Acute Renal Failure in Infancy and Childhood

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SUMMARY

The clinical features and management of 132 infants and children with severe acute renal failure are reviewed.

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Life-threatening fluid, electrolyte and acid-base imbalances occur within days of the onset of acute renal failure and present formidable and urgent problems of diagnosis and management.

This article deals with acute renal failure in 132 consecutive patients under the age of 13 years seen at Red Cross War Memorial Children's Hospital during 1970-1973. Based on this experience, the causes, clinical features, diagnostic measures and management of childhood acute renal failure are outlined. Only patients with blood urea levels of >200 mg/100 ml, for whom dialysis might be considered, were included.

AETIOLOGY

The over-all sex incidence of acute renal failure was approximately equal, and the racial incidence corresponded with the local hospital population: 97 Coloured, 18 Black, 17 White. The ages varied from a few weeks to 13 years.

A summary of the causes and outcome of treatment is given in Tables I, II, III. The list is representative of the common causes of acute renal failure in the paediatric age group.

The distinction between prerenal, renal and postrenal failure is useful, and indicates the initial steps needed in diagnosis and treatment.

Prerenal Failure

Circulatory insufficiency due to dehydration, hypovolaemia, hypotension and renovascular disease leads to decreased perfusion of the kidneys, with consequent impaired glomerular filtration without parenchymal damage. Unless rapidly corrected, intrinsic renal failure, which is not readily reversible, follows.

Prerenal failure occurred in 37 patients (28%): 4 patients (11%) died during the acute phase of the illness. Two children with renovascular disease died later in chronic renal failure after prolonged peritoneal dialysis (Table I). Gastro-enteritis with dehydration was the most common cause of prerenal failure; only one patient had a blood urea of more than 300 mg/100 ml.

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TABLE I. CAUSES OF PRERENAL FAILURE

	Total No. of patients	Deaths
Dehydration with gastro-enteritis	31	4
parathion poisoning	1	
neonatal meningitis	1	
Hypovolaemia with idiopathic nephrotic syndrome	1	
Renal artery occlusion (traumatic)	2	(2)
Renal vein thrombosis	1	
Total	37	4+(2)

Figures in brackets indicate deaths in chronic renal failure.

Intrinsic Renal Failure

This was present in 81 patients (61.4%); of these, 18 (22.2%) died in the acute phase, while a further 12 patients died of chronic renal failure months or years later (Table II).

TABLE II. CAUSES OF RENAL PARENCHYMAL FAILURE

	Total No. of patients	Deaths
Acute poststreptococcal glomerulonephritis	19	
Rapidly progressive glomerulonephritis	8	3+(3)
Membranoproliferative glomerulonephritis	2	(2)
Proliferative glomerulonephritis (non-poststreptococcal)	1	
Chronic glomerulonephritis	3	(1)
End-stage renal disease	1	
Acute pyelonephritis	2	
Chronic pyelonephritis	7	(3)
Acute tubular necrosis	12	2
Partial cortical necrosis	1	
Hepatorenal syndrome	1	1
Haemolytic-uraemic syndrome	5	2
Septicaemia	10	6
Right renal agenesis, left nephrectomy	1	1
Radiation nephritis	1	1
Bilateral renal hypoplasia	1	
Single dysplastic kidney and vesico-ureteric reflux	1	(1)
Single multicystic kidney	1	1
Hereditary nephronophthisis	2	(1)
Unknown associated with mongolism	1	1
Unknown associated with multiple congenital anomalies	1	1
Total	81	18+(12)

Figures in brackets indicate deaths in chronic renal failure.

The impairment of glomerular filtration due to glomerulonephropathies and pyelonephritis is the result of structural damage, though the exact pathogenesis is unknown in many instances.

Acute renal failure which follows shock, sepsis, transfusion reactions, injury and nephrotoxins, is known as acute tubular necrosis, though necrosis of the tubular epithelium is by no means the rule; the glomeruli and blood vessels are usually normal. Recent studies[1] indicate that alterations in renal haemodynamics, mediated locally via the renin-angiotensin system, are responsible for the striking reduction in glomerular filtration observed in acute renal failure. Tubular blockage by swollen necrotic cells, casts and interstitial oedema and back diffusion of essentially unaltered glomerular filtrate through damaged tubular lining, may be contributing factors.

