- Consider urgent coronary angiography in clinical setting of acute chest pain with evidence of myocardial ischemia.
- Treat hyperthermia promptly as it increases cardiac demand.
- Beta-blockers may worsen coronary vasoconstriction (because unopposed alpha agonism remains) and should be used with great caution if pt presents with signs of ischemia or acute cocaine toxicity.
- In management of short-lived arrhythmias, drug treatment should be avoided if possible, as antiarrhythmic agents and cocaine may cause a synergistic depression of contractile function.
- For sustained hemodynamically tolerated SVT associated with AV nodal reentry, adenosine is safe and free of major side effects. If adenosine is unsuccessful, administration of an α-antagonist and a beta-blocker in combination is likely to be both safe and effective. No reliable information on the safety and efficacy of other antiarrhythmic drugs.
- Supraventricular or ventricular tachyarrhythmias associated with hemodynamic compromise require urgent DC cardioversion.
- Avoid use of reversal agents including flumazenil or naloxone, because these may further precipitate cardiac dysrhythmia and autonomic instability.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, MI, dysrhythmias, myocarditis, cardiomyopathy, aortic dissection, endocarditis, premature coronary atherosclerosis, prolonged QT	Exposure Chest pain Palpitations	BP/HR Murmur	ECG ECHO CK-MB, troponins I and T
RESP	Pneumomediastinum, bronchoconstriction, pneumothorax, diffuse alveolar hemorrhage, pulm edema	Exposure Hemoptysis SOB	Wheezing Rales	CXR
HEME	Thrombocytopenia, enhanced platelet aggregation promoting thrombus formation	Bleeding problems, vasoconstriction		Plts
OB	Preterm labor, premature rupture of membranes, abruptio placentae, spontaneous abortion, meconium-stained amniotic fluid	Exposure Uterine contractions Abdominal pain	Vaginal bleeding	US
GU	Rhabdomyolysis, ARF, ESRD	Exposure	Oliguria, anuria	K^+, Cr, CK, urine myoglobin
CNS	Subarachnoid hemorrhage, intracerebral bleed, seizures, CVA	Headache, N/V	Neurologic exam	CT scan

Key References: Hernandez M, Birnbach DJ, Van Zundert AA: Anesthetic management of the illicit-substance-using patient, *Curr Opin Anaesthesiol* 18(3):315–324, 2005; Dwarakanath S, Cook AM, Fahy BG: Perioperative care of the cocaine-dependent neurosurgical patient, *J Anesthesiol Clin Sci* 2:12, 2013.

Perioperative Implications

Preoperative Concerns

- Outside of trauma, likelihood of pt presenting to the OR with acute intoxication is low because of rapid metabolism.
- Some recommend at least 1 wk cocaine-free interval before elective surgery.
- Pts who have been chronically abusing cocaine are at risk for catecholamine-induced cardiomyopathy. Inquire about exercise tolerance, chest pain, and DOE.
- Hx of smoking, alcohol use, positive syphilis serology, and use of other illicit drugs should alert to possibility of cocaine abuse.
- Difficult IV access due to sclerosis of peripheral veins.
- Consider urine screen (reliable for only 14–60 h after use). Tests typically screen for benzoylecgonine.
- Be alert for polysubstance abuse; rare that only one substance is abused. Cocaine is often "cut" with amphetamines. Check blood alcohol, comprehensive drug screen.

Monitoring

- Routine.
- Consider arterial line if Hx of acute intoxication or recent exposure. Consider central access for difficult IV access or if significant hemodynamic lability requiring use of vasoactive agents.

Airway

- Intranasal cocaine can cause perforation of nasal septum, oropharyngeal ulcers, and chronic sinusitis.
- Notify ENT surgeons if pt is chronically hypertensive, on MAO-I or a TCA. Usage of cocaine will precipitate hemodynamic instability.

Preinduction/Induction

- Benzodiazepines are helpful to decrease HR and BP.
- Severe Htn may occur during direct laryngoscopy.
- Usage of succinylcholine in acutely intoxicated pt can be associated with prolonged paralysis as cocaine is also metabolized by plasma cholinesterase. Succinylcholine may also compete for plasma cholinesterase metabolism and prolong acute cocaine effects. Use with caution.
- Use ketamine with caution; potentiates CV toxicity of cocaine.
- Neuraxial anesthesia may be associated with more frequent episodes of hypotension. Correct hypovolemia/coagulopathies first. Hypotension may be ephedrine resistant and thus more responsive to phenylephrine.

