# Clinical Pharmacology & Toxicology Pearl of the Week

## COLCHICINE – A Crocus a day to keep Gout away?

- ✓ Colchicine is a plant alkaloid isolated from the Autumn Crocus and Glory Lily flowers
- ✓ Used in Gout, Pseudogout, Beçet's disease, Pericarditis, Familial Mediterranean Fever, idiopathic vasculitis and Sweet syndrome.
- ✓ It exerts anti-inflammatory effects by inhibiting leucocyte function & recruitment
- ✓ Colchicine's pharmacokinetics contribute to its narrow therapeutic window:
  - Absorption: well absorbed orally, efflux from enterocytes and hepatocytes via P-Glycoprotein
  - Distribution: very lipophilic, distributes rapidly into all major organ systems
  - Metabolism: high first-pass metabolism, primarily by liver CYP3A4
  - Elimination: 40-65% renal excretion as unchanged drug; enterohepatic & biliary clearance
- ✓ Colchicine carries a high risk of toxicity that occurs in the setting of:
  - Concurrent use of CYP3A4 inhibitors: protease inhibitors, imidazoles, clarithromycin, grapefruit juice
  - Administration of P-GP inhibitors: clarithromycin, tacrolimus, cyclosporine
  - Renal and/or liver impairment
  - Co-prescription of statin medications, specifically: pravastatin, fluvastatin, lovastatin
  - Overdose (intentional vs. unintentional) or ingestion of the Autumn Crocus or Glory Lily

**Table 1: Phases of Colchicine Toxicity**

| Early Phase (0-24h) | Multi-organ failure Phase (1-7 days) | | Recovery Phase (7-21 days) |
|---|---|---|---|
| Nausea<br>Vomiting<br>Diarrhea<br>Abdominal pain<br>Dehydration | Respiratory: | Respiratory Distress Syndrome | Recovery of organ failure(s)<br>Leukocytosis<br>Alopecia<br>Persistence of:<br>neuropathies<br>myopathy<br>fatigue<br>depression |
| | Cardiovascular: | Congestive heart failure<br>Cardiac arrhythmia, cardiac arrest | |
| | Neurologic: | Seizures<br>Encephalopathy<br>Cerebral edema<br>Neuropathy, myopathy | |
| | Hematologic: | Cytopenias<br>Bone marrow suppression<br>Hemolysis, DIC | |
| | Metabolic: | Metabolic acidosis<br>HypoK, hypoNa, hypoP04,<br>hypoglycemia/hyperglycemia | |
| | Other: | Renal failure, Liver failure<br>Immune compromise & Sepsis | |

- ✓ Treatment includes aggressive GI decontamination (gastric lavage, single dose activated charcoal +/- multi-dose activated charcoal), IV fluids, ED observation for at least 8-12 hours if asymptomatic, antibiotics if infection suspected, dialysis if AKI is present, +/- G-CSF

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click **HERE** for clinical issues the CP service can assist with.

The Poison and Drug Information Service (**PADIS**) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.

**References can be found by scanning the QR code with a smartphone camera:**