

Personal practice

Renal failure in the newly born

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When urine output is absent or reduced and azotaemia develops renal failure is said to have occurred. It is acute if it happens over a period of days or weeks and chronic, often irreversible, when it takes months or years. Renal failure in the newly born infant is unique as it occurs after a period of intrauterine life and in a setting of immature renal function so that renal failure due to major anatomical abnormalities such as renal agenesis can present in the newborn as an acute problem.

During intrauterine life the placenta performs all the excretory functions necessary to maintain normal fetal homeostasis. The primary function of the kidney is the maintenance of normal amniotic fluid volume and the overall renal function of the fetus is low. Even when there is bilateral renal agenesis, azotaemia does not become evident until sometime after birth. At birth glomerular filtration rate averages 0.84 ml/minute/kg. It increases rapidly and doubles by the third week of life as the perfusion and function of the superficial cortical nephrons increases with greater renal plasma flow.^{1 2}

All functions of the kidneys of normal newborn infants operate very close to their maximum capacity. Under normal circumstances in a healthy infant this is not clinically important but there is a limited ability to vary renal function in response to stress.

It has been recognised for many years that a newborn has a limited ability to excrete a sodium load.³ This is probably due to enhanced distal tubular sodium reabsorption and high plasma aldosterone concentrations.⁴ In contrast the immature kidney loses salt and premature infants often become hyponatraemic due at least in part to immaturity of the tubular glomerular feedback mechanism.⁵

In response to severe dehydration the newborn kidney is unable to increase urine osmolality above 700 mmol/kg. This is largely due to the concentration of urea in the renal medulla.⁶ The ability to concentrate the urine increases with dietary protein intake. Conversely the newborn has an impaired ability to excrete large amounts of free water particularly during respiratory distress syndrome.⁷

It is also well known that the newborn easily becomes acidotic in stressful situations. This is mainly due to immaturity of net acid secretion.⁸ Consequently these infants are more susceptible to the metabolic insults associated with increased acid load and are unable to maintain normal homeostasis under stress.

Diagnosis

The cardinal feature of acute renal failure is azotaemia with or without oliguria.

Blood urea concentration is influenced by many extrarenal factors including dehydration and protein catabolism, and the plasma creatinine concentration is a more reliable index of glomerular function. At birth the plasma creatinine concentration (measured by the kinetic Jaffe reaction) approximates to that of the mother and ranges from 17 to 188 $\mu\text{mol/l}$. The concentrations fall rapidly and by the second week average 35 $\mu\text{mol/l}$.⁹ Interpretation of a single plasma creatinine concentration during this time is further complicated by analytical interferences caused by unconjugated bilirubin (causing falsely low concentrations), ketones, and many drugs—for example, cephalosporin (which causes falsely high concentrations). For these reasons plasma creatinine rising consistently by more than 20 $\mu\text{mol/l/24}$ hours is more important than a single high concentration.

The onset of urine flow in term babies is variable but is normally within the first 48 hours. Undetected spontaneous voiding during delivery may explain apparent anuria. Oliguria in the neonate is generally defined as a urine flow less than 0.5 ml/kg/hour. It is important to recognise, however, that renal failure can occur with normal urine flow rates of between 1–3 ml/kg/hour. The table shows a checklist of information that is needed in evaluating oliguria.

Haematuria is an unusual finding in the normal newborn, although about 10% will have a result of up to 1+ on dipstick testing (equivalent to 10 red blood cells/ μl). Proteinuria is rare but when it is present it is abnormal if the result on dipstick

Table Information required when evaluating oliguria in neonates

Clinical:	Daily fasting weight Blood pressure Evidence of infection Drugs (a) nephrotoxic—treatment stopped (b) excreted by the kidney—dose adjusted
Urine:	Flow rate (ml/kg/hour) Routine urinalysis—blood, protein, microscopy Sodium, creatinine, and urea concentrations, osmolality Culture
Blood:	Urea, creatinine, sodium, potassium, chloride, bicarbonate, calcium, magnesium, and glucose concentrations, osmolality Culture Arterial pH
Others:	Chest x ray Renal ultrasound

testing is greater than 2+.^{10 11} False positives for protein may occur when specimens are collected in vessels containing residual disinfectants based on quarternary ammonium compounds or chlorhexidine. Urine microscopy is important to identify red cells and casts. Red cell and granular casts may be seen in normal urine but more than one per high power field is abnormal.¹⁰ Careful microscopic examination of the urine particularly for frequent broad cast, red cells, and significant proteinuria are important features of parenchymatous renal disease.¹²

Chemical analysis of the urine has also been suggested to help distinguish between parenchymatous renal failure and decreased renal perfusion. The most generally used indices are the fractional excretion of sodium (FE_{Na}):

$$FE_{Na} = \frac{\text{Urine sodium} \times \text{plasma creatinine}}{\text{Plasma sodium} \times \text{urine creatinine}}$$

and the renal failure index (RFI):

$$RFI = \frac{\text{Urine sodium concentration} \times \text{plasma creatinine}}{\text{Urine creatinine}}$$