Maintenance

- Myocardial ischemia can manifest as CV instability, ECG changes.
- With acute exposure, anesthetic requirements may be increased (increased MAC with acute intoxication, decreased MAC with chronic abuser not using periop)
- Increased catecholamine levels due to inadequate anesthesia; cocaine in blood may result in cardiac dysrhythmias.
- Long-term cocaine abuse may downregulate postsynaptic catecholamine receptors such that indirect vasoconstrictors (ephedrine) are not as effective as direct vasoconstrictors (phenylephrine).
- Despite having alpha-antagonist effects, nonselective beta antagonist effects of labetalol are much more potent, leaving it as a questionable choice for hemodynamic control.
- Temperature rise, sympathomimetic effects associated with cocaine can mimic malignant hyperthermia.

Extubation

- No special issues

Adjuvants

- Ester local anesthetics and succinylcholine, which undergo metabolism by plasma ChE, may compete with cocaine, resulting in decreased metabolism of both.
- Cocaine decreases seizure threshold and enhances convulsant effect of other local anesthetics.
- Dexmedetomidine may be useful as an adjuvant because it counteracts cocaine's sympathomimetic cardiovascular effects. Use with caution if hemodynamics have not been optimized.

Postoperative Period

- Myocardial ischemia
- Pain medication requirements for chronic abusers are same as for nonabusers.
- Consider poor home social environment; may call for vigilant work with case management for pt's posthospital transitions in care that optimize longitudinal recovery.

Colchicine

Rae Stewart | Karina Gritsenko

Uses

- Specifically indicated for treatment and relief of pain in acute attacks of gouty arthritis. Often effective in aborting an attack when taken at initial sign of discomfort.
- Not an analgesic and should not be used for other causes of pain.
- Recommended for prophylaxis of gouty attacks with regular use between attacks.
- Well documented use in familial Mediterranean fever.
- Also used in other conditions such as Bechet disease, pericarditis, atherosclerosis, osteoarthritis, and prophylaxis for postop atrial fibrillation.

Preoperative Risks

- Narrow therapeutic window and possibility of toxicities. In view of its potential side effects—including renal, hepatic, respiratory, and gastrointestinal side effects—dosage adjustments must also be considered, especially in cases of renal and hepatic impairment.
- In animals, has been shown to alter neuromuscular function, intensify gastrointestinal activity, increase sensitivity to central depressants, heighten response to sympathomimetic compounds, depress the respiratory center, constrict blood vessels, cause hypertension through central vasomotor stimulation, and lower body temperature.

- Volume of distribution and total body clearance of colchicine are significantly reduced in the elderly, which can lead to higher plasma concentrations and increased risk of toxicity.
- Onset of toxic effects occurs several hours after acute overdose, initially with nausea, vomiting, abdominal pain, and diarrhea leading to extensive vascular damage and shock, kidney injury, muscle weakness, ascending paralysis, delirium, and ultimately death due to respiratory arrest.

Overview/Pharmacology

- Lipid-soluble alkaloid prepared from *Colchicum autumnale*.
- Has a long terminal half-life of 20–40 h. Bioavailability from 24–88%. About 40% of colchicine binds to albumin in the bloodstream. Peak plasma levels occur 1 h after administration, with maximal anti-inflammatory effects occurring over 24-48 h, reaching their highest concentration within leukocytes.
- Primarily eliminated by hepatobiliary excretion. Renal excretion accounts for 10–20% of colchicine elimination in pts with normal renal function.
- Preferentially binds tubulin, cytochrome P3A4, and P-glycoprotein. It persists on tubulin for 20–40 h, preventing fusion of autophagic vacuoles within lysosomes in neuronal, marrow, and muscle cells, risking damage of these organs. CYP3A4 metabolizes colchicine to 2- and 3-demethylcolchicine in hepatocytes and enterocytes. P-glycoprotein, an ATPase efflux pump, extrudes colchicine from the GI tract to limit GI absorption.
- Because of CYP3A4 interactions, there is decreased metabolism of colchicine in pts taking clarithromycin, fluoxetine, paroxetine, nefazodone, protease inhibitors, tolbutamide, azole antifungals, cimetidine, and several nondihydropyridine calcium channel blockers. P-glycoprotein may interact with macrolides, protease inhibitors, chemotherapeutic agents, glucocorticoids, statins, and calcium channel blockers.

