ACUTE RENAL FAILURE: ITS COURSE AND PROGNOSIS*

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There is no field of medicine or surgery in which the syndrome of acute renal failure may not be encountered. The majority of cases are due to acute tubular necrosis, a condition that is reversible provided appropriate management is applied from the onset. While it is a subject of importance to all medical practitioners, the experience of any single doctor is likely to be limited. There is an understandable temptation to treat the seemingly mild case locally. Not only is the course highly variable but the clinical status is a poor guide to the severity of the underlying biochemical disturbance. For adequate treatment early transfer to a specialized centre is essential. A 24-hour biochemical service and facilities for carrying out haemodialysis must be available.

This report is based on the experience of the renal service of Groote Schuur Hospital in the management of 148 patients with acute renal failure. Table I reflects the annual incidence for the years 1959 to 1962, including also the last 4 months of 1958 and the first 6 months of 1963. There appears to be a slight but definite increase in the incidence.

TABLE I. ANNUAL INCIDENCE OF ACUTE RENAL FAILURE, GROOTE SCHUUR HOSPITAL

Year	*Obstetric*	*Medical**	*Surgical†*	*All patients*	*Incidence per 1,000 admissions*
1958‡	7	0	5	12	1·7
1959	5	3	7	15	0·7
1960	8	5	11	24	1·1
1961	12	12	8	32	1·3
1962	11	9	21	41	1·6
1963¶	11	7	6	24	2·0
Total	54	36	58	148	

* Medical includes nephrotoxic group. † Surgical includes post-traumatic group. ‡ 4 months. ¶ 6 months.

The Course of Acute Renal Failure

In the first place both the course and prognosis are determined by the clinical setting. The arbitrary division of the cases into categories, viz. obstetric, medical, nephrotoxic, surgical and post-traumatic, is useful. In general, in the surgical and post-traumatic groups the course is one of rapid deterioration and the prognosis is poor, whereas in the obstetric and the nephrotoxic group the course is more benign and the outlook good. The medical group falls between these extremes.

Reversible Renal Failure

The course in any individual case is determined by a number of factors, but in general the sequence is predictable. After the onset phase, during which the precipitating condition frequently dominates the picture, the oliguric phase ensues (< 400 ml./day). This is usual, but by no means invariable. In 7 of the 148 patients this phase did not occur. In the early stages the urine output is frequently below 50 ml./day (miscalled anuria). In a previous study of recovered cases, the oliguric phase was found to last 11·1 ± 6·5 days.[1] A progressive stepwise increase in the urine output follows until the urine volume reaches 1 - 2 litres/day.

The patient may be entirely symptom-free for several days before the appearance of uraemic symptoms, which are usually anorexia, nausea, retching, vomiting, acidotic breathing, mental dulling, confusion, then stupor and finally coma. Repeated convulsions occur in some cases. Pulmonary oedema is not a feature of the appropriately treated case, nor is hypertension. Uraemic twitching and purpura are far-advanced signs of uraemia, as is the presence of pericarditis and uraemic frosts. A gross bleeding state, with incoagulable blood, is uncommon but occurred in 3 of our patients. In one case factor-VII deficiency was demonstrable.

The course and management are closely interwoven, and mismanagement may materially alter the course, with disastrous results. The principles of treatment are now well known and need not be recapitulated.

The course is gauged by daily investigation of blood-urea, serum-K, and CO_2 concentrations, and ECG monitoring for hyperkalaemia. Depending on the degree of catabolism, the blood-urea rise may be slow or rapid and in general a daily rise in blood urea > 35 mg./100 ml. is regarded as indicating a severe case. With the onset of

