be reached rapidly and serum-potassium concentration per litre may rise more than a milli-equivalent in the course of 24 - 48 hours. In such cases the rise is countered by the administration of glucose and insulin (1 G. glucose per unit of insulin). It is unnecessary to use cation-exchange resins prophylactically in all cases, but they are of value where the serum-potassium level has shown a sharp upward trend. The oral administration of a sodium-cycle resin* in amounts of 35 - 45 G. per day in ginger beer has been effective. A continuous infusion of a standard mixture of calcium and sodium with glucose may also be effective,[24] but we are reluctant to use it as part of our daily régime, despite the claim that sodium administration has no dire effects.

If these measures fail, dialysis should be performed without delay. If uraemic symptoms are present in addition to hyperkalaemia, the measures for reducing serum potassium outlined are used temporarily before urgent dialysis. We have observed that in 3 out of 5 post-abortal patients with marked intravascular haemolysis from severe *Cl. welchii* infection, the serum potassium failed to rise with the advance of the other clinical and biochemical indices of acute renal failure.

*Other Measures*

McCracken and Parsons' claim[25] that an anabolic agent, norenthandrolone, ('nilevar') was capable of reducing protein catabolism by approximately 70% in obstetric cases, but not in post-traumatic cases, needs to be confirmed. Norandrostenolone ('durabolin'), 25 mg. by injection every second day, has been given for 7 - 15 days in 21 cases, but we have been less impressed with its value. It should be noted that the obstetric cases in which it is claimed to be effective are, in any event, those with the best prognosis.

Antibiotics have not been used prophylactically, although they have not been withheld in cases of infection. Due regard is given to the disappearance rates of the appropriate antibiotic in serum. Penicillin, erythromycin, chlortetracycline, 'active' 'chloromycetin', and 'active' novobiocin behave normally.[26,27] In uraemic patients the glucuronic-acid conjugates of chloromycetin persist for many hours in the serum and their potential toxicity is unknown. When infection is already present, as it is in many cases, these antibiotics may be used with a normal loading and slightly reduced or normal maintenance dosage, with the possible exception of chloromycetin. Whenever possible the use of streptomycin, the other tetracycline antibiotics, and the nephrotoxic drugs, neomycin and kanamycin, has been avoided, since their half-lives are considerably prolonged. Polymyxin B and vancomycin tend to accumulate in uraemia and must be used with the utmost caution.

In addition to penicillin treatment, antigas-gangrene serum has been administered in all cases of suspected *Cl. welchii* infection. Where vomiting and restlessness are troublesome, promazine, chlorpromazine and trifluoperazine have been used in low dosage. A transfusion of fresh packed cells has been given when the haemoglobin level has fallen below 8 G. per 100 ml.

*Haemodialysis*

While many patients can be satisfactorily managed on the above régime, in some haemodialysis is necessary. The indications have been reviewed elsewhere,[28] but in general

* CTS-3 carboxylic-acid-type resin (sodium salt) supplied by courtesy of Eli Lilly & Co.

more weight is given to the early clinical signs and symptoms as opposed to the abnormal serum chemistry (marked hyperkalaemia excepted). Although it is frequently difficult to differentiate the milder symptoms of uraemia from those of severe infection, our practice is to dialyse even when symptoms are mild. Of the 55 patients, 30 underwent dialysis, and 6 needed a further dialysis. Of these patients, 16 were from the obstetric, 1 from the nephrotoxic, 4 from the miscellaneous, 5 from the postoperative, and 4 from the post-traumatic group.

Dialysis is carried out in a room specially designed for the purpose. The procedure is described in the appendix. Apart from occasional sudden hypotension at the start of dialysis, no great variation in the blood pressure has been observed during the procedure. As the dialysis proceeds the blood pressure may tend to rise, but the use of hypotensive agents has been unnecessary. The temperature has usually remained unchanged, and haemolysis has not occurred.

Sedation may be necessary to allay restlessness. Pethidine or an intermediate-acting barbiturate is usually given. Unless the patient is already getting an antibiotic, penicillin, ½ mega unit, is given twice in the 24 hours.

