Drug-Induced Kidney Injury

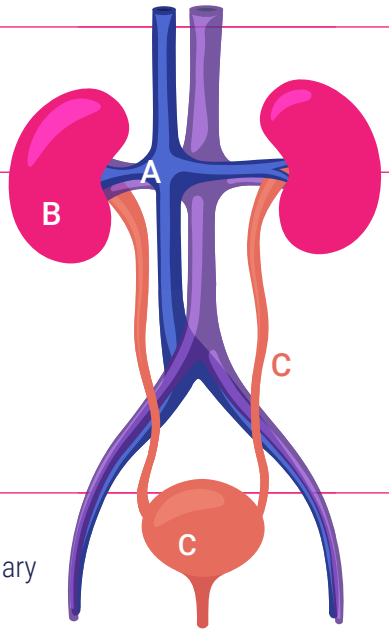
Drugs can cause acute kidney injury, which may progress into or worsen chronic kidney disease.

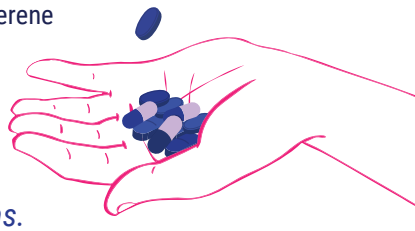
1 Risk Factors

- Previous acute kidney injury
- eGFR <60 mL/min
- Taking ≥2 nephrotoxic drugs
- Dehydration
- Hypotension, hypertension
- Diabetes, heart failure
- Hospitalization, surgery
- Age >60
- Female

Causes of Drug-Induced Kidney Injury

Type of Injury	Sample Nephrotoxic Drugs
A Pre-renal Decreased blood flow to the kidney	Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARBs), calcineurin inhibitors (cyclosporine, tacrolimus), diuretics, NSAIDs, sodium-glucose cotransporter-2 (SGLT2) inhibitors
B Intra-renal/ Intrinsic Damage to kidney itself	Anti-infectives (acyclovir, aminoglycosides, amphotericin, cephalosporins, foscarnet, indinavir/tenofovir, penicillin, pentamidine, quinolones, rifampin, sulfonamides, tetracycline, vancomycin); Anti-convulsants (carbamazepine, phenytoin, valproate); Immune/Oncology (azathioprine, calcineurin inhibitors, carbo/cisplatin, cyclophosphamide, ifosfamide, interferon, methotrexate, pamidronate); Other (allopurinol, Chinese herbs, cimetidine, contrast dye, clopidogrel, diuretics, ethylene glycol, fibrates, illicit drugs, lithium, NSAIDs, proton-pump inhibitors (PPIs), statins)
C Post-renal Obstruction of urinary flow out of kidney (e.g., crystals)	Acyclovir, calcium supplements, indinavir, ganciclovir, methotrexate, nelfinavir, quinolones, sulfonamides, triamterene





2 Signs and Symptoms

can occur days to months after starting a new drug. Most mild to moderate kidney injuries have no symptoms.

Important Things to Watch For

- ↑ Serum creatinine (SCr) of ≥27 μmol/L within 48 hrs
- ↑ SCr ≥50% within 7 days[1]
- Urine output <0.5 mL/kg/h for >6 hrs
- Worsened chronic kidney disease (eGFR ↓ by 25%)

Use SCr to watch for drug-induced kidney injury. eGFR is only useful in chronic kidney disease. eGFR overestimates kidney function in acute kidney injury.

Other Signs/Symptoms

- Lack of energy
- Confusion
- Nausea/vomiting
- Edema
- Sudden blood pressure increase
- Abnormal electrolytes
- Shortness of breath

Rare but serious (may be delayed):

- Rash
- Muscle/joint pain
- Discoloured urine
- ↑ urine, ↑ thirst

[1]KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney inter., Suppl. 2012; 2: 1–138.

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3 Take Action *and think through the following steps when prescribing or monitoring nephrotoxic drugs:*

Step 1 For ALL patients starting a nephrotoxic drug:

- Check baseline SCr
- Routinely check SCr, electrolytes, blood pressure
- Optimize blood sugar, blood pressure, and hydration to minimize risk of injury
- Educate everyone on kidney injury symptoms

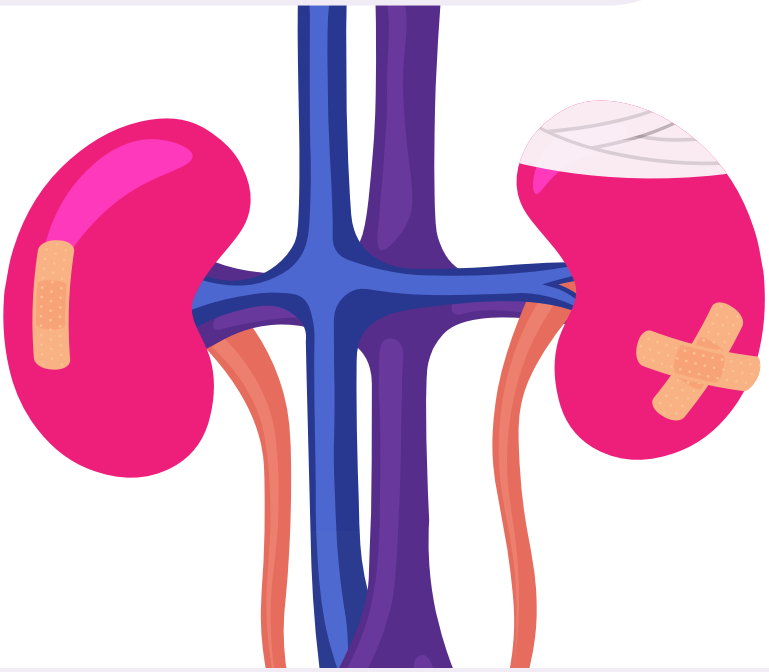
AND Step 2 If the patient ALSO has risk factors for kidney injury:

- Use non-nephrotoxic alternatives if possible
- Educate patient to HOLD **SADMANS**[2] meds if dehydrated (vomiting, diarrhea, fever)
- Adjust doses based on eGFR or dialysis

AND Step 3 If the patient is suspected of having a drug-induced kidney injury:

- Stop the nephrotoxic drug, if possible
- Adjust the dose if the benefit outweighs risk (e.g., antibiotics)
- Seek urgent medical attention (e.g., hospital or nephrology consult)

[2]**S** ulfonylureas, other secretagogues
A ngiotensin-converting enzyme (ACE) inhibitors
D iuretics, direct renin inhibitors
M etformin
A ngiotensin receptor blockers (ARBs)
N on-steroidal anti-inflammatory drugs (NSAIDs)
S odium glucose cotransporter-2 (SGLT2) inhibitors



Resources for Drug Dosing

The Renal Drug Handbook
http://www.gicu.sgul.ac.uk/resources-for-current-staff/supplementary-inpatient-prescription-charts/renalbook.pdf/

Drug Prescribing in Renal Failure
https://kdpnet.kdp.louisville.edu/

eGFR = estimated glomerular filtration rate

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