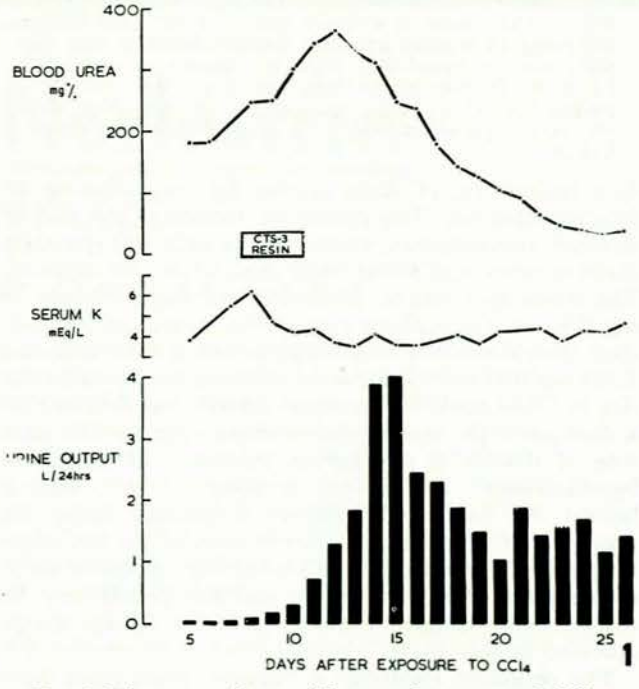

Fig. 1. The course in a mild case of acute renal failure due to carbon-tetrachloride poisoning. Note that the blood urea took 14 days to return to normal levels from the peak value of 368 mg./100 ml. (Previously published with an article by Friedman and Eales.[2])

*Presented by Prof. L. Eales at the 44th South African Medical Congress, Johannesburg, July 1963.

the diuretic phase the blood urea continues to climb for another 2-7 days and then usually declines rapidly. Intracellular components (K, Mg and PO_4) show a similar behaviour.

Fig. 1 depicts the course in a mild case of acute tubular necrosis due to CCl_4 poisoning.[2] The mean daily rise in blood urea was 28 mg./100 ml. Fig. 2 depicts the findings

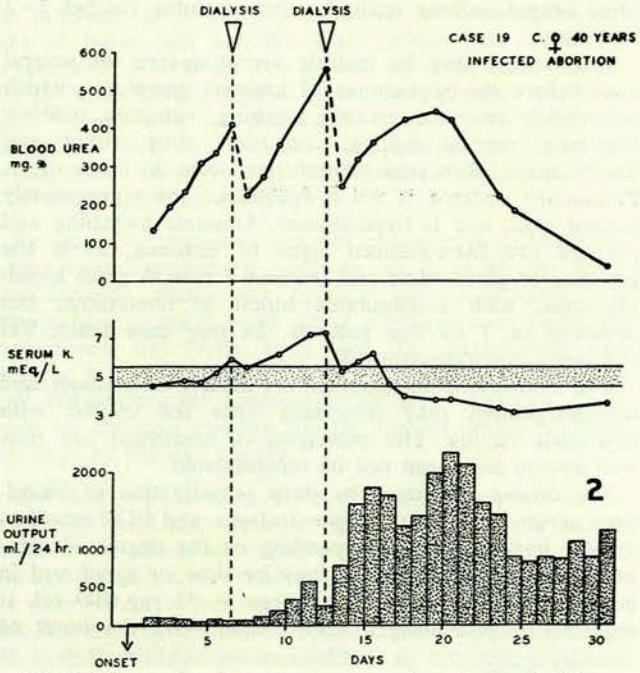

Fig. 2. The course in a severe case of acute renal failure following an infected abortion. Dialysis failed to alter the daily rate of blood-urea increase. Oliguria persisted for 13 days. Despite marked diuresis from the 14th day, decline in blood urea commenced on the 20th day. (Previously published with an article by Eales and Simenhoff.[1])

in a severe case of acute tubular necrosis following an infected abortion. The dangerous feature is the rise in serum-K concentration, which may be early and extremely rapid in cases with severe tissue destruction and infection. The mean daily rise in blood-urea concentration was 58 mg./100 ml. and without dialysis this patient would have died (the blood-urea concentration would have exceeded 1,000 mg./100 ml.). Dialysis in this case did not alter the rise in blood urea, but in others dialysis was followed by a decrease in the rate of urea synthesis (Fig. 3). The main role of dialysis is the prompt correction of dangerous hyperkalaemia. The dialysis procedure is not without hazard. We have lost 2 gravely ill patients during the procedure and have had at times to abandon the procedure before the full 6-hour period. During diuresis the serum-K concentration may fall rapidly and this period may be fraught with danger. Formerly a third of all deaths occurred in this phase.

