**ACUTE RENAL FAILURE**

*Dr Harley Powell – 2005*

**Introduction**

Normally a sudden huge increase in renal blood flow occurs at birth as the dialyzing effect of the placenta is lost. Acute and chronic renal failure at birth can be caused by failure of this increase in renal blood flow to occur. The cord blood serum creatinine is the same as the mother’s, as foetal blood is in dialysis equilibrium with the mother’s blood, and the newborn’s serum creatinine decreases from the maternal adult level (0.05-0.07mmol/L) to normal neonatal levels (0.02-0.03) in 2-3 days.

As renal failure may not be diagnosed before birth, neonatal renal failure is often not clearly acute or chronic at birth. A renal ultrasound will always be abnormal in babies with chronic renal failure but will show normal shaped kidneys in acute renal failure.

**Definition of Renal Failure**

The two million nephrons in the human body (about one million in each kidney) undertake many complex functions in generating the final urine. After glomerular filtration 75-80% of the filtrate volume is reabsorbed in the proximal tubules, with smaller amounts absorbed in the loops of Henle and distal nephrons. Failure of the various renal functions causes many well-defined diseases (eg. phosphate-wasting rickets and cystinuria due to proximal tubule dysfunction, Bartter’s syndrome due to Loop dysfunction, diabetes insipidus due to collecting duct dysfunction) but the renal function which is reduced in the condition called ‘renal failure’ is glomerular filtration.

Normal glomerular filtration rate in children and adults is about 100ml/min/1.73m² with a range of 80-150ml/min/1.73m². In neonates, normal glomerular filtration rate is much lower than in older children when expressed in terms of surface area (25-40ml/min/1.73m²) because neonates have a relatively large surface area compared to their body weight. **Renal failure is defined as glomerular filtration rate less than normal.**

Sometimes, minor reduction in renal function is referred to as ‘renal impairment’ and the term ‘renal failure’ is used for more seriously reduced function. Unless specific values become universally agreed, there is little point in making this distinction.

The normal GFR (say 100ml/min/1.73m²) is generated from the total filtration of the 2,000,000 nephrons in the two kidneys. Each nephron filters about 50 nanolitres/min and the total GFR of all the nephrons is 50 nl/min x 2,000,000 = 100ml/min. Clearly reduced GFR can be caused by a reduced number of nephrons or by a reduced single nephron GFR. Renal failure with reduced number of nephrons is **chronic** renal failure whereas renal failure due to reduced single nephron GFR is usually **acute** renal failure.

An alternative definition of renal failure is **inability to excrete the renal solute load.** This can be illustrated by an example:

**Example**

A well 9 year old boy weighing 27kg has a surface area of 1m². He is eating a diet which, after allowing for incorporation of some nutrients into body growth, provides 75mmol Na, 75mmol Cl, and 150mmol urea for excretion in the urine. These solutes constitute the main components of the renal solute load which will be about 75+75+150=300mmol (300 milli-osmols).

If this boy drinks an amount of water, which leads to 1000ml of urine each day, the renal solute load can be excreted in a urine containing 300mosm/L (isotonic urine). If he drinks a large amount of water so that his urine volume increases to 6
litres daily, the same 300mmol of solute will produce a urinary concentration of 50mosm/L, which is close to the most dilute urine that the kidneys are capable of producing. Alternatively, if he is partly deprived of water so that only 250ml of urine are produced daily, the renal solute load of 300mmol will need to be excreted in a urine with a concentration of 1200mosm/L (ie. maximally concentrated). As the kidneys cannot concentrate urine more than this, a urine flow rate less than 250ml will not allow excretion of the renal solute load, which then will accumulate in the body.

A urine flow rate of less than 250ml/m²/day (or approximately 0.5ml/kg/h) is sometimes used to define acute oliguric renal failure but this figure is only relevant if renal solute load is average and concentrating capacity is normal. Often in renal failure, catabolism increases renal solute load and concentrating capacity is impaired so definitions based only on urine flow rate need to be used with caution. Some causes of acute renal failure, such as antibiotic toxicity, do not lead to reduced urine flow.

**Aetiology of Acute Renal Failure**

Acute renal failure may be caused by disorders which either reduce renal perfusion (pre-renal causes), or affect renal parenchyma (renal causes), or obstruct urinary drainage (post-renal causes).

**Pre-renal hypo-perfusion** occurs in disorders with:

- Reduced blood volume (blood loss, hypoproteinaemia, dehydration) but also occurs in:
  - Vascular (venous) dilatation (eg: septicaemia) or
  - Cardiac Failure

Renal parenchymal disorders may be either:

- Glomerular (eg glomerulonephritis or thrombosis due to haemolytic-uremic syndrome and disseminated intravascular coagulation) or
- Tubular (eg. ischaemic or toxic acute tubular necrosis, or pigment tubular obstruction (myoglobin or haemoglobin).

**Post-renal obstruction** causing renal failure occurs in children with posterior urethral valves, with pelvic tumors or with obstruction of a solitary functioning kidney (eg. multicystic non-functioning kidney with contralateral pelvi-ureteric obstruction).

**Pathogenesis of Acute Renal Failure**

Renal blood flow and glomerular filtration rate are maintained over a large range of blood pressures (perfusion pressures) by constriction or dilatation of afferent arterioles by a mechanism, which requires changes in secretion of vasodilatory prostaglandins such as prostacyclin. This **autoregulation of renal blood flow fails** when perfusion pressure is sufficiently low. Drugs such as Indomethacin, which inhibit prostaglandin synthesis, make the kidney more susceptible to hypoperfusion damage.