Cortical necrosis, due to very severe ischaemia, is irreversible. Renal papillary necrosis was not recognised in this series.

Postrenal Failure

Obstruction to urine flow occurred in 14 cases (10,6%) (Table III). Three patients (21,4%) with severe obstructive uropathy died of overwhelming infection and in acute renal failure, while 2 patients died later in chronic renal failure. Total anuria is not invariable, and complicating urinary tract infection frequently first drew attention to the presence of obstructive uropathy.

TABLE III. CAUSES OF POSTRENAL FAILURE

	Total No. of patients	Deaths
Posterior urethral valves	5	2+(1)
Bilateral ectopic ureters + bladder neck obstruction	1	
Traumatic rupture of bladder	1	
Hydrometrocolpos	1	
Prune belly syndrome	2	1+(1)
Single kidney + calculus in ureter	1	
Calculus in one ureter + acute glomerulonephritis	1	
Ureteric valves + infection	1	
Sulphonamide anuria	1	
Total	14	3+(2)

Figures in brackets indicate deaths in chronic renal failure.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

A careful history and physical examination will often provide clues to the cause of the renal failure. The clinical features are partly dependent on the underlying disease or precipitating cause.

Uraemic symptoms may not be evident until the blood urea is over 200 mg/100 ml, and include anorexia, nausea, vomiting, occasionally haematemesis and melaena, hiccoughs, malaise, confusion, somnolence, stupor, muscle twitching, flapping tremor, convulsions, irregular respiration and fluctuating level of consciousness.

Sudden impairment of kidney function is usually manifest by a marked reduction in urine output to less than 400 ml/1,73 m^2/24 hours. Total anuria is uncommon, but occurred in this series with bilateral renal artery occlusion, severe acute glomerulonephritis and complete obstruction to urine flow. A few millilitres of 'bladder sweat' may sometimes be obtained even in total anuria; this finding does not exclude obstructive uropathy.

High output renal failure with increasing uraemia despite a normal or excessive urine output[2] was not seen except during the early diuretic phase of oliguric renal failure, and in some cases of acute-on-chronic renal failure.

In prerenal failure circulatory insufficiency will be readily apparent. In infants, severe dehydration without obvious shock may lead to acute tubular necrosis.

Signs of hypervolaemia such as oedema, hypertension, tachypnoea, elevated jugular venous pressure, congestive cardiac failure and/or pulmonary oedema should be looked for. Hypertension is unusual in acute tubular necrosis. The degree of sodium and fluid overloading may often be correlated with preceding intake.

Metabolic acidosis with deep sighing respiration may be the first clue to the presence of impaired renal function. Hyperkalaemia may be clinically manifest by muscle weakness and an irregular, slow pulse. Electrocardiographic abnormalities, however, are a more reliable guide to this hazardous complication.

Carpopedal spasm, a positive Chvostek's sign, muscle twitching, cramps, and convulsions indicate hypocalcaemia.

A bleeding tendency with bruising and purpura may be evident.

In older children enlarged kidneys are suggestive of intrinsic renal failure, regardless of the actual cause. The kidneys are normally palpable in the newborn infant. Renal vein thrombosis should be suspected if one or both kidneys become tender or enlarged, or haematuria and thrombocytopenia are present in infants with hyperosmolar dehydration, and in newborn infants of diabetic mothers. Massive enlargement may indicate polycystic or multicystic kidney disease or obstructive uropathy.

A persistently full bladder with dribbling suggests urethral obstruction in boys, or a neuropathic bladder. The bladder remains empty in bilateral ureteric obstruction.

Pallor, growth retardation and renal osteodystrophy indicate pre-existing chronic renal failure. In this situation treatment of intercurrent infection, dehydration, sodium depletion and hypotension may nevertheless result in considerable, though incomplete, recovery of renal function.

The incidence of renal failure due to congenital abnormalities of the kidney and urinary tract was 13,5%, and occurred mainly in the younger age group.

INVESTIGATIONS

Urine is examined for red blood cells, pus cells, casts, crystals, protein, sugar, haemoglobin, sodium and urea concentration, osmolality and culture. It may be necessary to obtain a catheter specimen of urine for the initial

diagnosis, but the introduction of infection in the presence of oliguria or obstructive uropathy is a significant risk. Modest proteinuria, haematuria, pyuria and varying casts are the usual findings.

