Acute kidney injury (AKI) is common. It is found in at least 20% of patients admitted to acute hospitals and 50% or more of patients admitted to specialist areas such as intensive care and cardiac surgery units. AKI has traditionally been viewed as a single disease, classified according to the anatomy of the kidney (i.e. prerenal, renal, and postrenal). We now know it is a complex clinical syndrome involving several different, often overlapping, diseases. These include the hepatorenal syndrome, cardiorenal syndrome, sepsis, and the use of nephrotoxic drugs. Each appears to have its own unique pathophysiology as well as treatment. A challenge in the diagnosis of AKI and its management is therefore recognising that these conditions often overlap and coexist, as illustrated in Figure 7.1. Because AKI often occurs as a result of other diseases, it can be considered a marker of severity of disease and a predictor of short- and long-term outcomes.

**Definitions**

The international consensus criteria for AKI were first introduced by the Acute Dialysis Quality Initiative, subsequently modified by the AKI Network, and finally by Kidney Disease Improving Global Outcomes (KDIGO). AKI is defined as any of the following:

An increase in serum creatinine to >1.5 times baseline, known or presumed to have occurred within the last 7 days
An increase in serum creatinine to >1.5 times baseline, known or presumed to have occurred within the last 7 days
A urine output ≤0.5 mL/kg/h for 6 hours

AKI is staged according to its severity, as illustrated in Table 7.1. Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function present for at least 3 months, with implications for health (see Table 7.2). ‘Acute kidney disorder’ refers to abnormalities present for 7 days to 3 months which could be AKI or CKD.

Single creatinine measurements are unhelpful in deciding whether a person has AKI or CKD. Creatinine is a nitrogenous waste product derived from muscle. Elderly people have less muscle mass and can have a ‘normal’ creatinine with impaired renal function. Likewise, athletes may have a ‘high’ creatinine with normal renal function. Therefore, labs in many countries routinely report an estimated glomerular filtration rate (eGFR) alongside creatinine measurements. The eGFR is an estimate of creatinine clearance based on creatinine,
Creatinine clearance can be calculated using the equation:

$$\text{Creatinine clearance} = \frac{(140 - \text{age}) \times \text{weight in kg}}{\text{creatinine in } \mu\text{mol/L}} \times 1.2 \text{ for men}$$

### Basic Renal Physiology

Renal blood flow in a 70 kg man is around 1200 mL/min, which is 20–25% of cardiac output, making the kidneys among the most highly perfused organs in the body. Various factors affect renal blood flow, as illustrated in Figure 7.2. There is autoregulation of renal blood flow between a mean arterial pressure (MAP) of 70–130 mmHg in the average healthy person. This is a vital homeostatic mechanism designed to protect the kidney from injury and allow it to maintain a relatively constant GFR necessary to clear waste.
products from the body. The ability of the kidney to maintain a relatively constant blood flow, GFR, and glomerular capillary pressure is mediated by the myogenic response of afferent arterioles working in concert with tubulo-glomerular feedback in response to changes in the concentration of sodium chloride reaching the distal tubules. Below a MAP of 70 mmHg, renal blood flow and GFR fall sharply, as illustrated in Figure 7.3. Autoregulation is impaired in people with hypertension, diabetes, and other forms of chronic kidney disease, which is one reason why these people are more susceptible to AKI in acute illness.
The pathophysiology of AKI varies according to the myriad of conditions associated with it and there is still a lot we do not understand. Most cases of AKI admitted to hospital are due to renal hypoperfusion, sepsis, and cardiorenal syndrome, often in combination with nephrotoxic drugs. Most cases of hospital-acquired AKI are multifactorial, for example, in people admitted for major surgery. ‘Renal’ causes of AKI (e.g. a rapidly progressive glomerulonephritis) are uncommon but are extremely important not to miss.

Renal Hypoperfusion

Renal hypoperfusion (e.g. due to hypovolaemia, low blood pressure, or reduced blood flow due to other causes) activates protective physiological mechanisms within the kidney in order to maintain GFR. If the hypoperfusion is sustained or the response is inadequate, GFR will decrease, initially without any structural damage. If renal perfusion is not restored within a few hours, then ischaemic necrosis can occur, along with endothelial injury, activation of inflammatory mediators, and further renal damage.