The period of restitution is variable. Most cases show marked improvement in the glomerular filtration rate by the 3rd or 4th week. Convalescence is usually prolonged. In a few cases temporary urinary-tract infection has occurred. An interesting sequel to treatment by dialysis has

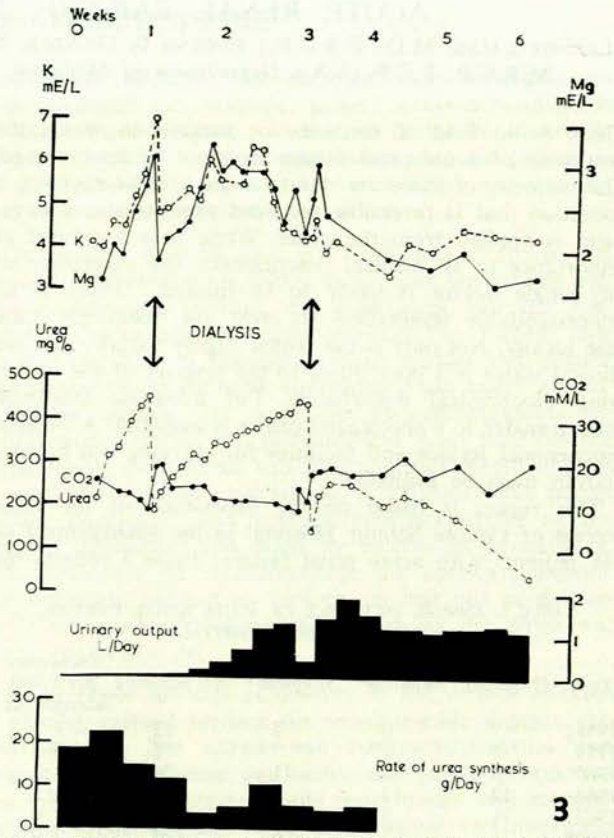

Fig. 3. The course in a severe case of acute renal failure owing to an infected abortion studied by Dr. H. Currie. Dialysis resulted in an alteration in the rate of urea synthesis. Note that serum K and Mg behaved similarly.

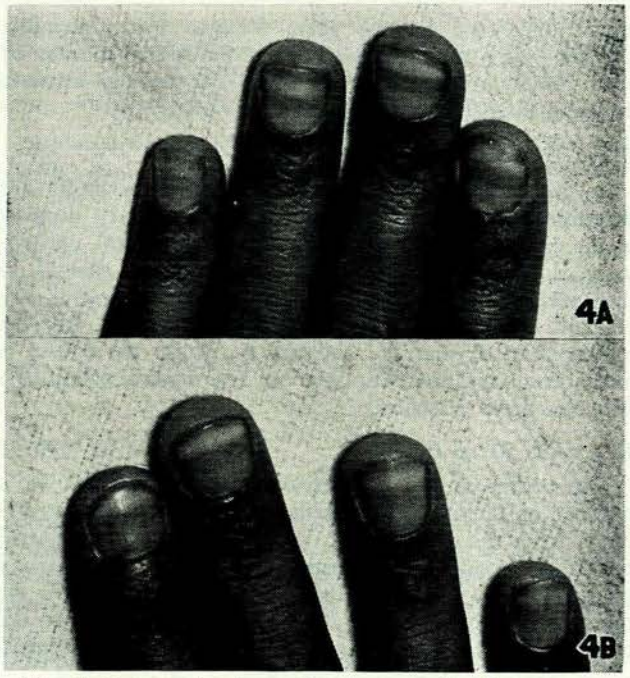

Fig. 4. Opaque bands on the finger nails after management of renal failure.

been the occurrence of a mild polyarthritis in 4 patients. Opaque bands on the nails are common (Fig. 4), and in one case a row of splinter haemorrhages was apparent on every nail. In some patients temporary mental depression has occurred during the recovery phase. This has been coupled at times with a dread of a future pregnancy, but it is of considerable interest that even a near-fatal episode of post-abortal acute renal failure has not deterred three of the patients from becoming pregnant at the earliest possible occasion!