A full blood count, including a platelet count, and blood culture are done on admission.

The major biochemical disturbances noted in acute renal failure are azotaemia, hyponatraemia, hyperkalaemia, metabolic acidosis, hypermagnesaemia, hypocalcaemia, hyperphosphataemia and hyperuricaemia. Since renal function is difficult to assess clinically, a good laboratory service is essential for correct management.

The blood urea level is influenced by factors other than renal function such as protein intake, gastro-intestinal bleeding and the rate of tissue catabolism. In severe acute renal failure the usual rate of rise of the blood urea is 25 - 30 mg/100 ml per day, but in hypercatabolic states this may reach 100 mg/100 ml in 24 hours. The serum creatinine is a more reliable measure of renal function.

Investigations into the cause and treatment of acute renal failure must be carried out simultaneously. On several occasions it was necessary to dialyse the child before undertaking diagnostic procedures.

A chest X-ray film, and a straight film of the abdomen for kidney size, nephrocalcinosis, radio-opaque renal calculi and bladder size, are obtained.

High-dose excretion urography with nephrotomography will often provide useful information, regardless of the level of blood urea. The renal outline can frequently be defined, but a diagnostic pyelogram is rarely obtained in oliguric states. Patients with uncomplicated acute tubular necrosis and oliguric acute pyelonephritis show an early dense persisting nephrogram, a pattern not seen in other forms of acute renal failure.[3] Hydronephrosis due to obstructive uropathy may be seen as filling defects in the nephrogram, or a delayed pyelogram may become apparent several hours after injection of the contrast medium. The use of intravenous hyperosmolar X-ray contrast media is contra-indicated in the presence of severe hypervolaemia.

Micturating cysto-urethrography is performed if lower urinary tract abnormalities are suspected. The risk of introducing infection is high, and if obstructive uropathy is found, the procedure should be followed by urgent relief of the obstruction. If a high obstruction to urine flow is suspected, cystoscopy and unilateral retrograde ureteric catheterisation is undertaken as soon as the patient is fit enough.

Renal arteriography is performed if renovascular lesions are suspected, renal masses and trauma require further evaluation, or if the presence of unilateral agenesis or dysplasia needs confirmation. Renal and inferior vena cava venography may be carried out in suspected renal vein thrombosis.

Renal scintiscan and radio-isotope renogram are of limited diagnostic value in acute renal failure.

Open renal biopsy is carried out if rapidly progressive glomerulonephritis or a collagen disorder amenable to immunosuppressive therapy is suspected and the diagnosis cannot otherwise be made. Needle biopsy in acute renal failure in childhood is risky, and open biopsy is preferred.

Further investigations depend on the likely aetiology, and include antistreptolysin 0 titre, throat swab or impetigo swab cultures, serum total complement, β_1C-globulin levels, lupus erythematosus cell preparations, antinuclear factors, blood cultures, and tests for disseminated intravascular coagulation and haemolysis.

MANAGEMENT

The first priority in the management of acute renal failure is to deal with rapidly reversible causes and avoid serious damage.

Prerenal Failure

Circulatory insufficiency is corrected with appropriate fluids:

(a) half normal saline in 2½% dextrose water if serum K is high
(b) dextrose 2½% in Darrow's solution if serum K is normal

} 20 ml/kg every hour until the circulation is restored; with added sodium bicarbonate if indicated

(c) blood or plasma 10 - 20 ml/kg when indicated, or concentrated salt-poor human albumin 20% 0,5 - 1,0 g/kg/day if significant hypoproteinaemia is present, as in the nephrotic syndrome with prerenal failure. In the latter situation diuretics are given only after albumin administration.

Hourly reassessment of the vital signs is necessary to ensure rapid correction and at same time avoid overhydration.

The dividing line between transient impairment of renal function and renal parenchymal failure is ill-defined. A urinary sodium of less than 20 mEq/litre, a ratio of urine urea:plasma urea greater than 5,[4] urine osmolality greater than 400 mOsm/kg water, or urine specific gravity of over 1,020 suggest that function will improve rapidly with volume replacement.