Renal hypoperfusion leads to **renin secretion** from the juxtaglomerular apparatus on the afferent arterioles of glomeruli. Renin leads to efferent arteriolar constriction, which raises glomerular capillary pressure thereby helping maintain glomerular filtration during hypoperfusion. Plasma renin levels are raised in most types of acute renal failure but are **low in acute post-streptococcal nephritis** where the patient is fluid overloaded and perfusion is reduced, not by low perfusion pressure but by glomerular capillary occlusion by cell proliferation. Severe prolonged hypoperfusion causes a form of renal injury with acute oliguric renal failure that does not respond to volume repletion and is the clinical condition called ‘**acute tubular necrosis**’. However in this condition renal biopsies show that there is often no actual
necrosis of tubules and the condition appears to be due to an intense renal **afferent arteriolar vasoconstriction** with a consequent drop in renal blood flow. There is evidence that this vasoconstriction is renin mediated, as kidneys of experimental animals seem protected from hypoperfusion injury if renin action is blocked by pre-treatment with ACE inhibitors or suppressed by saline loading. No protection occurs if these measures are given after the hypoperfusion injury.

It is speculated that hypoperfusion causes renin release, which initially constricts efferent arterioles and maintains glomerular filtration, but if sufficiently severe the released renin causes afferent constriction as well, so that perfusion is further reduced, more renin is released and the vasoconstriction is greater than the initial hypoperfusion demanded. This causes prolonged oliguria which does not improve with volume repletion.

Acute oliguria due to glomerular conditions such as proliferative nephritis or thrombotic disease like haemolytic uraemic syndrome reduce renal blood flow and renal function by interfering with glomerular perfusion.

**Clinical Features**

A child with acute renal failure will have symptoms and signs due to the underlying cause of the renal failure, such as pallor in HUS or haematuria in acute nephritis, plus symptoms and signs due to the oliguria. The clinical features due to the oliguria are caused by retention of the various urinary constituents in the body and are:

- **Water:** Water retention causes oedema.
- **Sodium:** Sodium is mainly an extracellular ion so its retention preferentially expands the plasma volume leading to hypertension.
- **Potassium:** Potassium retention (hyperkalaemia) causes arrhythmias.
- **Hydrogen:** Hydrogen ion retention leads to acidotic ventilation.
- **Urea:** Retention of urea and other nitrogenous products causes nausea and vomiting.
- **Phosphate:** Phosphate retention causes reduced ionized calcium with consequent tetany.

**Management of Acute Renal Failure**

Renal failure due to low perfusion pressure (blood pressure) requires urgent infusion of fluid to restore volume. Sometimes urine flow remains low when blood pressure appears to have been restored and the question then arises whether to give more fluids because of sub-clinical dehydration or to restrict fluids because the patient may have ‘acute tubular necrosis’. Giving a dose of frusemide (4mg/kg) intravenously will help resolve this dilemma. Patients with pre-renal hypoperfusion will respond to frusemide with an increase in urine flow within 45 minutes, whereas patients with established renal failure (‘acute tubular necrosis’) remain oliguric.

Examination of the sodium and osmolality in the oliguric patient sometimes gives a guide to the cause of the oliguria in hypoperfusion states. In hypovolaemic states with preserved tubular function the urine osmolality is high and the sodium is low (less than 40mmol/L) while in acute renal failure with loss of tubular function (tubular necrosis) the urine concentrations are more like unmodified glomerular filtrate (osmolality about 300 and sodium about 135). In practice, however, the response to frusemide is a more useful test of tubular function and also helps manage the oliguria.

If an oliguric patient responds to frusemide, indicating intact tubular function, it is likely that extra fluid will be rapidly required to restore renal perfusion. An exception to this is acute post-streptococcal nephritis which responds well to frusemide (as tubules are not involved in the disease) but is associated with fluid overload and hypertension.
Frusemide in acute nephritis and fluid replacement in frusemide-responsive hypoperfusion are generally all that is required in these conditions to manage the renal failure. If urine output is not restored by frusemide the patient will probably require dialysis.

The principle indication for dialysis in acute oliguric states is serum electrolyte abnormality (especially hyperkalaemia) or fluid overload with hypertension or cardiac failure in a patient with frusemide-resistant oliguria. If the patient does not respond to frusemide and remains oliguric the electrolyte or fluid problems can only get worse so even minor electrolyte abnormalities in oliguria indicate the need to for dialysis.

**Dialysis**, either peritoneal or haemodialysis, involves placing a dialysis fluid in dialysis equilibrium with the blood so that blood chemicals, which accumulate in uremia (potassium, phosphate, hydrogen ion, urea, and creatinine), can equilibrate with dialysis fluid which does not contain these uremic solutes. Water can be drawn out of the overloaded patient by using dialysis fluid, which is made hypertonic to plasma by addition of dextrose.

Dianeal is a commonly used peritoneal dialysis fluid at RCH and contains the following concentrations:

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<tr>
<td>Na+</td>
<td>132mmol/L</td>
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<td>Ca++</td>
<td>1.8mmol/L</td>
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<tr>
<td>Mg++</td>
<td>0.25mmol/L</td>
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<tr>
<td>Cl-</td>
<td>96mmol/L</td>
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<tr>
<td>Lactate</td>
<td>40mmol/L</td>
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Dialysis fluid has **1.5% dextrose**, which makes it slightly hyperosmolar to plasma (osmolality 346mosm/kg), **2.5% dextrose** (osmolality 386mosm/kg), or **4.25% dextrose** (osmolality 484), which is very hypertonic to plasma and draws off large quantities of water. The more hypertonic fluids are used in the most overloaded patients.

**Prognosis**

Patients with acute tubular necrosis usually recover renal function after a few days of dialysis but the occasional patient requires dialysis for many weeks before recovery.