Sepsis-Associated AKI

As described in Chapter 5, in sepsis there is macrovascular and microvascular dysfunction, immunological dysfunction, and abnormal cellular responses. Sepsis leads to an increase in circulating inflammatory cytokines and leucocyte activity which leads to the formation...
of capillary microthrombi and a redistribution of intrarenal perfusion. This produces kidney inflammation, oedema, reduced capillary blood flow, reduced oxygen delivery, and increased venous output pressures. Imbalances in reactive oxygen species or nitric oxide production also contribute to endothelial damage, increased vascular permeability, and worsening interstitial oedema.9

**Cardiorenal Syndrome**

Cardiorenal syndrome is the term used to describe a spectrum of disorders involving both the heart and kidneys in which acute or chronic dysfunction in one organ can induce acute or chronic dysfunction in the other. It occurs as a result of ‘haemodynamic cross-talk’ between the failing heart and the response of the kidneys and vice versa, as well as alterations in neurohormonal markers and inflammatory mediators. The condition known as type 1 cardiorenal syndrome reflects an abrupt worsening of cardiac function (e.g. acute or decompensated congestive heart failure) and can develop because of a low cardiac output, renal vein congestion, or both.10 The kidney plus cardiac dysfunction affects kidney perfusion pressures and compensatory mechanisms may be insufficient to maintain an adequate renal blood flow. Inflammation, neurohumoral activation plus the effects of drugs, and the presence of pre-existing CKD also contribute to the development of this syndrome.11 A common scenario is that when patients with decompensated congestive heart failure are admitted to hospital with a deterioration in renal function, their ‘nephrotoxic’ medications are suspended and they may even be given fluid. We now know this is detrimental and this topic is explored further in the mini-tutorial.

**Mini-Tutorial: Treatment of AKI in Decompensated Heart Failure**

Cardiorenal syndrome is a spectrum of disorders in which heart failure can cause renal dysfunction or renal dysfunction can cause heart failure.10 When a patient first presents, it may not be possible to identify in which organ the syndrome first originated. However, a common scenario in acute care settings is when patients on treatment for decompensated heart failure develop AKI.

Impaired renal function is common in patients with congestive heart failure and is associated with worse outcomes. Drugs used to treat heart failure, such as ACE inhibitors and angiotensin-receptor blockers (ARBs) improve long-term outcomes. National Institute of Health and Care Excellence (NICE) guidelines12 recommend that, following the introduction of ACE inhibitors or ARBs, a fall in eGFR of up to 25% or a rise in creatinine of up to 30% is acceptable. Hyperkalaemia may be a reason to reduce or stop drug treatment.

When a patient whose primary problem is heart failure presents with worsening oedema and AKI, more diuretics are required. The kidneys are ‘biochemically sacrificed’ in order to reduce preload and optimise cardiac output. Guidance on changes in renal function associated with drug treatment in heart failure13 can be summarised as follows:
Drug-induced AKI is important to detect because the offending drug can be stopped or substituted for one that is non- or less nephrotoxic. Nephrotoxic drugs are implicated in roughly one-fifth of critically ill patients with AKI. A list of commonly prescribed drugs that contribute to AKI is given in Box 7.1. Nephrotoxic drugs impact on the kidney in different ways. Antibiotics and endogenous toxins (e.g. myoglobin, uric acid) are filtered and concentrated and can reach toxic levels, having a direct cytotoxic effect on

**Box 7.1 Common Nephrotoxic Drugs**

- Acyclovir
- Aminoglycosides
- Amphotericin
- ACE inhibitors
- Angiotensin receptor blockers
- Antibiotics (e.g. flucloxacillin)
- Ciclosporin
- Cisplatin
- Methotrexate
- Non-steroidal anti-inflammatory drugs
- Radiocontrast agents
- Sulphonamides
- Tacrolimus

**Nephrotoxic Drugs**

Drug-induced AKI is important to detect because the offending drug can be stopped or substituted for one that is non- or less nephrotoxic. Nephrotoxic drugs are implicated in roughly one-fifth of critically ill patients with AKI. A list of commonly prescribed drugs that contribute to AKI is given in Box 7.1. Nephrotoxic drugs impact on the kidney in different ways. Antibiotics and endogenous toxins (e.g. myoglobin, uric acid) are filtered and concentrated and can reach toxic levels, having a direct cytotoxic effect on
renal tubular cells, affecting intrarenal blood flow or causing precipitation of metabolites or crystals. In acute interstitial nephritis, drugs or infectious agents can also activate an immune reaction in patients who are genetically predisposed, leading to an interstitial inflammatory cellular infiltrate which in turn stimulates the production of cytokines, eventually (if not interrupted) causing interstitial fibrosis and CKD.