If oligo-anuria is entirely due to circulatory insufficiency without acute tubular necrosis, urine flow may be expected to increase within a few hours of adequate fluid replacement. The blood urea should drop to less than half the admission figure within 24 hours.[5]

If oliguria persists after correcting of circulatory insufficiency, give:

(a) Furosemide 1 - 2 mg/kg *slowly* intravenously. If given rapidly transient ototoxicity[6] or cardiac arrest may occur, while repeated use, if effective, will lead to hypokalaemia.
(b) Mannitol 0,5 - 1,0 g/kg body weight intravenously as 20% solution over 30 minutes. This should result in more than 6 ml urine/kg body weight within 3 hours. If so, this dose may be repeated, or an infusion of 5% mannitol in 0,2% saline may be used to maintain diuresis. Mannitol must not be used if circulatory overload is present.

If haemoglobinuria or myoglobinuria is present, and after clamping aorta or renal pedicle, furosemide and/or mannitol are used to ensure adequate urine flow.

The central venous pressure should be monitored; frequent weighing, accurate intake and output measurement and serum and urine electrolyte estimations are necessary to avoid imbalance. If there is no response to the above measures acute tubular necrosis must be presumed.

Renovascular lesions require urgent surgical intervention and/or anticoagulant therapy.

Postrenal Failure

Obstructive uropathy is relieved at the earliest possible moment. Dialysis may be necessary in order to get the patient in a fit state to withstand major surgical procedures.

Established Renal Failure

The aim of treatment is to maintain body fluid composition within the range compatible with life until renal function is restored.

Fluid intake. The patient's thirst is no guide to his needs and glomerular filtration cannot be forced by overhydration. Before precise fluid restriction was introduced as a therapeutic measure, overhydration was a major cause of death in renal failure.

Fluid requirements:

(a) Insensible loss (minus endogenous water production) is replaced as water: 12 - 25 ml/kg/24 hours, the younger the child the greater the fluid requirement (250 - 300 ml/m²/24 hours or 20 - 30 ml/400 kJ expended/24 hours).[7]

(b) Urine output during previous 24 hours is replaced with 0,45% sodium chloride with dextrose 2,5%.

(c) Losses from the gastro-intestinal tract are replaced with electrolyte solutions as indicated by the nature of the loss.

For each degree rise in temperature above 37°C the calculated insensible loss is increased by 18%. Hot weather and hyperventilation also increase insensible loss.

Accurate fluid and electrolyte balance requires exact recording of all intake and losses, daily estimation of the serum electrolytes, sodium and potassium content of the urinary and gastro-intestinal losses, and weighing the child daily at the same time of day. Owing to the difficulties of maintaining adequate caloric intake, the child will lose up to 1% of his weight daily.

If fluid overload is present, ml for ml replacement will perpetuate this state; initially less should be given. In some cases of oliguric renal failure the urine output may be increased to near-normal volumes by intensive diuretic therapy. This facilitates management by the less rigid fluid restriction necessary, but does not always avoid dialysis.

Caloric intake. Minimal caloric needs are estimated at 1 600 kJ/m²/day.[7]

In general, carbohydrate and fat are metabolised completely to carbon dioxide and water, and the kidneys are necessary only for the excretion of excess water. The end-products of protein metabolism, on the other hand, rely primarily on adequate renal function for excretion. Protein intake is therefore restricted. Endogenous protein catabolism and thus the rate of rise of blood-urea is limited to some extent by a high carbohydrate intake, the maximum protein sparing effect being obtained with 2 - 3 g/kg or 75 g carbohydrate/m²/24 hours. This will also help to avoid hyperkalaemia.

Carbohydrate is given as follows:

(a) By mouth—Hycal (Bencard) (100 ml = 976 kJ) and/or Caloreen (Milner Scientific and Medical Research Co. Ltd) (1 g = 16 kJ) and/or 10% dextrose water (100 ml = 160 kJ).

(b) Intravenously—20 - 30% dextrose water via a catheter in a vena cava.

Hydrocortisone 10 mg/litre to avoid phlebitis and heparin 1 unit/ml to prevent thrombosis may be added; an infusion pump facilitates administration of small volumes.

Protein intake. After 5 - 7 days the rate of tissue catabolism slows and protein 0,5 - 1,0 g/kg/day is added as low sodium humanised milk (1,5 - 1,6 g protein/100 ml) or a modified Giordano-Giovannetti diet for bigger children.

