Renal Failure

By

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Acute kidney injury

- Acute kidney injury is a broad clinical syndrome of abrupt onset due to intrinsic kidney diseases as well pre-renal and post-renal causes. It includes, but is not restricted to, acute renal failure. It is one of a number of acute kidney diseases, and can coexist with other acute or chronic kidney diseases. The concept of acute kidney disorders is relatively new, and the definitions are evolving.
- The diagnosis of acute kidney injury, and staging of its severity, are based on changes in serum [creatinine] and urine output. Acute kidney injury is defined by any of the following.
- 1. increase in serum creatinine by 26.5 µmol/l or more within 48 hours;
- 2. increase in serum creatinine to 1.5 or more times baseline, which is known or presumed to have occurred within the previous 7 days;
- 3. urine output of less than 0.5 ml/kg/hour for 6 hours.

- Acute kidney failure is then a stage of acute kidney injury defined by a GFR <15 mL/min per 1.73 m2 body surface area, or the requirement for renal replacement therapy (i.e. dialysis or transplantation).
- By definition, this is renal disease of acute onset, severe enough to cause failure of renal homeostasis. Often oliguric, diuretic and recovery phases can be recognised, although a few patients maintain a normal urine output throughout the course of the illness.

Oliguric phase

- In this phase, less than 400 mL of urine is produced each day; if the renal failure is due to outflow obstruction, there may be anuria. The oliguria is mainly due to a fall in GFR.
- The urine that is formed usually has an osmolality similar to plasma and a relatively high [Na+], since the composition of the small amount of glomerular filtrate produced is little altered by the damaged tubules.
- Plasma [Na+] is usually low due to a combination of factors, including intake of water in excess of the amount able to be excreted, increase in metabolic water from increased tissue catabolism and possibly a shift of Na+ from ECF to ICF.
- Plasma [K+], on the other hand, is usually increased due to the impaired renal output and increased tissue catabolism, which is aggravated by the shift of K+ out of cells that accompanies the metabolic acidosis that develops due to failure to excrete H+ and also due to the increased formation of H+ from tissue catabolism.

- Retention of urea, creatinine, phosphate, sulphate and other waste products occurs. The rate at which plasma [urea] rises is affected by the rate of tissue catabolism; this, in turn, depends on the cause of the acute renal failure.
- In renal failure due to trauma (including renal failure developing after surgical operations), plasma [urea] tends to rise more rapidly than in patients with renal failure due to medical causes such as acute glomerulonephritis.
- To differentiate the low urinary output of suspected acute renal failure from that due to severe circulatory impairment with reduced blood volume, the tests summarized in Table 4.4 may be helpful.
- However, none of these tests can be completely relied upon to make the important and urgent distinction between renal failure and hypovolaemia .
- Careful assessment of the patient's fluid status, possibly including measurement of the central venous pressure, is also required.

Table 4.4 Investigation of low urinary output.

Investigation	Simple hypovolaemia	Acute renal failure
Urine osmolality	Usually >500 mmol/kg	Usually <400 mmol/kg
Urine [urea] : plasma [urea]	Usually >10	Usually <5
Urine [Na^+]	Usually <20 mmol/L	Usually >40 mmol/L

- For monitoring patients in the oliguric phase of acute renal failure, plasma [creatinine] or [urea] and plasma [K+] are particularly important, and need to be determined at least once daily.
- Decisions to use haemodialysis are reached at least partly on the basis of the results of these tests. The volume of urine and its electrolyte composition (and the volume and composition of any other measurable sources of fluid loss) should also be assessed in order to determine fluid and electrolyte replacement requirements.

Diuretic phase

- With the onset of this phase, urine volume increases, but the clearance of urea, creatinine and other waste products may not improve to the same extent. Plasma [urea] and [creatinine] may therefore continue to rise, at least at the start of the diuretic phase.
- Large losses of electrolytes may occur in the urine and require to be replaced orally or parenterally. Measurement of these losses is needed so that correct replacement therapy can be given; this requires urine collections, for urine [Na+] and [K+] measurement, and calculation of daily outputs.
- Plasma [K+] tends to fall as the diuretic phase continues, due to the shift of K+ back into the cells and to marked losses in urine resulting from impaired conservation of K+ by the still-damaged tubules. Usually, Na+ deficiency also occurs, due to failure of renal conservation. Throughout the diuretic phase, therefore, it is important to measure plasma [creatinine] and both plasma [Na+] and [K+] at least once daily, and to monitor the output of Na+ and K+ in the urine.

