1.Chronic kidney disease (CKD) is initially described as diminished renal reserve or renal insufficiency, which may progress to renal failure (end-stage renal disease). Initially, as renal tissue loses function, there are few noticeable abnormalities because the remaining tissue increases its performance (renal functional adaptation).

Decreased renal function interferes with the kidneys' ability to maintain fluid and electrolyte homeostasis. The ability to concentrate urine declines early and is followed by decreases in ability to excrete excess phosphate, acid, and potassium. When renal failure is advanced (glomerular filtration rate [GFR] ≤ 15 mL/min/1.73 m2), the ability to effectively dilute or concentrate urine is lost; thus, urine osmolality is usually fixed at about 300 to 320 mOsm/kg, close to that of plasma (275 to 295 mOsm/kg), and urinary volume does not respond readily to variations in water intake.

Creatinine and urea

Plasma concentrations of creatinine and urea (which are highly dependent on glomerular filtration) begin a hyperbolic rise as GFR diminishes. These changes are minimal early on. When the GFR falls below 15 mL/min/1.73 m2 (normal > 90 mL/min/1.73 m2), creatinine and urea levels are high and are usually associated with systemic manifestations (uremia). Urea and creatinine are not major contributors to the uremic symptoms; they are markers for many other substances (some not yet well defined) that cause the symptoms.

Sodium and water

Despite a diminishing GFR, sodium and water balance is well maintained by increased fractional excretion of sodium in urine and a normal response to thirst. Thus, the plasma sodium concentration is typically normal, and hypervolemia is infrequent unless dietary intake of sodium or water is very restricted or excessive. Heart failure can occur due to sodium and water overload, particularly in patients with decreased cardiac reserve.

Potassium

For substances whose secretion is controlled mainly through distal nephron secretion (eg,

potassium), renal adaptation usually maintains plasma levels at normal until renal failure is advanced or dietary potassium intake is excessive. Potassium-sparing diuretics, angiotensin-converting enzyme inhibitors, beta-blockers, nonsteroidal anti-inflammatory drugs, cyclosporine, tacrolimus, trimethoprim/sulfamethoxazole, pentamidine, or angiotensin II receptor blockers may raise plasma potassium levels in patients with less advanced renal failure.

Calcium and phosphate

Abnormalities of calcium, phosphate, parathyroid hormone (PTH), and vitamin D metabolism can occur, as can renal osteodystrophy. Decreased renal production of calcitriol (1,25(OH)2D, the active vitamin D hormone) contributes to hypocalcemia. Decreased renal excretion of phosphate results in hyperphosphatemia. Secondary hyperparathyroidism is common and can develop in renal failure before abnormalities in calcium or phosphate concentrations occur. For this reason, monitoring PTH in patients with moderate CKD, even before hyperphosphatemia occurs, has been recommended.

Renal osteodystrophy (abnormal bone mineralization resulting from hyperparathyroidism, calcitriol deficiency, elevated serum phosphate, or low or normal serum calcium) usually takes the form of increased bone turnover due to hyperparathyroid bone disease (osteitis fibrosa) but can also involve decreased bone turnover due to adynamic bone disease (with increased parathyroid suppression) or osteomalacia. Calcitriol deficiency may cause osteopenia or osteomalacia.

pH and bicarbonate

Moderate metabolic acidosis (plasma bicarbonate content 15 to 20 mmol/L) is characteristic. Acidosis causes muscle wasting due to protein catabolism, bone loss due to bone buffering of acid, and accelerated progression of kidney disease.

Anemia

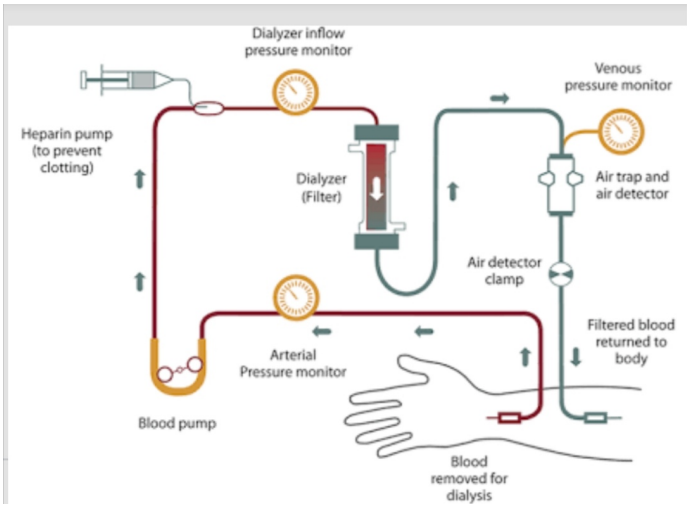
Anemia is characteristic of moderate to advanced CKD (≥ stage 3). The anemia of CKD is normochromic-normocytic, with an Hct of 20 to 30% (35 to 40% in patients with polycystic

kidney disease). It is usually caused by deficient erythropoietin production due to a reduction of functional renal mass (see Overview of Decreased Erythropoiesis). Other causes include deficiencies of iron, folate, and vitamin B12.

The pathophysiology of AKI is multifactorial and complex. The most common cause of AKI is ischaemia, which can occur for a number of reasons (Table 3). Physiological adaptations, in response to the reduction in blood flow can compensate to a certain degree, but when delivery of oxygen and metabolic substrates becomes inadequate, the resulting cellular injury leads to organ dysfunction. The kidney is highly susceptible to injury related to ischaemia, resulting in vasoconstriction, endothelial injury, and activation inflammatory processes.66 This susceptibility can be explained in part from structural associations between renal tubules and blood vessels in the outer medulla of the kidney, with ischaemia compromising blood flow to critical nephron structures present therein. Following the reduction in effective kidney perfusion, the epithelial cells are unable to maintain adequate intracellular ATP for essential processes. This ATP-depletion leads to cell injury and if it is severe enough can lead to cell death by necrosis or apoptosis. During an ischaemic insult all segments of the nephrons can be affected but proximal tubular cells are the most commonly injured. In addition, the nephron's natural function is to filter, concentrate and reabsorb many substances from tubular lumen, and the concentration of these substances may reach toxic levels for the surrounding epithelial cells. A detailed description of the sequence of events and the cellular changes during ischaemic AKI can be found elsewhere.67–69

AKI is also very common in the setting of sepsis. In sepsis the circulation is hyperdynamic and blood flow is altered, albeit not necessarily in the ischaemic range, and GFR drops rapidly.70 The pathophysiology of septic-AKI is very complex and involves inflammation, oxidative stress microvascular dysfunction and amplification of injury via secretion of cytokines by tubular cells.71 The traditional classification of AKI into pre-renal, intrinsic-renal and post-renal has recently been challenged since histological diagnosis is performed very rarely and distinction between pre-renal azotaemia and tubular damage cannot be confirmed and only hypothesised retrospectively.

2.


Dialyzer inflow pressure monitor
Venous pressure monitor
Heparin pump (to prevent clotting)
Dialyzer (Filter)
Air trap and air detector
Air detector clamp
Filtered blood returned to body
Arterial Pressure monitor
Blood pump
Blood removed for dialysis