During dialysis less rigid fluid and protein restriction is necessary, and with repeated dialyses it becomes important to replace the protein lost in the dialysate. Once the blood urea drops below 100 mg/100 ml minimal protein restriction is required.

Fats have protein sparing effects but are poorly tolerated orally. Intravenous fat emulsions have been used, but we have no experience with them.

The use of appropriate amino-acid precursors such as the alpha-keto and alpha-hydroxyacid analogues may prove a valuable adjunct in the dietary management of renal failure.[8] Adequate vitamin supplementation is essential.

Anabolic steroids are of limited, if any, benefit in reducing endogenous protein breakdown.

Hyperkalaemia. This is common and due to protein and fat catabolism, breakdown of devitalised tissue, metabolic acidosis and haemolysis. A serum K > 8 mEq/litre or > 7 mEq/litre with ECG abnormalities constitutes a medical emergency.

The ECG abnormalities are: mild—peaked, tented T waves; moderate—prolonged P-R interval, disappearing P wave, widened QRS, increased peaking T waves; severe —further widening of QRS, S-T segment lost in ascending limb of T wave, sine wave ending in cardiac arrest.

Treatment is as follows:[7,9]

(a) timely elimination of K intake and early administration of ion-exchange resin (see below) may prevent hyperkalaemic emergencies;

(b) 10% calcium gluconate 0,5 ml/kg slowly intravenously over 5-10 minutes. If the pulse rate drops by more than 20 beats/minute slow down or temporarily discontinue infusion;

and/or

(c) 2 - 3 mEq 8,5% $NaHCO_3$/kg intravenously (1 ml 8,5% $NaHCO_3$ = 1 mEq Na and HCO_3). Note that by increasing the pH, the fraction of ionised calcium is lowered and tetany may be precipitated; the sodium load may result in hypertension and circulatory overloading;

and/or

(d) intravenous glucose 1 - 3 g/kg with or without soluble insulin; 1 unit for every 4 g glucose given over 1 hour.

Calcium does not alter the serum K but acts by decreasing the threshold potential and thus myocardial excitability. Calcium infusion is the most rapidly effective method for treating severe cardiac toxicity, though the effect is relatively transient if the hyperkalaemia is not also reduced by other methods. The other measures also act rapidly and shift extracellular potassium into the cells, but their effect lasts a few hours only.[10]

Potassium is removed from the body by

(a) Na − K ion exchange resin (sodium polystyrene sulphonate) (Kayexalate; Winthrop) orally or rectally 0,5 − 1 g/kg suspended in 10% dextrose water (1 g resin in 4 ml dextrose water). It is frequently used concomitantly with one or more of the above measures. The resin is more effective when given as a high retention enema (30 - 40 minutes) since the colon is a major site for K exchange.[10] The resin acts within 30 minutes when given rectally and within 2 hours orally, and lasts 4 - 6 hours, lowering the serum K by about 1 mEq/litre. The administration may be repeated 2 or 3 times in 24 hours. Each 1 g of resin takes up ± 1 mEq K as well as some hydrogen and calcium, and donates 3 mEq Na. For the latter reason a Ca-K ion exchange resin is preferable but less readily available.

(b) Dialysis if the serum K remains higher than 7 mEq/litre despite the above measures.

Metabolic acidosis. Hydrogen ions, derived from the oxidation of sulphur-containing amino-acids, phosphorus residues and incompletely metabolised organic acids are normally excreted by the kidney. Adequate caloric intake lessens H+ production.

Treatment is as follows:

(a) Partial correction with intravenous $NaHCO_3$ is indicated if the plasma pH is <7,2 or the standard bicarbonate <12 mEq/litre. (Formula for full correction: mEq $NaHCO_3$ required = 0,3 × base excess × weight in kg.) The dangers of sodium bicarbonate have been emphasised in the section on hyperkalaemia. If severe hypocalcaemia is present intravenous calcium is given before administering sodium bicarbonate.

(b) Dialysis if metabolic acidosis is severe and uncontrollable, or if fluid volume overload makes administration of more sodium hazardous.

Hyponatraemia. Hyponatraemia associated with **oedema** (serum Na <130 mEq/litre) is due to retention of water derived from excessive intake and the catabolism of fat and carbohydrate, and is not due to sodium depletion. Unless the serum sodium is less than 120 mEq/litre, central nervous system signs of water intoxication, such as reduced level of consciousness, convulsions and coma seldom occur.