Not only may the drugs given be dialysable, but the electrolyte concentration may influence their action. In a digitalized patient a sudden drop in serum potassium may precipitate digitalis intoxication, with the development of dangerous arrhythmia. Regular ECG control is therefore essential throughout the procedure.

Apart from the bursting of defective coils on 2 occasions, intermittent irregularity of the arterial inflow in 4 patients, and intermittent venous obstruction in 1, the procedure has been trouble-free and accomplished without fatality. Deaths during dialysis have, however, been recorded.[31] The main complication has been transient hypotension. Other complications have included a case of ventricular tachycardia in 1 patient, troublesome epistaxis in 2 and gastro-intestinal haemorrhage in 2. In 1 the haemorrhage was of such gravity that it led us to abandon dialysis after 3 hours. In 4, cut-down wounds became infected.

*Biochemical Changes caused by Dialysis*

The improvements following dialysis are shown in Table III. The reduction in the blood-urea and serum-creatinine levels is considerable. Hyperkalaemia is corrected in all patients and acidosis relieved or greatly ameliorated in most. Abnormal sodium and chloride concentrations show a return towards normal levels. The phosphate and uric-acid concentrations are reduced materially, while hypocalcaemia, if present, is corrected. While all cases show biochemical improvement, it is clear that without dialysis certain patients (e.g. case 19, Fig. 1) would not have survived.

TABLE III. MEAN AND STANDARD DEVIATIONS OF BLOOD AND SERUM VALUES

| *Substance* | *Before dialysis* | *After dialysis* |
|---|---|---|
| Blood urea—mg. per 100 ml. (31) .. .. .. .. | 376 ±111·6 | 182 ± 82·3 |
| Serum creatinine—mg. per 100 ml. (23) .. .. | 15·4± 4·8 | 8·6± 3·1 |
| Serum potassium — mEq./l. (30) .. .. .. .. | 6·6± 1·6 | 4·6± 1·0 |
| Serum $CO_2$—mEq./l. (24) .. | 10·9± 4·2 | 19·3± 4·9 |
| Serum sodium—mEq./l. (23) | 133·7± 4·4 | 135·9± 3·6 |
| Serum chloride—mEq./l. (25) | 88·8± 7·6 | 93·6± 6·0 |

Bracketed figures represent number of observations.

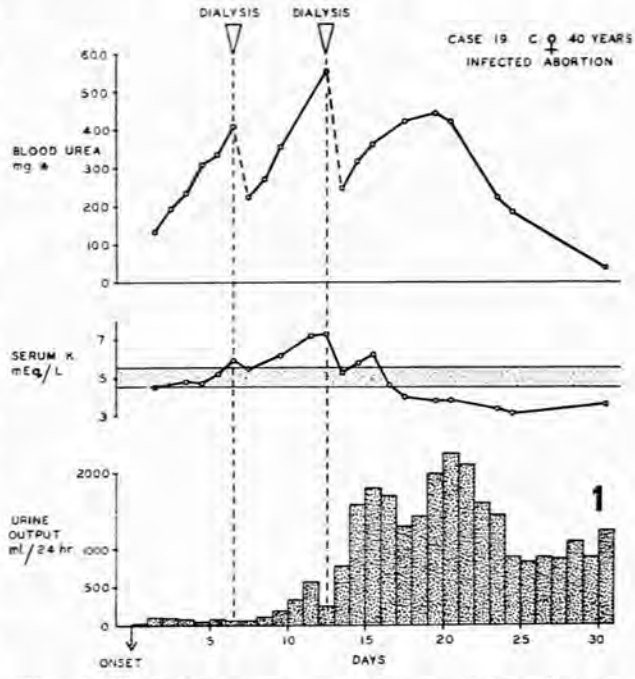


*Fig. 1.* Illustrating severe uraemia necessitating dialysis on 2 occasions.

The magnitude of the fall in the blood-urea and serum-creatinine levels was considerable, averaging 186 and 6·7 mg. per 100 ml. respectively. The fall in blood urea exceeded 300 mg. per 100 ml. in only 2 patients, and 200 mg. per 100 ml. in 11; it was less than 100 mg. per 100 ml. in 3. In the earlier cases bath water was not changed.