Normal values for both are the same and a renal failure index or fractional excretion of sodium greater than 3 is said to suggest parenchymatous renal failure. A urine to plasma osmolality ratio of less than one has been found in newborns with renal failure and may be helpful in distinguishing acute renal failure from the syndrome of inappropriate antidiuretic hormone.¹³ The results of these indices are usually difficult to interpret, however, due to the effects of the immaturity of the urinary concentrating mechanism, the effects of low protein diet on urine osmolality, and the high urinary sodium excretion in premature babies.⁵ More often than not

the diagnosis of parenchymatous renal failure or hypovolaemia is made on the basis of sound clinical judgment supported by simple urine analysis and microscopy. The diagnosis of hypovolaemia may be suggested when the blood urea is raised out of proportion to the plasma creatinine concentration. The urine indices are often unhelpful. The diagnosis may be further complicated by the knowledge that hypovolaemic renal failure may progress to renal parenchymal failure.

Incidence

It is difficult to estimate the true incidence of acute renal failure in the neonate. It has been calculated that 6% of babies admitted to one neonatal intensive care unit had renal failure.¹⁴ In the Yorkshire region an average of seven newborn babies are dialysed each year because of acute renal failure (0.2 per 1000 live births) but many more are managed conservatively and not referred for dialysis treatment. This comprises 25% of all children dialysed in the Yorkshire region for acute renal failure each year.

Aetiology

Because of the unique circumstances of the newborn, major anatomical abnormalities of the kidneys and urinary tract may present as acute renal failure.

Bilateral hydronephrosis due to urethral valves can now be detected by skilful antenatal ultrasound examination of the fetus and as a result it is no longer the acute medical problem it was. Bilateral renal hypoplasia or dysplasia may not progress to renal insufficiency until several weeks after birth, although in severe cases the features of Potter's syndrome or pulmonary dysplasia will be immediately apparent.

Aggressive modern intensive care has resulted in the resuscitation of many ill newly born term and extremely premature infants. In these children the aetiology of acute renal failure is often complex. Respiratory distress syndrome appreciably depresses glomerular filtration rates,⁷ and renal failure develops after severe asphyxia.¹² Renal venous thrombosis may complicate any severe illness in the newborn particularly if there is a history of sepsis, maternal diabetes, or prediabetes. Undetected hypotension in the baby after antepartum haemorrhage and septicaemia, particularly if treated in judiciously with nephrotoxic antibiotics, are also important causes. Congenital heart disease is the single commonest abnormality associated with acute renal failure. In the Yorkshire region it accounts for 25% of the babies with renal failure in the first month of

life. Anomalies with left ventricular outflow tract obstruction or a prolonged period of cardiopulmonary bypass are associated with increased risk.¹⁵

Management

A successful conclusion to the management of renal failure in the neonate requires ready access to the expertise of a neonatal intensive care unit and the combined skills of a neonatologist, paediatric nephrologist, surgeon, radiologist, and biochemist. It is unwise to attempt treatment without this team.

Obstructive uropathy and other anatomical anomalies of the urinary tract must be excluded by an abdominal ultrasound examination and the bladder catheterised with a fine feeding tube. This also allows the accurate measurement of the urine flow rate facilitating fluid balance management. If there is doubt about the extent of a prerenal component then there are those who suggest a fluid challenge of 10 ml/kg of isotonic sodium chloride solution over an hour¹⁶ or a mannitol infusion.⁷ Both are potentially dangerous and should only be done when there is ready access to dialysis. The use of frusemide 1 mg/kg body weight has been well established in the treatment of acute renal failure in adult patients but there is no evidence of its value in the newborn.¹⁷ It does have the virtue, however, of being relatively safe. If in doubt it is much wiser to restrict fluids from the baby for 24 hours by which time the diagnosis is usually more clear.

Meticulous attention to the details of fluid and electrolyte balance are fundamental. Water losses from urine, gastrointestinal loss, and urine output should be calculated and replaced. The insensible water loss of a normal newborn is estimated to be 50 ml/kg/day.¹⁸ One third of this is respiratory loss, which is negligible during artificial ventilation. Insensible fluid loss is 30% greater under radiant heat incubators than in conventional incubators.¹⁹ Sodium or potassium replacement are usually unnecessary in oliguric renal failure unless there are appreciable gastrointestinal losses, but correction of the acidosis is important. This requires a combination of skilful ventilation and sodium bicarbonate supplementation to keep the blood arterial pH as near normal as possible. The amount of bicarbonate required varies depending upon the severity of the acidosis but it should be remembered that one mmol of sodium is given with every mmol of bicarbonate, and the infusion of bicarbonate carries several risks including cerebral haemorrhage. Severe acidosis in renal failure is often best treated by early dialysis.