Treatment is as follows:

If asymptomatic—rigid fluid restriction.

If symptomatic, in addition to fluid restriction give:

(a) Normal saline—40 ml/kg raises serum sodium by 10 mEq/litre.

(b) Saline 3% (emergencies only)—12 ml/kg raises serum sodium by 10 mEq/litre.

(c) Cerebral oedema may be treated with glucose 0,5 g /kg or mannitol 0,5 g/kg as a 20% solution intravenously over 20 minutes with transient relief of the hypo-osmolaric state.

(d) Dialysis with hypertonic solutions.

It must be stressed that saline infusion is hazardous and may lead to pulmonary oedema and/or hypertension. It is unnecessary to increase the serum Na level above 125 mEq/litre.

Hyponatraemia with **dehydration** is indicative of sodium depletion and requires saline infusion as discussed under prerenal failure.

Hypernatraemia. Treatment is difficult and in established renal failure is best managed by dialysis if indicated for other reasons.

Hypocalcaemia. Moderate hypocalcaemia is frequent in severe renal failure, though rarely symptomatic except during rapid correction of metabolic acidosis.

Oral calcium carbonate (Titralac; Riker Laboratories) 1 - 4 g/day or intravenous 10% calcium gluconate up to 120 ml/m²/day, and oral phosphate-binding antacids (Amphojel; Wyeth Laboratories) 10 - 120 ml/day help to correct hypocalcaemia, but normal levels are not usually attained. Multiple transfusions with citrated blood require 10 ml 10% calcium gluconate intravenously for each 4 units transfused.

Congestive cardiac failure and pulmonary oedema. This very serious complication of acute renal failure is due to sodium and water overload and hypertension. Myocardial efficiency may be affected by uraemia and electrolyte imbalance. Congestive cardiac failure further reduces glomerular filtration. In our experience pulmonary oedema may occur without marked uraemia.

Treatment is as follows:

(a) Rigid sodium and water restriction.

(b) High dosage diuretic therapy—furosemide up to 5 mg/kg slowly intravenously. Provided the glomerular filtration rate is >5 ml/min/1,73 m², it is usually possible to obtain a moderate diuresis.

(c) Antihypertensive measures.

(d) Medical venesection with rotating tourniquets or removal of 50 - 200 ml blood may be lifesaving.

(e) Oxygen.

(f) Sedation—morphine 0,1 mg/kg subcutaneously.

(g) Dialysis with hypertonic solutions.

(h) Uraemic pericarditis and cardiac tamponade must be excluded: pericardiocentesis and dialysis may be indicated.

(i) Digitalisation is rarely necessary; rather, urgent measures to reduce the fluid overload are indicated. Digoxin is excreted via the kidney and intoxication readily occurs in renal failure, particularly when the serum K is lowered. Considerable individual

variation in response and tolerance occurs; frequent ECG monitoring and, if available, digoxin radioimmunoassays are advisable to avoid toxicity and assess adequacy of digitalisation. A normal loading dose is given and a daily maintenance dose of one-tenth to one-eighth the digitalising dose during the period of oligo-anuria.[11] The formula

$$\frac{(14 + \text{creatinine clearance})}{5}\ \%$$ of the loading dose[12] as maintenance therapy has been suggested for adults but it is uncertain whether this is applicable in children.

Convulsions. These may be due to hypertension, hyponatraemia, hypocalcaemia, hypoglycaemia, uraemia, or concurrent disease not necessarily related to renal failure, and should be treated accordingly. Convulsions are often preceded by muscle twitching and neuromuscular irritability which do not respond to calcium infusion.

Treatment is as follows:

(a) intravenous diazepam (Valium) 0,25 - 0,33 mg/kg slowly;
(b) diphenylhydantoin sodium (Epanutin) 3 - 5 mg/kg orally or intramuscularly;
(c) paraldehyde 0,1 - 0,2 ml/kg intramuscularly.

Phenobarbitone should not be given since it accumulates in renal failure, but short-acting barbiturates may be used.