Drug Class/Mechanism of Action/Usual Dose

- Tricyclic alkaloid antiinflammatory agent used to treat acute attacks of gouty arthritis.
- Binds tubulins, blocking microtubule assembly and polymerization, arresting microtubule growth at low doses, and promoting depolymerization at higher doses.
- Antiinflammatory effects due to disruption of microtubules and downstream cellular functions of leukocytes. Inhibition of neutrophil chemotaxis, adhesion and mobilization, superoxide production, NALP3, and interleukin 1B processing and release.
- Lactic acid production is reduced; there is decreased uric acid deposition and a reduction in phagocytosis, leading to a decreased anti-inflammatory response.
- Its CV effects are via inhibition of intimal hyperplasia and VEGF expression
- For acute gout, ACR guidelines recommend a loading dose of 1.2 mg followed by 0.6 mg. In the treatment of osteoarthritis, 0.5 mg twice daily. In treatment of recurrent pericarditis 1-2 mg day 1 and maintenance 0.5–1.0 mg/day. For postpericardiotomy syndrome on POD3, 1 mg twice daily and for maintenance, 0.5 mg twice daily.
- Recommend reducing dose by up to 50% in pts >70 y.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Circulatory collapse	Within 7 d of ingestion	Vital signs	
RESP	Respiratory failure		Vital signs	ABG
GI	N/V diarrhea	Symptoms within 24 h of ingestion		LFTs
RENAL	Renal failure	Within 7 d of ingestion		BUN/Cr
MS	Rhabdomyolysis, muscle weakness	Within 7 d of ingestion; concomitant use with statins		Creatinine kinase, LDH
HEME	Blood dyscrasias, marrow failure	Within 7 d of ingestion		CBC
CNS	Delirium, ascending paralysis, convulsions	Within 7 d of ingestion	Mental status exam, neurologic assessment	EEG

Key References: Leung YY, Yao Hui LL, Kraus VB: Colchicine—update on mechanisms of action and therapeutic uses. *Semin Arthritis Rheum* 45(3):341–350, 2015; Ismaeil MS, Tkachenko I, Hickey RF, et al.: Colchicine inhibits isoflurane-induced preconditioning. *Anesthesiology* 91(6):1816–1822, 1999.

Perioperative Implications

Preoperative Concerns

- Surgery and even minor procedures can precipitate acute gouty arthropathy. Prophylaxis against attacks of gout in pt undergoing surgery can be initiated 3 d before and 3 d after surgery.
- Narrow therapeutic index can cause toxicities in the setting of renal impairment or drug interactions.
- Recommended that colchicine be held on the morning of surgery and resumed when pt is again able to tolerate oral medications.

Monitoring

- Standard ASA monitoring

Induction/Maintenance

- Colchicine has been shown to abolish the myocardial protective effect of pretreatment with isoflurane.
- Owing to alterations in neuromuscular function, colchicine may increase sensitivity to CNS depressants, heighten response to sympathomimetic compounds, and depress the respiratory center.
- To decrease risk of toxicity, adequate urine output must be maintained and renal impairment avoided.

Possible Drug Interactions

- Interactions with calcium channel blockers, glucocorticoids, macrolides, statins, cimetidine, clarithromycin, fluoxetine, paroxetine, nefazodone, azole antifungals, protease inhibitors, tolbutamide, and chemotherapeutic agents owing to metabolism with CYP3A4 and P-glycoprotein.

Anticipated Problems/Concerns

- Colchicine IV is not available in USA; therefore if pt should develop an acute flare of gout postop and be unable to tolerate oral medications, intra-articular or systemic steroids can be used.

Cromolyn Sodium

Gregory A. Wolff | Christopher Ciarallo | Lee A. Fleisher

Uses

- Approved by the FDA in 1973 as the first prophylactic nonsteroidal drug available for treatment of chronic asthma.
- Alternative initial maintenance therapy for mild persistent and moderate persistent asthma.
- Preventative only; not effective during acute episodes of bronchospasm.
- Beneficial for allergic-component and exercise-induced asthma.
- May be beneficial in allergic rhinitis and atopic ocular diseases.
- Oral formulations for the management of mastocytosis, ulcerative colitis, and food allergies.
- Leukotriene receptor antagonists have largely replaced cromolyn sodium as the non-corticosteroid treatment of choice in the treatment of asthma.

Overview/Pharmacology

- Inhibits antigen-induced degranulation of pulm mast cells, eosinophils, neutrophils, monocytes, and lymphocytes.
- Prevents release of histamine, leukotrienes, and other autacoids.
- Reverses and suppresses leukocyte activation.
- Inhibits cough reflex.
- Does not directly relax bronchial smooth muscle.
- No apparent steroid-sparing effects and considered inferior to inhaled corticosteroids on measures of lung function and morbidity in 2006 Cochrane Review.
- Administered by inhalation to treat asthma.
- 8–10% of inhaled dose reaches lung parenchyma and is readily absorbed.
- $T_{½}$: 80–90 min; peak plasma concentration within 15 min.
- Active drug excreted unchanged in urine (50%) and bile (50%).
- Can be taken prophylactically 15–20 min before exercise or exposure to known allergen to prevent bronchospasm.