Iodinated radiocontrast agents are an important cause of AKI. Contrast agents are directly toxic to tubular epithelial cells, but there are also vasomotor changes mediated by endothelin, nitric oxide, and prostaglandins. The outer renal medulla has a relatively low partial pressure of oxygen, making it particularly susceptible to the hemodynamic effects of contrast in situations where there is also a high metabolic demand. Patients with pre-existing kidney disease, the lowest levels of kidney function, and those receiving higher doses of contrast are most at risk. Contrast-associated AKI is associated with increased mortality, but it is not clear whether it is a mediator or simply a marker of adverse outcomes, as there are currently no adequately powered trials showing that prevention of contrast-associated AKI reduces mortality. The increments in plasma creatinine levels that are used to define acute kidney injury are common in patients who have undergone procedures using contrast, but this is also true of hospitalised patients in general. However, the incidence of severe acute kidney injury due to contrast material (i.e. creatinine >50% of baseline, or requiring dialysis) is very low – 1.2% in one study of elective coronary angiography patients with CKD and 0.3% of patients undergoing contrast CT scans. Intravenous sodium chloride 0.9% in the few hours before and after the procedure (e.g. at a rate of 125 mL/h) probably prevents contrast-associated AKI (although caution may be required in patients with congestive heart failure). There is no evidence that using oral n-acetylcysteine offers a protective benefit. Bottom line: if your patient needs an urgent intervention because of a serious (even potentially life-threatening) acute illness – proceed with the intervention and explain the risks and benefits to the patient. Stop nephrotoxic medication, administer intravenous sodium chloride 0.9%, use the lowest dose of contrast medium possible, and monitor renal function closely following the procedure.

**Hepatorenal Syndrome**

Hepatorenal syndrome is the most extensively studied form of AKI in terms of neurohumoral changes. In this syndrome, there is intense renal vasoconstriction due to renin–angiotensin–aldosterone activation, accompanied by fall in systemic blood pressure due to splanchnic vasodilatation. This compromises renal blood flow. In patients with decompensated liver disease and tense ascites, increased intra-abdominal pressure can also contribute to a reduction in renal perfusion. This is why treatment of this syndrome includes: suspending nephrotoxic drugs, fluid resuscitation and correction of hypotension, terlipresin (see Chapter 5), and drainage of tense ascites.

**AKI in Major Surgery**

AKI is common in patients undergoing major surgery and is associated with poor short- and long-term outcomes. Surgery is a leading cause of AKI acquired in hospital, with an incidence
of 5–7.5% among general in-patients and 50–60% of critically ill patients. Patients most at risk are those who are older with hypertension, diabetes, or CKD. The highest rates of AKI are found after cardiac surgery. In major surgery, fluid losses (e.g. blood loss, insensible losses, and extravasation of fluid in to the third space) and the effects of anaesthetic drugs (e.g. peripheral vasodilation, myocardial depression) are thought to be the main causes of AKI.20

Obstruction

Extrarenal (e.g. prostatic hypertrophy) or intrarenal (e.g. stones) obstruction leads to an increase in intratubular pressures in the kidney, leading to impaired blood flow and inflammation that can result in AKI, depending on previous kidney function and the severity of the obstruction.

Preventing AKI

The first and most important principle is to anticipate and mitigate all potential causes or triggers of AKI before they happen. The second principle is to ensure that further insults are avoided after AKI occurs.21 Intravascular volume depletion should be corrected. Mean arterial pressure should be optimised so that renal perfusion is maintained, thereby minimising further damage. Nephrotoxic drugs should be stopped. The assessment of intravascular volume status can be monitored by physical examination (see Chapter 5). Dynamic tests such as the response to fluid challenges and passive leg raising may provide additional information.