Hypertension. The commonest cause of hypertension in acute renal failure is extracellular fluid volume overload. The renin-angiotensin system may contribute.[5] Treatment is necessary when hypertension is symptomatic or becomes life-threatening (levels exceeding 150/110 mmHg).

Treatment is by one of the following:

(a) Rigid restriction of sodium and fluid intake.
(b) Intensive diuretic therapy.
(c) Antihypertensive drugs.
 (i) 1,4-Dihydrazinophthalazine (Nepresol) 0,3 mg/kg *slowly* intravenously up to 12,5 mg per dose, while pulse and blood pressure are monitored to avoid excessive tachycardia and hypotension. This dose may be repeated once or twice at intervals of an hour. The drug may also be given intramuscularly.
 (ii) Intramuscular reserpine (Serpasil) 0,02 - 0,05 mg/kg per dose is effective in 2 - 3 hours and lasts 4 - 6 hours. Maximum single dose is 1 mg. Reserpine may be combined with hydralazine 0,15 mg/kg intramuscularly.[13]
 (iii) Intravenous diazoxide (Hyperstat; Scherag) 5 mg/kg as a bolus injection is effective within a few minutes but is of variable duration.
(d) Avoid blood transfusion and other volume expanders.
(e) Dialysis to relieve sodium and fluid overload when the hypertension is refractory to treatment.
(f) If hypertensive encephalopathy appears imminent intravenous sodium amytal (5 - 10 mg/kg) or diazepam (Valium) 0,25 - 0,33 mg/kg is given.

Hyperchloraemia, hyperuricaemia and hypermagnesaemia are not directly life-threatening and are corrected by dialysis if this is indicated for other reasons.

Anaemia. The main causes are blood loss, haemodilution, shortened red cell survival time and decreased erythropoiesis.

Unless there is active bleeding or severe haemolysis, transfusion is not necessary until the haemoglobin has dropped below 6 g/100 ml, the packed cell volume has fallen below 20%, or the child has symptoms of anaemia. Packed fresh red cells (5 - 10 ml/kg) are given slowly over 4 - 6 hours, preferably during dialysis. Owing to the limited vascular compliance in acute renal failure with hypervolaemia, minor expansion or blood volume may result in severe hypertension and circulatory overload. Partial exchange transfusion may be preferable; 10 ml/kg packed red cells (Hb ± 25 g/100 ml) exchanged for the same volume of the patient's blood (Hb ± 5 g/100 ml) will increase the haemoglobin by 2,5 g/100 ml.[5] Fresh blood is used to lessen the hazard of hyperkalaemia.

The bleeding tendency in uraemia is due to platelet dysfunction and thrombocytopenia, and may be reversed by dialysis.

Infection. The host response to infection is depressed in uraemia despite the frequent finding of a polymorphonuclear leucocytosis. Infection played a major role in the causation of the renal failure initially, as well as determining the outcome in 18 of our patients who died in the acute phase. In this series septicaemia complicated by renal failure and disseminated intravascular coagulation was common under 1 year of age but rare in the older age groups. Gram-negative organisms were usually implicated, an important fact when considering antibiotic therapy.

The method of prevention would be to isolate the patient, avoid catheterisation, provide good nursing care, and prevent chest infection by physiotherapy and early ambulation. An antibiotic ointment applied at catheter sites is useful, and bladder irrigation with an antibiotic solution (Polybactrin soluble GU; Calmic) and gamma globulin may be indicated.

Drugs and antibiotics excreted by the kidney require adjustment of dosage to avoid accumulation and toxic effects[14,15] (Table IV). Bactericidal rather than bacteriostatic antibiotics should be given. Serum antibiotic bioassays allow more accurate dosage administration.

Dialysis. Thirty-seven patients were dialysed (28%), including one treated with both peritoneal dialysis and haemodialysis.

The indications are assessed for each patient individually. Dialysis should supplement good conservative care, and not supersede it. There are few contra-indications to peritoneal dialysis, and the procedure is not difficult, though a certain degree of expertise and experience is required.[16] Infants of <2 kg have undergone peritoneal dialysis successfully in this hospital.

The decision to dialyse is determined more by an assessment of the probable course of the renal failure, than by arbitrary biochemical criteria.

The following indications are therefore merely a guide:

(a) Blood urea >250 - 300 mg/100 ml. Serum creatinine >10 - 15 mg/100 ml.
(b) Clinical uraemia with central nervous system manifestations and/or uraemic pericarditis.