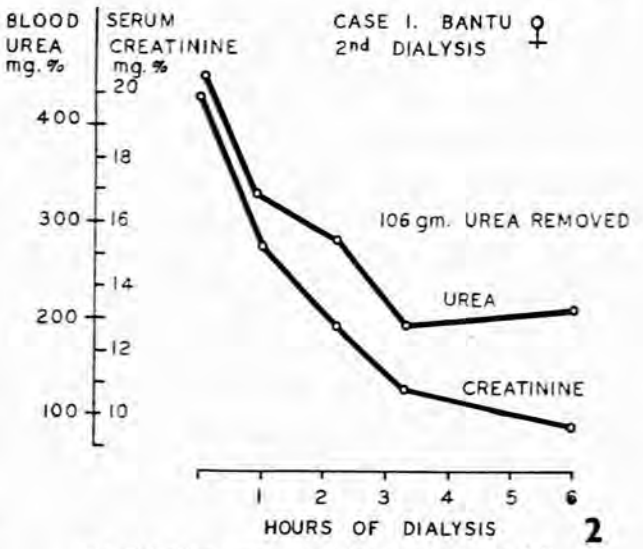


*Fig. 2* Unlike urea, creatinine continues to fall.

and hence the fall was less than in subsequent cases. In addition, however, there are marked differences in the clearance of urea at comparable levels of blood urea. Variation in dialysance of urea may be related to the tightness of the coil packing, resulting in inefficient perfusion, and the recently suggested remedies[32] have been adopted.

Changing the bath fluid influenced the fall in blood-urea concentration, but not that of creatinine (Fig. 2). There is a rapid fall in blood-urea concentration in all cases up to 3 hours and a levelling out thereafter in cases in which bath fluid is unchanged. When the fluid is changed the level continues to fall. The serum-creatinine level falls gradually throughout dialysis and changing the bath water has little effect.

Fig. 3 compares the urea levels in serum and bath fluid. With the fall in urea concentration there occurs a

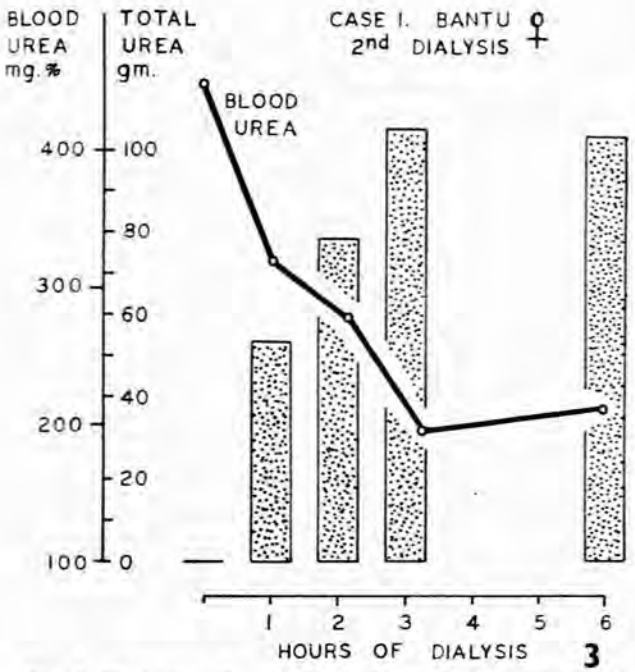


*Fig. 3.* Illustrating the changes in concentrations of blood and bath urea during dialysis without change of bath water. (Shaded areas represent bath-urea concentrations.)

reciprocal rise in the bath urea — to as much as 139 G. Potassium behaves similarly. Normal serum-potassium values are achieved by the end of the second hour. Although the increase in bath potassium is small when the initial bath concentration is 5 mEq./l., it has amounted to 350 mEq. with a bath concentration of 2·5 mEq./l. Gjǿrup and Thaysen, when dialysing against a potassium-free solution throughout, found the amount of potassium removed to average 419 mEq.[33] Although this exceeded the calculated excess potassium in their patients, the serum values remained within normal limits.

Bacteriological and chemical investigations have provided no explanation for the alteration in the colour of the bath fluid, which changes gradually to a yellow-green colour. This is maximal at the end of 1 - 2 hours in some cases. A characteristic odour is also present.