Irreversible Renal Failure

Among the 148 cases there were 7 patients who died from uraemia owing to irreversible changes (Table II). When severe oliguria persists beyond the first week, and the urine is bloodstained and hypertension develops, a diagnosis

TABLE II. URAEMIC DEATHS DUE TO IRREVERSIBLE RENAL FAILURE

Race Sex Age	*Diagnosis*	*Day of death*	*PM findings*
BM—45	Multiple injuries	9	Bilateral cortical necrosis
CM—25	Multiple injuries	6	Bilateral cortical necrosis
WM—44	Acute beriberi. Alcoholism	9	Bilateral cortical necrosis
WF—37	Mitral valve replacement	6	Bilateral cortical necrosis
CF—42	Concealed accidental haemorrhage	63	Bilateral cortical necrosis
BF—32	Premature induction. Severe postpartum haemorrhage	17	Fibrinoid necrosis of interlobular arteries
CF—42	Pre-eclamptic toxaemia	36	Patchy cortical necrosis and fibrinoid necrosis of interlobular arteries

W = White, C = Coloured, B = Bantu, M = Male, F = Female.

of bilateral, patchy or massive cortical necrosis is probable. However, the clinical differentiation of the patchy type of cortical necrosis from acute tubular necrosis may be impossible.

Although bilateral cortical necrosis is recognized to be most commonly associated with concealed accidental haemorrhage in the last trimester of pregnancy, it has been noted in many other clinical settings.[3] While most of the women affected are multiparous and over 30 years of age, it may occur in children as a result of diarrhoea and dehydration, and in males it is usually the result of severe infections or poisons. Three of our patients were males, 2 with severe multiple injuries, and one an alcoholic patient with acute beriberi.

The course does not differ materially from that of acute tubular necrosis except that severe oliguria persists well beyond the usual period of 11·1 ± 6·5 days. Although we have noted recovery from acute renal failure after 29 days of oliguria, the diagnosis of renal cortical necrosis is to be seriously considered when oliguria persists for more than 3 weeks. Renal biopsy and X-ray of the kidney areas for calcification should be done. The course in patient 127 with bilateral cortical necrosis is illustrated in Fig. 5. On the 12th day tomograms and retrograde pyelograms, apart from possible enlargement of the kid-

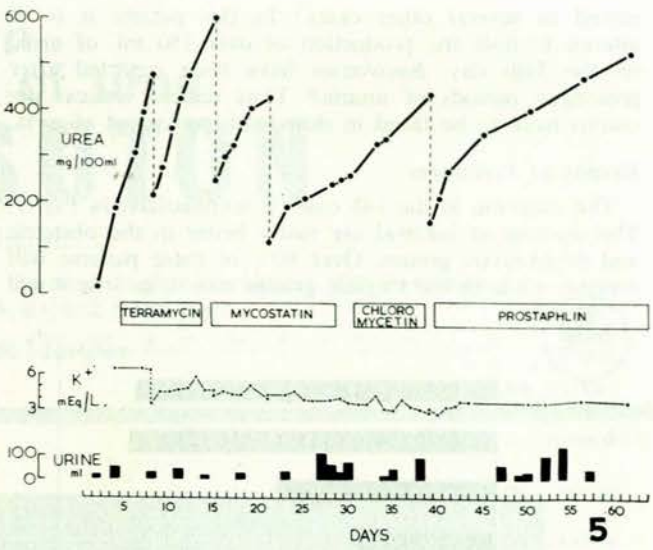

Fig. 5. Case 127. CF aged 42 (grav-20, para-13, 30-weeks pregnant, accidental haemorrhage). Illustrating the course in bilateral cortical necrosis. Note the rapid rise in blood-urea concentration (±80 mg./day) up till the time of the 2nd dialysis, and the much slower rate of rise subsequently. The 'terramycin' administration coincided with the period of rapid blood-urea increase. The 'chloromycetin' was given for a urinary-tract infection by proteus organisms and subsequently 'prostaphlin' for staphylococcal skin infection. Renal biopsy was performed on the 25th day after the 3rd dialysis. In view of the continuing small urinary output a 4th dialysis was undertaken.