TABLE IV. DRUGS IN RENAL FAILURE (modified from Hedger[15])

	Drugs requiring reduced dosage	Drugs requiring no modification of dosage
Antibiotics	Cephaloridine	Penicillin
	Gentamicin	Cephalothin
	Streptomycin	Erythromycin
	Kanamycin	Chloramphenicol
	Isoniazid	Doxycycline
	Colistin	
	Amphotericin	Propranolol
	Vancomycin	
	Lincomycin	
		Hydralazine
CVS drugs	Digitalis	Reserpine
		Ganglion blockers
Antihypertensive drugs	Alpha-methyldopa	Guanethidine
Sedatives/	Phenobarbital	Secobarbital
anticonvulsants	Chlorpromazine	Chloral hydrate
	Prochlorperazine	Diazepam
		Paraldehyde
	Salicylates	Diphenylhydantoin

(c) Hyperkalaemia >7,0 mEq/litre which is resistant to conservative measures.
(d) Uncontrollable metabolic acidosis with a plasma standard bicarbonate less than 12 mEq/litre.
(e) Severe hypervolaemia with circulatory overload.
(f) Severe poisoning with dialysable agents.

It is better to dialyse early rather than to wait until the patient is *in extremis*.

Continuing Care

A flow sheet recording pulse, temperature, blood pressure, central venous pressure, weight, intake, urinary output and extrarenal losses, serum biochemistry and haemoglobin greatly facilitates management. Assessment of fluid and electrolyte requirements should be made at 8 - 12-hour intervals.

Treatment Directed Towards Specific Causes

Heparin is no longer favoured for the haemolytic-uraemic syndrome in this hospital and there is support for this policy elsewhere.[15]

Good results have been reported with anticoagulant therapy, dipyridamole and immunosuppressive agents in severe progressive forms of glomerulonephritis.[18] We have not yet been able to reproduce these results in a few cases so treated. Anticoagulant therapy has also been used in renal vein thrombosis.

Allopurinol and alkalinisation of urine is indicated in uric acid nephropathy. Hypercalcaemia requires urgent correction.

In haemoglobinuria or myoglobinuria the prognosis is improved by forced diuresis and alkalinisation of the urine.

In general, corticosteroids are contra-indicated since they are ineffective, aggravate hypertension and by their catabolic action increase hyperkalaemia and uraemia. Exceptions are the idiopathic nephrotic syndrome of childhood with prerenal failure, and possibly glomerulonephritis associated with lupus erythematosus and polyarteritis nodosa.

Diuresis

Diuresis is mainly due to excretion of accumulated water, urea and electrolytes as renal function improves. It is frequently less dramatic than recorded in earlier descriptions, and this probably reflects the more rigid fluid restriction of today. In the face of the existing circulatory overload, failure to continue fluid restriction during the early diuretic phase will perpetuate hypervolaemia.

Blood urea levels may continue to rise for a few days despite increasing urine output, since initially renal function is inadequate to cope with the load of breakdown products. In acute tubular necrosis diuresis almost invariably occurs within 35 days of the onset of renal failure. On the other hand, diuresis may never occur, as in malignant glomerulonephritis. Massive diuresis may follow operative relief of urinary tract obstruction.[19]

Frequent reassessment of fluid and electrolyte balance remains important during the recovery phase. The hazard of infection, too, remains serious.

Prognosis

This depends on the underlying disease process and the standard of care provided. Twenty-five of our patients died in the acute phase (19,8%), while a further 16 (12%), after initial partial recovery, died months or years later in chronic renal failure (Tables I - III).

Excluding patients with posterior urethral valves, prune belly syndrome and gross extrarenal congenital abnor-

malities, 17 patients who died might have benefited from long-term haemodialysis and/or kidney transplantation, had facilities been available. One 4-year-old boy, who was first referred here with end-stage renal failure, received a kidney homograft from his father at another centre.

Acute renal failure in infancy and childhood occurs too infrequently for other than large units to acquire the necessary experience in management. Early referral to a specialised centre is necessary, and in addition the after-care is often complex. However, treatment must be initiated before referral to prevent sudden deaths from hyperkalaemia, pulmonary oedema and hypertensive encephalopathy during transport.

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