Chronic kidney disease

- Most of the functional changes seen in chronic renal impairment can be explained in terms of a full solute load falling on a reduced number of normal nephrons. The GFR is invariably reduced, associated with retention of urea, creatinine, urate, various phenolic and indolic acids, and other organic substances.
- The progress and severity of the disease are usually monitored by measuring plasma [creatinine] and [urea], and by calculating the eGFR.
- Chronic kidney disease (CKD) affects up to 10% of the population and is often asymptomatic until renal function is severely reduced. Furthermore, mild CKD is a significant risk factor for cardiovascular disease. Detection of asymptomatic progressive CKD could allow patients to be actively treated to preserve renal function and reduce cardiovascular risk. [Creatinine] gives an indication of GFR and is readily performed, but can be misleading. In particular, [creatinine] is influenced by muscle mass (and hence by sex and age) as well as by GFR. A small elderly woman could lose a large proportion of her GFR and still have a [creatinine] within the population reference range and less than that of a young more muscular man, so a 'normal' [creatinine] can be misleading in such a patient.

- By incorporating age and sex into its calculation, the eGFR circumvents these problems, although it is not always applicable.
- eGFR is the basis for the detection and classification of CKD (Table 4.5). It should be emphasised that an eGFR >60 mL/min/1.73 m2 should be regarded as normal in the absence of any other indication of kidney disease.
- This can be structural, such as polycystic kidney disease, or a urine abnormality, such as proteinuria or haematuria .

Table 4.5 Classification of CKD.

Stage	eGFR mL/min/1.73 m2	Description	Treatment stage
1*	90+	Normal kidney function	Observation Control blood pressure
2*	60–89	Mildly impaired kidney function	Observation Control blood pressure and risk factors
3	30–59	Moderately impaired kidney function	Observation Control blood pressure and risk factors
4	15–29	Severely impaired kidney function	Planning for end-stage renal failure
5	<15	Established kidney failure	Treatment choices for renal replacement therapy

*In addition to eGFR results, the diagnosis of stage 1 or 2 CKD requires a structural abnormality of the kidneys (such as polycystic kidney disease) or a functional abnormality (such as persistent proteinuria or haematuria. In the absence of these an eGFR between 60 and 89 is not abnormal.

- **Sodium, potassium and water**
- The renal handling of Na+, K+ and water by normal kidneys and in chronic renal failure has already been considered above.
- **Acid-base disturbances**
- The total excretion of H+ is impaired, mainly due to a fall in the renal capacity to form NH+ 4. Metabolic acidosis is present in most patients, but its severity remains fairly stable in spite of the reduced urinary H+ excretion. There may be an extrarenal mechanism for H+ elimination, possibly involving buffering of H+ by calcium salts in bone; this would contribute to the demineralisation of bone that often occurs in chronic kidney disease.

- **Calcium and phosphate**
- Plasma [calcium] tends to be low, often due, at least partly, to reduced plasma [albumin]. Plasma [phosphate] is high, mainly due to the reduction of GFR.
- Virtually all patients with the later stages of chronic kidney disease have secondary or, much less often, tertiary hyperparathyroidism, and they may develop osteitis fibrosa. Plasma [calcium], which is decreased or close to the lower reference value in patients with secondary hyperparathyroidism, increases later if tertiary hyperparathyroidism develops. Many patients with a low plasma [calcium] have reduced activity of renal cholecalciferol 1α-hydroxylase, the enzyme responsible for the synthesis of the most active form of vitamin D.
- They can potentially develop osteomalacia or rickets, but this would be uncommon in adequately treated patients. A few patients show a third type of bone abnormality: increased bone density (osteosclerosis). It is not clear why any particular one of these various types of renal osteodystrophy should develop in an individual patient.

Other laboratory abnormalities

- Other findings in chronic kidney disease may include impaired glucose tolerance (IGT) and raised plasma [magnesium]. These may need appropriate treatment, but are of no particular diagnostic significance.
- Impaired renal erythropoietin synthesis contributes to the anaemia which is often present in patients with chronic kidney disease.
- Biosynthetic erythropoietin can be used to treat this.