In critically ill patients, invasive haemodynamic monitoring and vasopressor drugs may be required to increase mean arterial pressure. The use of hydroxyethyl starch has been shown to result in increased rates of AKI especially in patients with sepsis.22 The use of sodium chloride 0.9% has been shown to increase the risk for composite death, dialysis, and persistent renal dysfunction compared to more balanced solutions such as Hartmann’s.23

Theoretically, loop diuretics may protect the loop of Henle from ischaemia by decreasing its transport-related workload. However, no results from double blinded randomised controlled trials of suitable size have shown that these agents reduce the incidence of AKI.24 Although no specific drug-based intervention has been shown to be of benefit, avoidance of nephrotoxic drugs probably shortens the course of AKI. For those patients at particular risk of contrast-associated AKI (i.e. interventional cardiology and oncology patients), intravenous n-acetylcysteine or sodium bicarbonate do not provide additional benefit beyond hydration therapy alone.25

Assessment of Patients with AKI

In deciding what has caused AKI, and whether renal impairment is due to AKI, CKD, or AKI on a background of CKD, the patient’s history usually gives the answer. In the majority of admissions to hospital with AKI, there is an acute and identifiable cause: hypovolaemia
Chapter 7 Acute Kidney Injury

(e.g. diarrhoea and vomiting), sepsis, decompensated heart failure, often in combination with nephrotoxic drugs. Obstruction causing retention of urine due to an enlarged prostate, cancer, haematuria, or stones can also usually be diagnosed on history, physical examination, and a bedside bladder scan (but remember that basic bladder scanners cannot detect a urine volume in the presence of ascites).

In some cases, AKI is due to intrinsic kidney disease. Of these, vasculitis, glomerulonephritis, and interstitial nephritis are the most common. The clinical features suggesting one of these diagnoses range from non-specific symptoms (e.g. malaise, darker/less urine) to symptoms that point towards kidney disease (e.g. oedema, proteinuria, microscopic haematuria, and hypertension) to systemic manifestations of classical syndromes (e.g. Henoch–Schönlein purpura, scleroderma). There may also be temporal association with starting a drug known to cause interstitial nephritis. When there is no clear ‘pre-renal’ cause or obstruction, bedside urinalysis to look for proteinuria and/or microscopic haematuria and urine microscopy is important. Urine microscopy can suggest pathological glomerular changes such as fragmented red cells, red cell casts, white cell casts, or granular casts. The urine microscopy score (based on the quantification of tubular cells and casts) correlates with worsening AKI, need for renal replacement therapy, and hospital mortality.26

Kidney disease is usually a silent condition and therefore AKI can also be diagnosed in the absence of an acute illness when there is a reduction in kidney function within the past 3 months, with or without a change in urine output. Some patients present with abnormal kidney function of unknown duration and the challenge is to decide whether this is AKI or the first presentation of CKD or both (AKI on CKD). In these situations, the history (e.g. presence of risk factors), the presence or absence of albuminuria, kidney size on ultrasound (small in CKD), and the presence of features of CKD (e.g. normocytic anaemia, hyperphosphataemia, and high parathyroid hormone levels) can be helpful in distinguishing between AKI and CKD.

Management of AKI

Early action can save kidneys. In general, the management of AKI involves six simple steps:

1) Treat hyperkalaemia first (see Box 7.2)
2) Correct volume depletion
3) Treat hypoperfusion
4) Exclude obstruction
5) Stop nephrotoxins
6) Treat the underlying cause
Remember that pseudohyperkalaemia is most commonly caused by in vitro haemolysis and the presence of haemolysis is usually reported by the lab. In true hyperkalaemia, both the absolute value of serum potassium and the rate of change are risk factors for electrocardiogram (ECG) changes, and some susceptible individuals may develop cardiac arrhythmias at lower levels of hyperkalaemia. The ECG changes in hyperkalaemia include 'tented' (tall) T waves, a prolonged PR interval, and then loss of P waves, QRS widening, and arrhythmias.

In critically ill patients with established AKI, fluid overload is often present, and maintaining nutrition and administering crucial drugs often requires the administration of at least 1500 mL of fluid per day. Early renal replacement therapy is the best treatment in this situation, as fluid overload has been recognised as a major contributor to increased mortality in patients with AKI.28

### Box 7.2 Treatment of Hyperkalaemia

Hyperkalaemia is defined as:

- **Mild**: 5.5–5.9 mmol/L (meq/L)
- **Moderate**: 6.0–6.4 mmol/L (meq/L)
- **Severe**: >6.5 mmol/L (meq/L)

The principles of treatment of severe hyperkalaemia are:

- Protect the heart
- Shift potassium into cells (this is only temporary)
- Remove potassium from the body
- Prevention of recurrence

This is done by administering:

- Intravenous calcium
- Intravenous insulin and dextrose
- Nebulised salbutamol can be added but is not effective in up to 40% of patients with end-stage renal disease – the potassium-lowering effect of nebulised salbutamol occurs within 30 minutes and lasts for up to 2 hours. The serum potassium level may fall by between 0.5 and 1.0 mmol/L when 10–20 mg of nebulised salbutamol is delivered.27
- Stop drugs that may contribute to hyperkalaemia, institute low potassium diet, treat AKI

The patient should have frequent capillary glucose monitoring and repeat potassium levels.
Renal Replacement Therapy

In some patients, AKI is severe enough to require renal replacement therapy. The indications for starting renal replacement therapy in AKI include:

- Oliguria/anuria
- Resistant hyperkalaemia
- Fluid overload
- Severe metabolic acidosis (pH < 7.2)
- Uraemia (urea > 30 mmol/L or BUN > 83 mg/dL) including its complications (e.g. encephalopathy, pericarditis, and seizures)

Three forms of renal replacement therapy are available: continuous, intermittent (either as intermittent haemodialysis or slow low-efficiency dialysis), and peritoneal dialysis. Continuous renal replacement therapy can involve filtration alone (e.g. continuous veno-venous haemofiltration) or diffusion alone (e.g. continuous veno-venous haemodialysis) or both (continuous veno-venous haemodiafiltration). Peritoneal dialysis is rarely used in AKI due to clearance limitations and difficulty with fluid removal; however, it is often used to start patients with established kidney disease safely on renal replacement therapy.

Evidence from various small- and medium-sized trials suggest little difference in patient outcomes between intermittent renal replacement therapy or continuous renal replacement therapy.
There is also little difference in patient survival rates or time to recovery from AKI with increasing intensity of renal replacement therapy. There is also little difference in patient survival rates or time to recovery from AKI with increasing intensity of renal replacement therapy. 

**Prognosis of AKI**

Nearly two-thirds of AKI cases resolve within 7 days. When AKI does not resolve, substantially worse clinical outcomes can be expected. Patients with stage 2–3 AKI who resolve within 7 days and remain alive and free of renal dysfunction by hospital discharge have a 1-year survival of more than 90%. In contrast, patients whose AKI never resolves have a 47% hospital mortality and among those who are discharged alive, the 1-year survival is 77%. In the long term, several studies have demonstrated a link between AKI and the subsequent development of CKD. Not all episodes of AKI lead to death or CKD, but patients with risk factors for progression (e.g. diabetes, hypertension, and heart failure) should be followed up long term.

**Key Points: AKI**

- AKI is common and diagnosed when there is an acute reduction in kidney function, with or without a change in urine output
- AKI is a complex clinical syndrome involving several different, often overlapping, conditions
- Renal blood flow is autoregulated between a MAP of 70–130 mmHg and this is impaired in people with hypertension, diabetes, and other forms of chronic kidney disease
- AKI can be prevented
- A simple checklist can be used to treat most cases of AKI – but treatment of AKI in decompensated heart failure and some other conditions may be different
- Two-thirds of cases of AKI resolve within 7 days but some patients need renal replacement therapy and patients with risk factors for progression to CKD should have long-term follow-up
- The prognosis of unresolved AKI is poor

**Self-Assessment: Case Histories**

1. A 31-year-old man is admitted to hospital after being found on the floor of his apartment. He had taken intravenous heroin the night before. His vital signs are: drowsy, blood pressure 93/61 mmHg, pulse 108/min, temperature 35°C, respiratory rate 8/min, and oxygen saturations 95% on air. His blood results show a normal full blood count, sodium 131 mmol/L, potassium 6.5 mmol/L, urea 30 mmol/L (BUN 83 mg/dL), creatinine 600 μmol/L (7.2 mg/dL), and calcium 1.9 mmol/L (7.6 mg/dL). He looks dehydrated. What is your management?
Chapter 7 Acute Kidney Injury

2 An 82-year-old year man is admitted with ‘general deterioration’ and not eating or drinking. He is usually treated for heart failure and is taking the following medications: ramipril 10 mg daily, furosemide 80 mg daily, and allopurinol 300 mg daily. He was treated for a chest infection 1 week previously with amoxicillin and also took ibuprofen for pleuritic chest pain. His vital signs are: drowsy, blood pressure 90/60 mmHg, pulse 90/min, temperature 37°C, respiratory rate 20/min, and oxygen saturations 95% on air. His blood results show: sodium 133 mmol/L, potassium 5.1 mmol/L, urea 29 mmol/L (BUN 80 mg/dL), and creatinine 483 μmol/L (5.7 mg/dL). His last available blood results are from 2 months ago and show a urea of 7 mmol/L (BUN 19.5 mg/dL) and creatinine 120 μmol/L (1.44 mg/dL) with an eGFR of 53.4 mL/min/1.73 m². At that time, his blood pressure was 140/80 mmHg. On physical examination, there are no signs of fluid overload and his lungs are clear. He has dry axillae. What is your management?

