**Clinical Pharmacology & Toxicology Pearl of the Week**

**~ Naloxone ~**

* First synthesized in 1960, naloxone is a competitive opioid antagonist at mu, kappa and delta receptors.
* It is most potent at the mu receptor (the receptor responsible for analgesia, sedation, miosis, euphoria, respiratory depression, and decreased GI motility)
* Naloxone can be administered intravenously, intramuscularly, subcutaneously, intranasally, intraosseously, intralingually, nebulized or via an endotracheal
tube. Onset is fastest when given IL (30 seconds) and slowest when given IM
(6 minutes)
* Duration of action is 20-90 minutes and elimination half-life is 60-90 minutes
* Indications for naloxone administration in patients with opioid-associated
CNS depression include: hypoventilation (respiratory rate < 12/min) and /or hypoxia (oxygen saturation < 90%).
* Naloxone has also been used in management of overdoses of non-opioids such as ethanol, clonidine, captopril and valproic acid. Mechanism of action may be due to reversal of endogenous opioid peptides at opioid receptors. Clinical improvement in these situations is neither as dramatic nor consistent as with opioids.
* **Dosing:**
	+ Adult starting dose:
		- 0.4 mg IV/IM/IO/SQ for non-opioid dependent patients
		- 0.04 mg IV/IM/IO/SQ for opioid-dependent patients
	+ Pediatric starting dose:
		- 0.1 mg/kg IV/IM/IO/SQ for non-opioid dependent patients
		- 0.001 mg/kg IV/IM/IO/SQ for opioid-dependent patients
	+ Repeat with escalating doses every 2-3 minutes as needed
	+ If there is no response after 10-12 mg naloxone, search for other causes of CNS depression.
	+ If starting an infusion, the infusion should be started at two-thirds of the effective naloxone dose per hour, and titrated as needed. The effective dose of naloxone is the dose that resulted in improvement of respiratory and CNS depression.
	+ A naloxone infusion in an adult can be prepared by multiplying the effective naloxone dose by 6.6, adding that quantity to 1000 ml of normal saline, and running the infusion at 100 ml/hr.
	+ Naloxone may need to be continued for > 24 hours post-exposure.
	+ In patients admitted for 24 hours of observation who are receiving repeat intermittent dosing or continuous infusion, monitor the patient for at least 6 hours after naloxone is discontinued.
* **Naloxone-associated acute opioid withdrawal:**
	+ Naloxone can potentiate withdrawal in opioid-dependent patients.
	+ Opioid withdrawal is typically not life threatening, but is extremely uncomfortable for the patient.
	+ In rare cases, acute lung injury may occur in the setting of precipitated opioid withdrawal, possibly due to massive catecholamine release or unmasking of opioid-induced hypoxia.
	+ Clinical features of opioid withdrawal include: yawning, rhinorrhea, nausea, vomiting, diarrhea, lacrimation, piloerection, muscle aches, weakness, perspiration, anxiety, dilated pupils, tremors, tachycardia, and hypertension. Seizures may be seen in neonatal opioid withdrawal.
	+ If the patient develops withdrawal after a bolus dose of naloxone, allow the effects of the bolus to abate. Symptoms resolve over 1 hour as the naloxone inhibition of opioid receptors decreases.
	+ If the patient develops withdrawal during an infusion of naloxone, stop the infusion until the withdrawal symptoms abate, and restart the infusion at half the initial rate.
	+ In addition to adjusting the naloxone dosing, treatment of naloxone-associated opioid withdrawal may involve the following depending on the symptoms :
		- IV fluid boluses for volume depletion.
		- Antiemetics (e.g. ondansetron) for nausea and vomiting.
		- A small dose of a short-acting opioid (e.g. fentanyl 25-50 µg IV) may be sufficient to relieve withdrawal symptoms.
		- H2 blockers (e.g. ranitidine) for gastrointestinal reflux symptoms.
		- Clonidine 6 µg/kg PO as a single dose for control of autonomic symptoms (elevated HR and BP).
		- Benzodiazepines (e.g. midazolam, lorazepam, diazepam) only for seizures.
		- Loperamide for diarrhea.
		- NSAIDS (e.g. ibuprofen) for myalgias.
		- Oxygen and positive pressure ventilation for acute lung injury.

**The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click** [**HERE**](https://cumming.ucalgary.ca/ermedicine/files/ermedicine/calgary-clin-pharm-consult-service-poster.pdf) **for clinical issues the CP service can assist with.**

**The Poison and Drug Information Service (**[**PADIS**](https://www.albertahealthservices.ca/topics/Page11975.aspx)**) is available 24/7 for questions related to poisonings.
Please call 1-800-332-1414, and select option 1.**