The strict fluid restrictions seriously limit a baby's nutrition, and hypoglycaemia is a common complication. A vigorous attempt to maintain a caloric

intake of at least 0.21 MJ/kg/day should be made if necessary by parenteral nutrition. This may be difficult within the restrictions imposed by the fluid allowance and early dialysis treatment is often necessary so that adequate nutrition can be maintained.

Poor nutrition leads to catabolism, which aggravates the acidosis and hyperkalaemia. Conservative measures to lower plasma potassium concentrations with glucose infusion (insulin often induces severe hypoglycaemia and is not recommended) or ion exchange resins (1 g/kg body weight in a 10% mannitol solution) are effective for only a few hours and are at best temporary measures while preparation is made for dialysis. Hypocalcaemia and hypomagnesaemia are frequent findings in acute renal failure,²⁰ and potentiate the toxic effects of hyperkalaemia on the heart. It is important to maintain plasma concentrations of calcium and magnesium within the normal ranges with 10% calcium gluconate (0.5–1 ml/kg over two minutes).

The drug chart should be examined, nephrotoxic drugs stopped and those known to be excreted by the kidney carefully controlled by frequent measurements of blood concentrations whenever possible.

Infection is often associated with acute renal failure either as a cause or a complication and should be excluded by urine and blood culture.

Dialysis treatment is indicated when there is fluid overload, severe acidosis (pH less than 7.2), hyperkalaemia, and progressive uraemia. Fluid overload when associated with gross peripheral oedema, hypertension, or pulmonary oedema requires treatment by early dialysis. It is often necessary to remove fluid to 'make room' for infusions of inotropic drugs, blood, nutrition, or other essential supportive drugs. Severely ill oliguric newborn infants readily become acidotic. Sodium bicarbonate infusion can be hazardous in these circumstances and it is wiser to initiate dialysis treatment early rather than infuse bicarbonate, which will result in further fluid overload.

A plasma potassium concentration of 6.0 mmol/l or more and a blood urea of greater than 10 mmol/l that is rising by more than 6 mmol/l a day indicates catabolism and rapidly progressing uraemia, and it should prompt referral for dialysis treatment.

Peritoneal dialysis is the method of choice in the neonate. It is a simple technique but not without difficulties even in the most skilled and experienced hands. The most often encountered complications are failure to achieve satisfactory drainage of dialysate and peritonitis. There is a risk of perforating a major vessel in a paralysed baby on a ventilator. Water and urea are removed efficiently and in most cases the acidosis improves rapidly, but

occasionally it does not. This is probably because standard peritoneal dialysis solutions have lactate as the source of bicarbonate. Some infants, especially those with a severe lactic acidosis, are unable to metabolise it and remain acidotic despite dialysis. A bicarbonate dialysis solution would be preferred, but is not manufactured, and an acetate solution, which had some theoretical advantages, is no longer manufactured.

Haemodialysis is difficult in the newborn but may be necessary if peritoneal dialysis is not possible because of abdominal surgery or other technical difficulties. Vascular access is usually achieved by a Hickman line inserted in the external jugular vein. Treatment is usually for two to three hours at a time.

Continuous arteriovenous haemofiltration is being used increasingly in the newborn.²¹ This method requires the catheterisation of an artery (usually the femoral or umbilical arteries). The blood passes continuously, often for 24 hours or more, across a small haemofilter comprising a number of hollow fibres, and is then returned to the baby's veins. The filtrate that is produced is measured, discarded, and simultaneously replaced by an appropriate volume of electrolyte solution. It is a gentler procedure than haemodialysis and we have found it to be a simple and effective alternative to peritoneal dialysis, particularly in babies with renal failure after cardiac surgery.

Prognosis

The prognosis reflects the nature of the underlying cause of acute renal failure. Three quarters of those who develop renal failure after perinatal anoxia survive, but 40% of the survivors had either cerebral or renal damage.¹² In contrast 75% of newborns who had renal failure after cardiopulmonary bypass surgery died and 50% of the survivors had neurological damage.¹⁵

During the last two years we have dialysed 14 neonates. Eight had medical causes of renal failure: four after sepsis, two after hypovolaemic shock from antepartum haemorrhage, and two because of prematurity and asphyxia; of these two died. In contrast six neonates were dialysed after surgical procedures for congenital anomalies: three after cardiopulmonary bypass surgery, two with diaphragmatic herniae, and one with prune belly syndrome with renal dysplasia; of these three died.

Up to 40% of the survivors may have decreased creatinine clearances and a smaller proportion will have a renal tubular acidosis or a concentrating defect indicating residual renal tubular dysfunction.¹⁴

The increasing vigour with which neonatal intensive care is being applied has resulted in an increase

in acute renal failure. Treatment is a challenge and can be rewarding as the results and techniques improve. One must be constantly mindful, however, of the painful consequences of the long term neurological and renal complications before embarking upon a course of treatment that can be difficult to stop.

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