3 A 34-year-old woman is admitted with breathlessness that started 1 week ago. The chest X-ray shows bilateral patchy shadowing and she reports coughing up small amounts of blood with no sputum. Her vital signs are: alert, blood pressure 181/85 mmHg, pulse 81/min, temperature 37.5°C, respiratory rate 20/min, and oxygen saturations 94% on air. She has no history of vomiting or diarrhoea and appears to be euvolaemic on physical examination. Her blood results show a normal full blood count, sodium 135 mmol/L, potassium 4.2 mmol/L, urea 33 mmol/L (BUN 91.6 mg/dL), and creatinine 451 μmol/L (5.41 mg/dL). What is your management?

4 You are asked to see a 55-year-old man on a surgical ward. He is being treated for ascending cholangitis and had a failed endoscopic retrograde cholangio-pancreatogram (ERCP) today to retrieve a common bile duct stone. His medication chart shows a beta-blocker, calcium channel blocker, and a nitrate for angina. He has no other past medical history. His vital signs are: alert, blood pressure 87/62 mmHg, pulse 85/min, respiratory rate 28/min, temperature 38.1°C, and oxygen saturations 95% on air. He has warm hands and feet. He also has a left nephrectomy scar from 15 years ago. He has been given gentamicin for his infection. The nurse alerts you to his urine output which has been 10 mL/h for the last 3 hours. What is your management?

5 A 63-year-old woman is admitted with diarrhoea and vomiting which she has had for 4 days. Her usual medication comprises bendroflumethiazide and ramipril for hypertension. On admission, her vital signs are: alert, blood pressure 94/67 mmHg, pulse 108/min, temperature 37.7°C, respiratory rate 22/min, and oxygen saturations 98% on air. She reports passing less urine in the last 24 hours. Her blood results show: sodium 145 mmol/L, potassium 4.0 mmol/L, urea 25 mmol/L (BUN 69.4 mg/dL), and creatinine 309 μmol/L (3.70 mg/dL). From her records, her eGFR was normal 1 month ago. What is your management?

6 An 84-year-old woman is admitted after sustaining a fractured neck of femur. Her vital signs are: alert, blood pressure 180/80 mmHg, pulse 75/min, temperature 36.6°C, respiratory rate 14/min, and oxygen saturations 95% on air. On admission, her haemoglobin is
13.5 g/dL, sodium 139 mmol/L, potassium 4.0 mmol/L, urea 6 mmol/L (BUN 16.6 mg/dL), and creatinine 55 μmol/L (0.66 mg/dL). She is prescribed a non-steroidal anti-inflammatory drug for pain. In theatre, she had a 10 minute period of hypotension (85/60 mmHg). Two days postoperatively her blood results are as follows: haemoglobin 10.5 g/dL, sodium 130 mmol/L, potassium 3.8 mmol/L, urea 23 mmol/L (BUN 63.8 mg/dL), and creatinine 254 μmol/L (3.05 mg/dL). What is your management?

7 A 52-year-old man with early diabetic nephropathy is admitted to the coronary care unit with an inferolateral myocardial infarction. He suffers a VF arrest and has no cardiac output for 5 minutes. He has a period of hypotension following this and is treated with inotropes. Although his cardiac condition recovers, his renal function deteriorates. On admission, his urea was 12 mmol/L (33.3 mg/dL) and creatinine 157 μmol/L (1.88 mg/dL). Forty-eight hours later his urea is 27 mmol/L (75 mg/dL) and creatinine 317 μmol/L (3.8 mg/dL). What are the possible reasons for the change in renal function and what is your management?