## RESULTS

Of 25 patients managed conservatively, 16 survived. Of the 9 who died, 7 were considered to have died as a result of the primary condition or its complications. One of these died of septicaemia when well over the acute renal failure. Case 28 died as a result of fulminating enterocolitis, while case 25 died from uraemia before dialysis could be started. Thirty patients were dialysed with 15 deaths, but there were no fatalities during dialysis.

While dramatic improvement frequently followed haemodialysis, the final assessment is judged simply as death

TABLE IV. RESULTS OF TREATMENT IN 55 CASES OF ACUTE RENAL FAILURE ††

| | *Patients* | *Dialysed** | *Died* | % *Mortality* |
|---|---|---|---|---|
| Group I: | | | | |
| Obstetric .. | 25 | 16 | 5** | 20 |
| Nephrotoxic .. | 2 | 1 | 0 | 0 |
| Miscellaneous .. | 8 | 4 | 3† | 37 |
| Total .. | 35 | 21 | 8 | 23 |
| Group II: | | | | |
| Postoperative .. | 13 | 5 | 7 | 54 |
| Post-traumatic .. | 7 | 4 | 6 | 86 |
| Total .. | 20 | 9 | 13 | 65 |

* Six patients were dialysed twice.

** In 3 of the obstetric cases the renal lesion was irreversible—2 with bilateral cortical necrosis and 1 with 'failed reflow' kidney.

† One patient with beriberi had bilateral cortical necrosis.

or survival. The results in all cases are summarized in Table IV, and the causes of death are given in Table V.

In group I, 8 of 35 patients died (23%). Whereas the mortality in the obstetric group was 20%, it should be noted that only 3 of the 5 deaths could reasonably be attributed to uraemia *per se*. Thus, case 24 had an irreversible parenchymal renal lesion ('failed reflow' kidney). Case 9 was *in extremis* with gross overhydration when referred for treatment. Pelvic peritonitis was also present. In case 25, in addition to a liver lesion of eclampsia, there was evidence of commencing recovery from acute tubular necrosis. Autopsy, however, failed to reveal any explanation for her sudden death. In the remaining 2, infection was responsible for the fatal outcome. In case 10 the severity of the septicaemia with acute endocarditis was sufficient in itself to cause death. Case 15 had recovered from the acute renal failure and the blood-urea level had been within normal limits for 12 days, when a recurrence of septicaemia resulted in death on the 22nd day. In the miscellaneous group, 2 of 3 deaths were attributable to uraemia. In the patient with burns (aged 67 years) fluid loss from fulminating diarrhoea contributed materially, while case 35 had bilateral renal cortical necrosis. The third patient died from the primary condition — a mesenteric thrombosis with infarction of the bowel.

In group II, 13 of the 20 patients died (65%). In the

†† Since the submission of this paper for publication, a further 13 patients have been treated, with the following results:

| | *Patients* | *Dialysed* | *Died* |
|---|---|---|---|
| Obstetric .. | 6 | 3 | 0 |
| Miscellaneous .. | 4 | 4 | 2 |
| Postoperative .. | 3 | 2 | 2 |

TABLE V. CAUSES OF DEATH

| Group | Case no. | Cause of death |
|---|---|---|
| Group I: | | |
| Obstetric | 9 | Septicaemia; uraemia and overhydration |
| | 10 | Septicaemia with acute endocarditis |
| | 15 | Staphylococcal septicaemia |
| | 24 | Uraemia—'failed reflow' kidney |
| | 25 | Uncertain—eclampsia |
| Medical | 28 | Uraemia—electrolyte imbalance |
| | 30 | Mesenteric thrombosis |
| | 35 | Uraemia—renal cortical necrosis |
| Group II: | | |
| Postoperative | 36 | Staphylococcal pyaemia with pulmonary abscess |
| | 39 | Cerebrovascular accident |
| | 41 | Pulmonary and popliteal embolism |
| | 42 | Cerebrovascular accident and myocardial infarction |
| | 45 | Cardiac arrest—myocardial infarction |
| | 47 | Pulmonary embolism |
| | 48 | Suppurative cholangitis |
| Post-traumatic | 49 | Intercurrent influenza and bronchopneumonia |
| | 50 | Uraemia—renal cortical necrosis |
| | 51 | Uraemia — gastro-intestinal haemorrhage |
| | 52 | Uraemia—renal cortical necrosis |
| | 53 | Bronchopneumonia and overhydration |
| | 54 | Fat embolism |