neys, showed no gross abnormalities. Renal biopsy, however, performed on the 25th day confirmed the diagnosis of cortical necrosis. The patient died after 63 days of 'anuria'. (Alwall *et al.*'s two patients survived for 79 and 116 days respectively.[4]) The degree of calcification of the kidneys is shown in Fig. 6*. This finding has been ob-

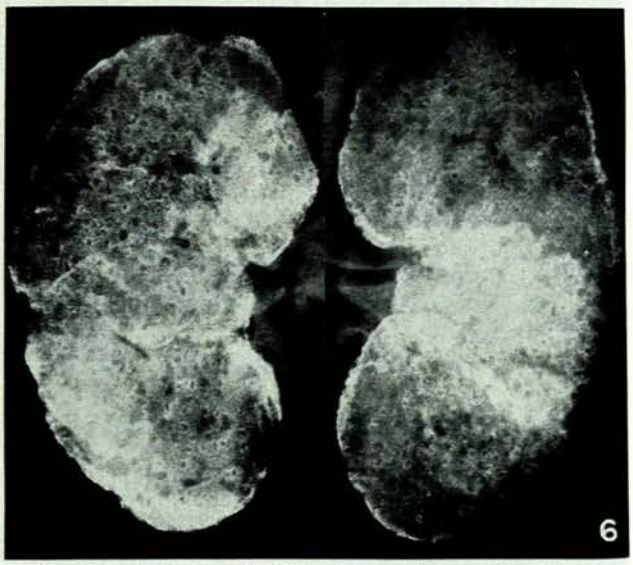

Fig. 6. Postmortem X-rays of the kidneys showing the gross degree of calcification. Note the cortical concentration of the calcium and islands of surviving tissue.

*The radiological and pathological findings will be reported elsewhere.[7]

served in several other cases.[5] In this patient it is of interest to note the production of over 150 ml. of urine on the 54th day. Recoveries have been reported after prolonged periods of anuria.[6] Thus difficult ethical decisions have to be faced in cases with prolonged oliguria.

Results of Treatment

The outcome in the 148 cases is summarized in Fig. 7. The chances of survival are vastly better in the obstetric and nephrotoxic groups. Over 80% of these patients will survive, while in the surgical groups only 1 in 3 or 4 will

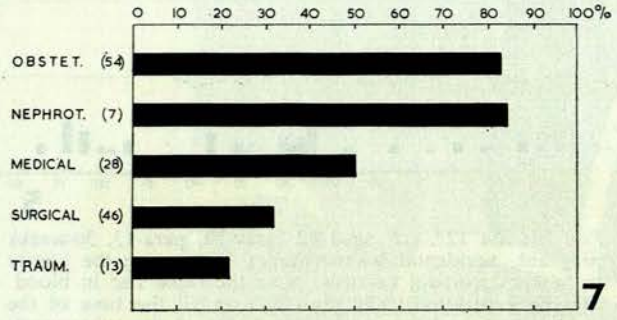

Fig. 7. Acute renal failure. Percentage recovery in 148 cases. Note that over 80% of the obstetric and nephrotoxic cases but only 20 - 30% of the surgical and traumatic cases survived. The medical cases fall between these two extremes. (The bracketed figures represent the numbers in each group.)

survive. The adverse factors affecting the course and prognosis of reversible renal failure are overhydration, delay, tissue destruction, infection, jaundice, advanced age, and underlying renal disease. Of these the first two are avoidable:

1. *Overhydration.* Scrupulous maintenance of water balance during the oliguric phase in hospital has removed the danger of pulmonary oedema, formerly a frequent cause of death. Patients, however, are still being admitted with gross fluid overloading and pulmonary oedema. We have had 6 such patients; Figs. 8 and 9 represent X-rays of the chest of a patient before and after dialysis.