8 A 56-year-old woman undergoes an elective abdominal aortic aneurysm repair. The aneurysm was located above the renal arteries and the aorta was cross-clamped for 30 minutes. She returns to the intensive care unit from theatre still ventilated. Her vital signs are: pulse 110/min, blood pressure 120/80 mmHg, CVP 10 mmHg, and temperature 36.5°C. Her arterial blood gases on 35% oxygen show: pH 7.2, PaCO₂ 4.0 kPa (30.7 mmHg), base excess (BE) 10, and PaO₂ 25.0 kPa (192 mmHg). Her urine output has been 20 mL/h for the last 2 hours. What is your management?

9 A 70-year-old man is referred by the community heart failure team because of increasing breathlessness, peripheral oedema, and a reduction in renal function. On admission, his vital signs are: alert, blood pressure 110/60 mmHg, pulse 103/min, temperature 36.7°C, respiratory rate 22/min, and oxygen saturations 93% on air. On examination, he has pitting oedema of his lower limbs and abdominal wall. His chest X-ray shows bilateral pleural effusions and interstitial oedema. His diuretics had been increased recently, but his breathlessness and oedema did not improve and his renal function deteriorated. On admission, his urea is 13 mmol/L (36.1 mg/dL) and creatinine 236 μmol/L (2.83 mg/dL) with an eGFR of 25.3 mL/min/1.73 m². His blood results 3 months ago showed an eGFR of 35 mL/min/1.73 m² and his renal function has been steadily declining since. What is your management?

Self-Assessment: Discussion

1 Management starts with assessing and treating problems with A (airway), B (breathing), C (circulation), and D (disability). In this case, this will include fluid challenges and intravenous or intramuscular naloxone. Lower doses of naloxone should be given to long-term opiate users. While this patient’s previous renal function may be unknown, information from the history suggests acute kidney injury rather than CKD. Normal sized kidneys on ultrasound would support this. A ‘long lie’ (lying on the floor...
for more than 1 hour and unable to get up) and some drug overdoses can cause rhabdomyolysis. Myoglobin and urate from muscle breakdown mediate kidney injury. This can be confirmed by measuring creatinine kinase levels, which are usually in the tens of thousands, and testing the urine for myoglobin (alternatively blood+++ on urinalysis but no red cells on microscopy). The typical picture of severe rhabdomyolysis is a high creatinine relative to urea, hyperkalaemia, high phosphate, and low calcium. Aggressive fluid resuscitation is the single-most important treatment. The patient's limbs should be checked for evidence of potential compartment syndrome caused by crush injury.

2 The history points to AKI on a background of CKD. This case is a multifactorial combination of dehydration (diuretics), the action of ACE inhibitors and NSAIDs on the kidneys, infection, and hypotension. Unlike patients admitted with decompensated heart failure and AKI, this patient has no signs of decompensated heart failure. Treatment would consist of the AKI checklist: correct volume depletion, treat hypoperfusion (stop ACE inhibitor, NSAID, and aim for a MAP of at least 70 mmHg), exclude obstruction, stop nephrotoxins, and treat any other underlying causes (e.g. ongoing infection, and consider penicillin-induced acute interstitial nephritis if his AKI does not resolve quickly). The dose of allopurinol should be reduced in renal impairment.

3 This patient appears to be well, with normal vital signs. The combination of haemoptysis plus AKI in a well patient should make you think of a pulmonary-renal syndrome (e.g. granulomatosis with polyangiitis, formerly known as Wegener’s, or anti-GBM disease, formerly known as Goodpasture’s). In a sick patient, the common cause of bilateral patchy shadowing on the chest X-ray, haemoptysis, and AKI is pneumonia, although the haemoptysis is usually mixed in with sputum. Urinalysis and urine microscopy are important in this case and she should be referred to a renal specialist as soon as possible. Blood can be sent for ANCA (anti-neutrophil cytoplasmic antibodies) and anti-GBM (glomerular basement membrane) antibodies. Underlying causes of AKI can be suspected when ‘classical’ clinical patterns present, as illustrated in Table 7.3.

4 AKI is defined as an acute rise in serum creatinine or a urine output ≤0.5 mL/kg/h for 6 hours. This patient is at high risk of AKI due to oliguria, cholestasis (which causes renal vasoconstriction), sepsis, gentamicin therapy, and a previous nephrectomy – early action is essential to prevent irreversible damage to his single kidney. Persisting hypotension and oliguria despite adequate volume replacement should trigger a referral to the intensive care unit within a few hours (see Chapter 6). Urinary obstruction should be excluded by urgent ultrasound. His anti-hypertensive medication and any nephrotoxins should be stopped. (Beta-blockers in low doses tend not to lower blood pressure and ideally should not be stopped suddenly as rebound angina or fast atrial fibrillation can occur.) The underlying cause (biliary infection and obstruction) should be treated as soon as possible.