postoperative group there was a 50% mortality rate. In 5 of 7 cases death was attributable to a complication of the primary condition which accompanied acute renal failure and which may have, in any event, resulted in death. Case 45, who died of cardiac arrest, was found at autopsy to have a recent myocardial infarction. In the 7th case there was gross overhydration and severe complicating pyaemia.

Only 1 of the patients in the post-traumatic group survived. Two patients who died had extensive renal cortical necrosis and another had fat embolism. Case 49, with a severe chest injury and multiple fractures of long bones, developed influenza during an outbreak in the ward, while making good progress, and succumbed rapidly from bronchopneumonia. Case 51 died, during the early diuretic phase following the 2nd dialysis, from uncontrollable gastro-intestinal haemorrhage resulting from uraemic ulceration of the bowel. Case 53, who was referred on his fourth oliguric day with gross overhydration, succumbed 2 days later from severe bronchopneumonia. Thus, in this group 3 had irrecoverable disease, 2 died of complicating infection, and 1 of severe haemorrhage ascribable to the uraemic state itself.

## DISCUSSION

The necessity for prompt diagnosis of acute renal failure has been emphasized. While there are difficulties in diagnosis, these can be avoided by directing attention to the quantity of urine and its composition. While, in general, blood-urea levels appear to reflect the clinical status of the uraemic patient, discrepancies are well known. Some of our patients were relatively symptom-free with blood-urea levels of over 400 mg. per 100 ml. Hyperkalaemia, acidosis, electrolyte imbalance and uraemic symptoms are integral features of acute renal failure, all of which can be corrected with efficient treatment. This treatment can best be achieved by referring suspected cases *as soon as possible* to a renal centre with an experienced haemodialysis unit. Such centres, with their trained and experienced personnel, are best equipped to deal with the complicated problems of fluid and electrolyte balance, the efficient prevention and control of infection and the other complications of the uraemic state. Early transfer of patients will permit of timely dialysis, and patients should be referred not later than the 3rd day of oliguria. The indications for dialysis have been considered elsewhere.[28] The majority of patients have a good clinical and biochemical result from dialysis, but there are some cases in which the degree of reduction in the blood urea is disappointing. It is our impression, however, that there is a beneficial effect despite very moderate reduction in the blood-urea level.

Death in acute renal failure results from: (1) the underlying primary condition, and (2) acute renal failure and its complications. Apart from an irrecoverable primary condition and an irreversible renal lesion (cortical necrosis), death from acute renal failure should be reduced to a minimum with modern methods of management. In the past the chief causes of death were hyperkalaemia, pulmonary oedema and uraemic coma. In this series there were only 6 recoverable cases in which death was ascribable to uraemia itself. In 2 instances patients were referred when moribund and in an overhydrated state, and in 1 of these infection was also present.

The frequency of the complications of acute renal failure increases with delay in the use of the artificial kidney. The main factors contributing to fatality are:

(*i*) *Infection*. This is the most important factor and has been stressed by many authors.[13,31,34,35] It accounts for from 45% to 72% of the deaths. It should be noted that, while Balch *et al.*[35] pointed out that infection was responsible for 45% of deaths from post-traumatic renal insufficiency, Balch[36] claimed that there was no evidence that patients with post-traumatic renal insufficiency are more susceptible to infection. He considered factors such as extent of tissue damage, delay in treatment, and inadequacy of debridement of wounds, to be of major importance. Nevertheless, infection is frequently present in cases of acute renal failure, and it is difficult to control. In the uraemic state there is delayed wound healing[37] with resultant poor localization of infection. Apart from the possible lethal effect of infection, morbidity is prolonged. Patients should be barrier-nursed under strict anti-infective precautions, and antibiotics should not be used prophylactically. Staphylococcal enteritis has been a much feared complication.[31] Avoidance of unnecessary urethral catheterization, active physiotherapy (especially breathing exercises), and early mobilization all contribute to the prevention of infection.

