

Drug-Induced Nephrotoxicity

Practical bedside approach • Adults

01 RECOGNISE RISK AND SUSPECT THE DRUG

- Drugs may cause **haemodynamic dysfunction, tubular injury, interstitial nephritis, crystal obstruction or glomerular injury**. More than one mechanism may coexist.
- Risk increases with **CKD, older age, dehydration, sepsis, heart failure, high doses, prolonged exposure and multiple nephrotoxic drugs**.
- Review prescribed/OTC drugs, supplements and recent contrast. Compare kidney function with baseline and drug timing.

02 COMMON DRUGS AND MECHANISMS

- **NSAIDs**: reduce afferent arteriolar vasodilation and may cause AKI, sodium retention and hyperkalaemia; can also cause interstitial nephritis. Risk is high during hypovolaemia.
- **ACE inhibitors/ARBs**: lower intraglomerular pressure; a modest initial creatinine rise can be expected. AKI risk increases with hypovolaemia or bilateral renal artery stenosis.
- **The triple whammy**: ACE inhibitor/ARB + diuretic + NSAID markedly increases haemodynamic AKI risk.
- **Aminoglycosides, vancomycin, amphotericin B, cisplatin and tenofovir disoproxil**: may cause tubular injury; use exposure monitoring and renal dosing when appropriate.
- **Beta-lactams, proton pump inhibitors, NSAIDs and immune checkpoint inhibitors**: may cause acute interstitial nephritis (AIN). Fever, rash and eosinophilia are often absent.
- **Acyclovir, methotrexate and some sulfonamides**: may cause crystal nephropathy, especially with dehydration/high exposure.
- **Tacrolimus/cyclosporine**: vasoconstriction, hyperkalaemia and chronic injury; occasionally thrombotic microangiopathy. Check levels and interactions.
- **Lithium**: nephrogenic diabetes insipidus and chronic tubulointerstitial injury. Review levels, hydration and interacting drugs.

03 INVESTIGATE SUSPECTED DRUG-RELATED AKI

- Assess volume status, BP, urine output and creatinine. Check **potassium, bicarbonate, urinalysis and sediment**.
- Exclude sepsis, obstruction and other causes. Check drug concentrations when indicated; ultrasound helps exclude obstruction.
- **Urine eosinophils do not reliably diagnose AIN**. Kidney biopsy may be needed for persistent AKI or diagnostic uncertainty.
- Trimethoprim can raise creatinine by inhibiting tubular secretion **without reducing GFR**, but may also cause true AKI and hyperkalaemia. Interpret the whole clinical picture.

04 PREVENT AND MANAGE INJURY

- **Stop the suspected culprit when appropriate**; correct hypovolaemia carefully and treat reversible causes.
- Adjust renally cleared medications, avoid additional nephrotoxins, review interactions and monitor creatinine, electrolytes and urine output.
- Provide an individualised acute-illness medication plan, including when to restart temporarily withheld drugs. **Do not permanently stop kidney-protective therapy without reassessment**.
- Suspected AIN: withdraw the culprit and discuss early nephrology review; selected patients may need glucocorticoids after diagnostic assessment.
- **Metformin accumulation in AKI increases lactic acidosis risk; it is not directly nephrotoxic**. An early SGLT2-related eGFR dip is not necessarily injury.

05 IODINATED CONTRAST AND RED FLAGS

- Distinguish **contrast-associated AKI** (temporal association) from proven contrast-induced AKI. Risk from modern IV contrast is lower than historically assumed.
- Assess AKI and severe CKD risk; consider IV isotonic saline prophylaxis for AKI or eGFR <30 when appropriate, accounting for heart failure. Do not delay essential imaging solely from fear of contrast.
- **Oliguria, rapidly rising creatinine, severe hyperkalaemia, pulmonary oedema or suspected TMA** requires urgent assessment; dialysis follows standard clinical indications.

KEY MESSAGE

Review drugs whenever kidney function worsens. Identify the mechanism, remove reversible risks and distinguish true injury from expected haemodynamic or creatinine-secretion effects.

REFERENCE

KDIGO 2024 CKD Guideline. Kidney Int. 2024;105(Suppl):S117-S314 (medication stewardship). ACR-NKF Consensus on IV Iodinated Contrast in Kidney Disease. Radiology. 2020;294:660-668.