5 This is a typical combination of volume depletion in combination with infection and nephrotoxic medication which should be corrected using the AKI checklist: correct
volume depletion, treat hypoperfusion (stop ACE inhibitor, bendroflumethiazide, and aim for a MAP of at least 70 mmHg), exclude obstruction, avoid nephrotoxins, and treat the underlying cause. Regular vital signs and fluid balance should be recorded. After correcting volume depletion and stopping her medication, the rest of the management involves ensuring adequate nutrition, monitoring her renal function, and ensuring she is followed up after discharge to ensure no progression to CKD.

The perioperative period can be associated with episodes of hypoperfusion because of volume depletion from many causes and hypotension due to anaesthesia. Perioperative medication may precipitate AKI, especially if the patient has predisposing risk factors: old age, diabetes, hypertension, and CKD. Use the AKI checklist: correct volume depletion, treat hypoperfusion (stop any nephrotoxic drugs and aim for a MAP of at least 70 mmHg), exclude obstruction (has she gone in to urinary retention?), and look for any other underlying causes (did she fall because of an infection?).

This patient was at risk of developing AKI because of pre-existing kidney disease coupled with a major cardiovascular event. A period of hypoperfusion probably precipitated AKI, but he may have also had a primary coronary angioplasty for his myocardial infarction involving the administration of contrast. As well as paying attention to A (airway) and B (breathing) in this case, management is as per the AKI checklist: treat hyperkalaemia first, correct volume depletion, treat hypoperfusion (stop any nephrotoxic drugs and aim for a MAP of at least 70 mmHg), exclude obstruction, and look for any other underlying causes. If his renal function continues to deteriorate, then renal replacement therapy may be necessary to support the patient through this acute

### Table 7.3  ‘Classical’ clinical patterns in renal disease.

<table>
<thead>
<tr>
<th>Symptom + impaired renal function</th>
<th>Consider this diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>Any connective tissue disease</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Haemolytic uraemic syndrome</td>
</tr>
<tr>
<td>Diarrhoea in a transplant patient</td>
<td>Cytomegalovirus infection, mycophenolate mofetil toxicity</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>ANCA + vasculitis, anti-GBM disease</td>
</tr>
<tr>
<td>Hypercalcaemia and back pain</td>
<td>Myeloma</td>
</tr>
<tr>
<td>Long lie</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Microscopic haemoproteinuria in a well patient</td>
<td>IgA nephropathy</td>
</tr>
<tr>
<td>Miscarriages</td>
<td>Lupus, antiphospholipid syndrome</td>
</tr>
<tr>
<td>Peripheral oedema</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>ANCA + vasculitis</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Thrombotic thrombocytopenic purpura (TTP)</td>
</tr>
</tbody>
</table>

These patterns mean the diagnosis should be considered, they do not confirm the diagnosis.
event. His renal function should be monitored closely with regular blood tests and a urinary catheter should be inserted for close monitoring of urine output.

8 The combination of volume depletion associated with major surgery, transient hypotension due to anaesthesia or blood loss, and cross-clamping of the aorta all put this patient at risk of developing postoperative AKI. The AKI checklist is still relevant in this situation, with the added consideration of whether and when to administer intravenous sodium bicarbonate (see mini-tutorial). Renal replacement therapy may be necessary if her creatinine rises significantly or she develops complications of AKI.

9 The priority for management in this situation is treating the patient's fluid overload. In this particular cardiorenal syndrome, the renal impairment is secondary to decompensated heart failure. His renal function may get worse with diuretic treatment; however, a further deterioration is often accepted as a ‘trade-off’ in this context. If he were taking 80 mg of oral furosemide twice a day at home, this could be increased by 25–50% and administered as a daily intravenous infusion, with close monitoring of his renal function. Once diuresis and weight loss are established, he can be switched to an oral twice a day regimen. Provided the patient has heart failure with a reduced ejection fraction, there is no hyperkalaemia, and his creatinine does not rise by more than 30%, any renin–angiotensin blockers do not need to be stopped.

References


Chapter 7 Acute Kidney Injury