(*ii*) *Cardio-pulmonary complications*. These include arrhythmias (usually in those with previous cardiovascular disease and/or during digitalis therapy), pulmonary oedema and acute respiratory failure. Pulmonary oedema results from overhydration and should no longer be a frequent and lethal complication of acute renal failure. Nevertheless, at least 15 of Salisbury's 31 fatal cases had

TABLE VI. RESULTS OF TREATMENT OF ACUTE RENAL FAILURE FROM VARIOUS CENTRES

| | *Group I (obstetric and medical)* | | | | *Group II (postoperative and post-traumatic)* | | | |
|---|---|---|---|---|---|---|---|---|
| | *Total* | *Dialysed* | *Died* | *% Mortality* | *Total* | *Dialysed* | *Died* | *% Mortality* |
| Swann and Merrill (1953) [5] | 63 | 17 | 25 | 40 | 22 | 41 | 14 | 64 |
| Anthonisen *et al.* (1956) [39] | 17 | 17 | 10 | 59* | 18 | 18 | 14 | 78 |
| Bull *et al.* (1956 - 8) [40-43] | 67 | 5 | 26 | 39 | — | — | — | — |
| Teschan *et al.* (1958) [6] | — | — | — | — | 51 | 31 | 27 | 53 |
| Parsons and McCracken (1959) [31] | 38 | 26 | 6 | 16 | 25 | 19 | 18 | 72 |
| Bluemle *et al.* (1959) [34] | 62 | 29 | 22 | 35 | 38 | 22 | 28 | 74 |
| Hammersmith (1960) [21,44] ** | 36 | 17 | 8 | 22 | 74 | 39 | 59 | 80 |
| Jackson *et al.* (1960) [45] | 33 | 18 | 18 | 55* | 22 | 17 | 11 | 50 |
| Kiley *et al.* (1960) [46] | 23 | 14 | 2 | 9 | 57 | 35 | 37 | 65 |
| Groote Schuur Hospital (present series) | 35 | 21 | 8 | 23 | 20 | 9 | 13 | 65 |

* The unusually high mortality is attributable presumably to the exclusion of undialysed cases (Anthonisen *et al.*) and to the inclusion of 11 fatal cases of glomerulonephritis (Jackson *et al.*).
** Group I figures are taken from Loughridge *et al.*,[21] and Group II figures from Shackman *et al.*[44].

pulmonary oedema.[28] Most renal units have had to treat patients with overhydration. Despite repeated emphasis, the importance of a restricted fluid and salt intake is not yet sufficiently appreciated.

*(iii) Central-nervous-system complications.* Coma and convulsions and the attendant danger of inhalation pneumonia may result in death, and are likely to be seen in advanced cases when referred too late. Almost two thirds of Bluemle's[34] patients with coma developed pneumonia.

*(iv) Bleeding.* Numerous bleeding defects have been demonstrated — vascular abnormalities, platelet defects, prothrombin depression, etc., while epistaxis, and oozing from wounds and into injection sites were found in a few patients — in only 1 of our patients was intractable bleeding considered responsible for death.

Comparison of mortality rates from different centres presents difficulties on account of the variable nature of the clinical material and the differences in management. Nevertheless, the mortality rate in this series, when compared with others, reveals a remarkable consistency (Table VI). In general, it is obvious that the mortality in the group I patients (despite the frequency and severity of infection in our cases) was very much lower than that in group II. There is little doubt concerning the gravity of the post-traumatic cases. The mortality from different centres has consistently been above 50% and is often above 70%. The differences may be related to:

1. The severe accelerated uraemia of the postoperative and, in particular, post-traumatic cases. Whereas the daily rate of rise in blood-urea concentration is usually below 35 mg. per 100 ml. in group I patients, it is considerably greater in the group II patients and may amount to 50[6] and 51[10] mg. per 100 ml. (blood-urea nitrogen) for post-traumatic cases.

2. The grave and often fatal nature of the underlying primary condition and its complications.

3. In the postoperative group the greater age and infirmity of many of these patients is undoubtedly a factor which is not sufficiently stressed. In fact, Bluemle *et al.*[34] stated there is no correlation between mortality and age. Kiley *et al.*,[46] in noting the effect of age, also emphasized the bad prognosis in patients following aneurysmectomy.