2. *Delay.* The patient must be sent to an adequately equipped and staffed centre as soon as possible. Serum-K concentration may rise alarmingly in 24 hours to dangerous levels. Delay in transfer should not extend beyond the 3rd oliguric day. We have had 9 gravely ill patients referred to us in a moribund condition. Of these we lost 2 while preparing for and 2 during haemodialysis, 1 died after dialysis, and 4 survived.

3. *Tissue Destruction.* Of this there are 2 main causes: (a) trauma, and (b) the postoperative state.

(a) *Trauma.* Post traumatic patients with gross crushing injuries have constituted the most serious cases, with extremely rapid increases in blood-urea and serum-K levels. Early dialysis is essential.

(b) *The postoperative state* and, in particular, surgery of the heart and great vessels (Table III). Of 19 cardiovascular patients who have developed acute renal failure, only 6 have survived.

TABLE III. PERCENTAGE CONTRIBUTION OF SURGICAL AND CARDIOVASCULAR CASES TO TOTAL MORTALITY

	% in surgical group	*% in cardiovascular cases*
1959	45	33
1960	42	9
1961	45	40
1962	49	40

The skill and the ingenuity of the cardiac surgeon in effectively repairing or replacing damaged valves is undeniable, but it should be remembered he is often working with what amounts to a heart-lung preparation and the hazards that may follow are formidable. Although the operative procedure may be successful and immediate cardiocirculatory complications overcome, there is a chance of emboli to distant areas and the development of acute renal failure with or without liver and bowel necroses. The patient still has to face the ever-present

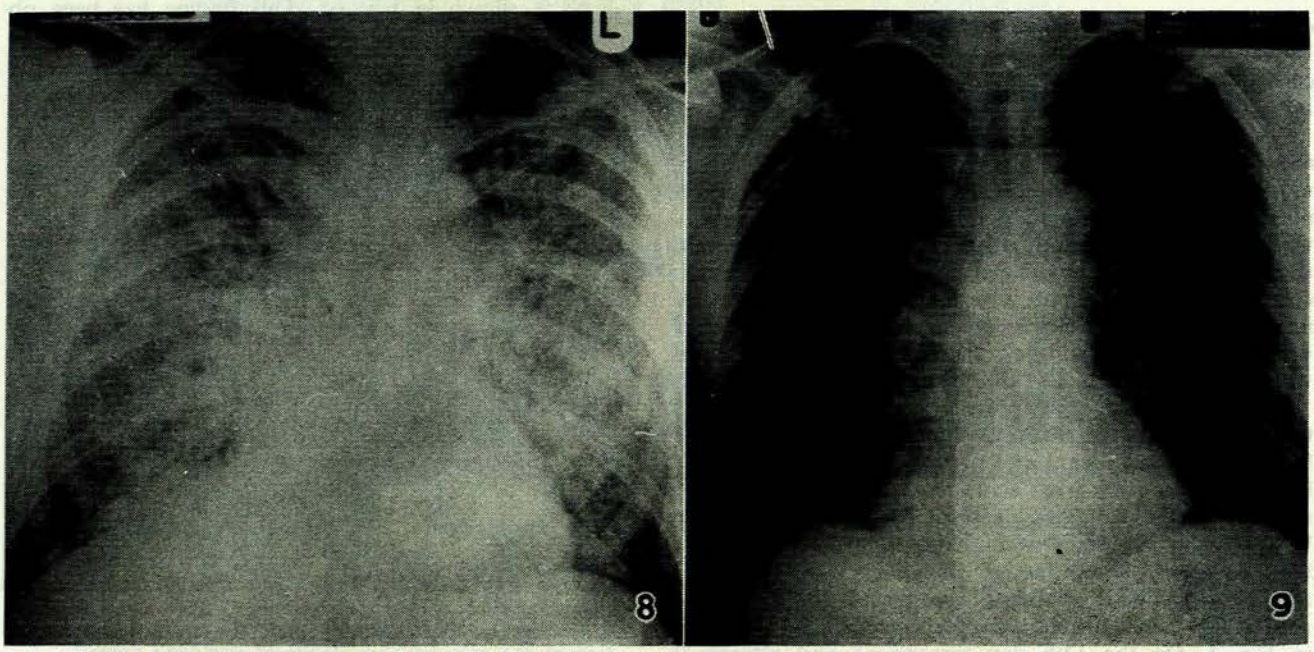

Fig. 8: X-ray of chest in case 122 before dialysis illustrating the severe pulmonary oedema from failure to restrict fluid intake.
Fig. 9: X-ray of chest in same patient 5 days later showing marked clearing of the pulmonary oedema.