Of 50 patients with acute renal failure resulting from surgical conditions, 12 were jaundiced, but in no instance did Shackman *et al.*[44] consider jaundice primarily responsible for the condition. Jaundice, from hepatic disease, and acute renal failure have long been held to be a particularly unfavourable combination. Jackson *et al.*[45] have suggested separation of such jaundiced patients within the group of acute recoverable renal failure 'to avoid presenting an unnecessarily poor prognosis'. While none will deny that jaundice may contribute to an unfavourable outcome, the claim that the poor prognosis in all cases of renal failure with jaundice from hepatic disease is primarily attributable to the hepatic disease, is open to question. In their series, no less than 5 of 7 such fatal cases had undergone major surgery and, therefore, we would have included them in any event in group II with its poor prognosis.

In 2 cases in the post-traumatic group the renal lesions were irreversible. It is common to find such cases excluded from a consideration of acute renal failure, but irreversibility may only become apparent after protracted treatment, and there is always a possibility that cortical necrosis may be partial or mild, with a definite, although slight, prospect of survival. The possibility of improving mortality in the potentially reversible cases lies in earlier reference of such cases. Thus, with the avoidance of ill-considered overhydration, the prompt institution of scrupulous anti-infective precautions, and the opportunity for earlier dialysis, some improvement in prognosis may be expected. In the severe cases dialysis should be undertaken well before the 6th day, and probably before the 4th day.

The benefits of prophylactic dialysis have been advocated by Teschan *et al.*[6] and it remains to be seen whether this procedure will materially affect the poor outlook of the post-traumatic cases. The stated aim of maintaining the blood non-protein nitrogen at about 150 mg. per 100 ml., so that patients can enjoy a liberal food intake, has merit, but one can only view with considerable apprehension the prolonged retention of indwelling cannulae, and the statement that transient bacteraemia with fever and chills occurred in some of their patients within an hour of the beginning of dialysis is hardly reassuring. Despite general improvement and 'well-being', marked anaemia and some mental defect persisted, and there were 3 deaths among their 15 patients. There is a case for early dialysis and more frequent repetition, if necessary, but the advantages of daily dialysis have to be established, as has the harmlessness of such a procedure.

While the Kolff-Brigham rotating-drum kidney has been

preferred on the grounds of greater efficiency, there is the possible danger of overhydration, with pulmonary oedema. We have little doubt that the 'fixed' capacity and the advantage of ultrafiltration of the twin-coil kidney more than compensates for its lesser efficiency.

Improvements in the performance of the twin-coil kidney have resulted from minor modifications in design, and the effects of using a coil of longer surface area remain to be explored.[22] It is hoped that unnecessarily frequent dialysis may be avoided.

No matter what procedure is used, the most important means of reducing mortality in patients with severe accelerated uraemia is the avoidance of ill-considered parenteral administration of salt and water, and the prompt transfer to a renal centre. Only then will the distressing experience of death within hours of arrival[21] be avoided.


## SUMMARY

Two years' experience in the diagnosis and management of acute renal failure, including the use of the twin-coil artificial kidney, is described.

The cases are considered in 2 groups: group I (medical and obstetric cases) has a very much better prognosis than group II (postoperative and post-traumatic cases).

The factors underlying the differences in mortality are discussed. The avoidance of ill-considered parenteral therapy and the importance of prompt transfer of such patients to a renal centre is stressed.


## APPENDIX

*Dialysis Procedure*

In the event of dialysis, 6 pints of fresh blood are reserved and compatibility tests are carried out against the patient's blood and between each unit of blood as well. The patient is weighed before dialysis and again after the procedure. This is the most accurate way of assessing fluid loss during dialysis (the disposable-coil artificial kidney is an ultrafilter as well as a dialyser). Following skin preparation in the ward, and observing scrupulous aseptic technique, artery and vein exposures are carried out in the artificial-kidney room by surgical colleagues in the artificial-kidney team. Brachial block performed by an anaesthetist has been used in most of our cases with excellent results. The procedure provides very satisfactory anaesthesia and vasodilation. One patient developed a pneumothorax as a direct result of the brachial block, but this complication is rare in good hands. A severe bleeding tendency and any significant respiratory pathology are contraindications to the performance of brachial block. After calibrating the flow rate, the coils are filled to a pressure of 180 mm.Hg and usually need about 1,000 ml. of heparinized blood.

In most of our patients the radial artery (coil inflow) and deep cubital veins (coil outflow) of the same arm have been cannulated. When this has not been feasible, a catheter has been inserted into the inferior vena cava *via* the femoral vein. For venous cannulation we have used an ordinary Baxter infusion set, previously sterilized in 'zephiran'. For the radial artery, a No. 4 polythene catheter has usually been passed with little difficulty, except in very small vessels, when a No. 3 has been used. Smaller calibre catheters do not give adequate flow rates, and in these cases it is better to use the inferior vena cava as the inflow. Once the catheters are *in situ*, they are kept patent by continuous flushing through of heparinized saline.

Heparinization follows — initially 100 units per kilo., and then 1,000 units hourly. Administration is stopped an hour or two before the end of the procedure (usually 6 hours). Although the clotting time was initially repeatedly checked with the aim of keeping it between 15 and 20 minutes, in practice it is so markedly prolonged with the above dosage that we now only carry out the procedure in the last hours of dialysis. We have had no experience with regional heparinization.[29,30] Oozing from cut-down sites, especially if covered, should be carefully looked for throughout dialysis. Oozing from sores on the lips has been an irritating, but minor, complication in some patients. Repeated firm packing is usually sufficient to control oozing. Where oozing or other bleeding is severe, protamine sulphate (50 mg. per 5,000 units heparin) is given at the end of dialysis. The electrolyte composition* of the bath fluid is similar to that of plasma. Where hyperkalaemia is present, the amount of added potassium chloride is reduced or omitted altogether. A flow rate between 200 and 300 ml. per minute has been used. As dialysis proceeds, this speed diminishes and may be increased if necessary. The bath fluid is changed every 3 hours, and the procedure usually lasts 6 hours.

Initially, blood pressure, pulse and respiration rate are measured every minute, then at 5-minute intervals, and after 1 hour every 15 minutes. The danger period is that which follows immediately on the commencement of dialysis. A sudden drop in blood pressure may occur, probably from an abrupt diminution in the circulating blood volume, since the tubing of the artificial kidney is distensible. This can be prevented by clamping the coil outflow initially for a few seconds and then releasing it. Sudden flooding of the patient's circulation with at least 2 units of citrated blood may, by depressing the serum calcium, cause a drop in the blood pressure. Sometimes the low blood pressure persists; this is usually easily countered by elevation of the foot of the bed and the administration of 200 - 300 ml. of blood.

* Electrolyte composition:

| *Component* | *Milli-equivalents per litre* | | | | | |
|---|---|---|---|---|---|---|
| | *Na+* | *K+* | *Ca++* | *Mg++* | *Cl−* | *HCO3−* |
| NaCl .. | 97 | — | — | — | 97 | — |
| $NaHCO_3$ .. | 36 | — | — | — | — | 36 |
| KCl .. | — | 5 | — | — | 5 | — |
| $CaCl_2$ .. | — | — | 5 | — | 5 | — |
| $MgCl_2$ .. | — | — | — | 1·5 | 1·5 | — |
| Total .. | 133 | 5 | 5 | 1·5 | 108·5 | 36 |

Invert sugar 0·4%. Lactic acid to adjust pH to 7·4.

Acknowledgment is made to the Medical Superintendent of Groote Schuur Hospital, Dr. J. G. Burger, for the excellent facilities; to our colleagues Drs. S. J. Saunders, I. Bouchier, S. Bank, L. Isaacson and J. Foster for their help in operating the artificial kidney; to the departments of Anaesthesia, Surgery, and Obstetrics for assistance and willing cooperation; to Prof. J. C. Kench and the Department of Chemical Pathology for many of the biochemical determinations; and to Misses J. Seward, B.Sc., and M. Naude, B.Sc., for their help with the biochemistry as part of the activities of the CSIR/UCT renal-metabolic group.

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