danger of the hospital staphylococcus or, more alarming, the prospect of a gram-negative septicaemia and irreversible hypotension. Of this group of patients acute renal failure has not usually been the actual cause of death. In 4 of the patients diuresis had already occurred and in only 2 could death be attributed to uraemia. Secondary infection and general haemodynamic failure are the main causes of death.

4. *Infection.* While many patients are admitted with serious infections, uraemic patients are very prone to develop secondary infections resulting in gross catabolic changes and an acceleration of the uraemic process. Furthermore, infection is the main cause of death. The use of antibiotics is often necessary, but there is evidence that tetracycline exerts an anti-anabolic effect that may result in a rise in the blood-urea concentration.[8]

5. *Jaundice.* This is a much feared adverse accompaniment to acute renal failure, but it is the underlying condition that confers the unfavourable prognosis. 48 of our patients were jaundiced and of these 24 died, but scrutiny of Fig. 10 will show that among the surgical cases, a group whose prognosis in any event is very poor, 100% of the jaundiced cases were fatal. Five patients with stones in the common bile duct and

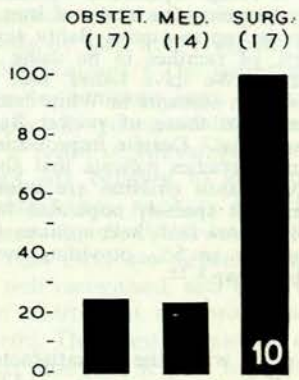

Fig. 10: Acute renal failure with jaundice. Percentage mortality. Note the striking difference between the surgical and the other two groups. The surgical group includes traumatic cases, and the medical group the nephrotoxic cases. (The bracketed figures represent the numbers in each group.)

complicating cholangitis, and 2 patients with severe cholecystitis, died, but in 4 of these diuresis had already occurred, and in all of them infection was the cause of death.

6. *Advanced Age.* Many elderly patients are in good health, but the poor outlook in frail elderly patients who have widespread atherosclerosis coupled with chronic bronchitis and emphysema needs no emphasizing.

7. *Underlying Renal Disease.* It is obvious that the prognosis of acute renal failure in such patients is poor.

The Main Cause of Death in Acute Renal Failure

Before the use of haemodialysis became general, the main causes of death were pulmonary oedema, hyperkalaemia and uraemia, and death in half of the fatal cases occurred within 6 days. Since the introduction of conservative management and haemodialysis, infection has supplanted pulmonary oedema and uraemia as the main cause of death.[9]

There were 63 deaths in our 148 patients. Although multiple factors contribute, a dominant cause of death can usually be determined. Thus the main cause of death in 24 of the 63 patients was considered to be infection (primary 15, secondary 9). Uraemia was primarily responsible in 14 patients; in 7 of these the underlying condition was irreversible. Cardiocirculatory complications were responsible in 14 patients, thrombo-embolic catastrophes in 6, haemorrhage and liver failure in 2 each, and fat embolism in 1. It is noteworthy that death occurred after diuresis was established in 17 patients.

SUMMARY

Based on an experience of 148 cases, the course of acute renal failure was discussed. Of these patients 7 had irreversible disease, including 6 patients with bilateral cortical necrosis, 3 of whom were males. The factors affecting prognosis adversely included delay in instituting treatment, overhydration, extensive tissue destruction, infection, and advanced age. Although jaundice is regarded usually as an adverse factor, it is the underlying condition that confers the adverse prognosis.

The main cause of death was infection. Uraemia and cardiocirculatory failure were the next most frequent causes.

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