Overdose Toxidromes

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Health Sciences North
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Learning Objectives

- To review antidote kit stock including indications for use, dosing & administration, and mechanisms of action
- To apply concepts to a clinical case

Case Study

Meet Patient OD

- 63 year old female found by husband in home with empty pill bottles of **citalopram** (180 mg), **hydrochlorothiazide** (375 mg), **zopiclone** (105 mg), and **acetaminophen**
- Also took husband's medications, **bisoprolol** and **amlodipine**

Meet Patient OD

Past Medical History:

- Previous overdose attempt (March 2017)
- Advanced adjustment disorder with depressed mood
- Chronic pain
- Generalized anxiety disorder
- Hypothyroidism

Meet Patient OD

Relevant Labs/Investigations:

- HR= 35 bpm in junctional escape rhythm
- Na= 132 mmol/L
- K= 5.1 mmol/L
- Cl =99 mmol/L
- SCr = 133 µmol/L
- AST = 118 U/L
- ALT = 31 U/L
- Acetaminophen level = 645 µmol/L

Antidote Kit

Taking Stock…

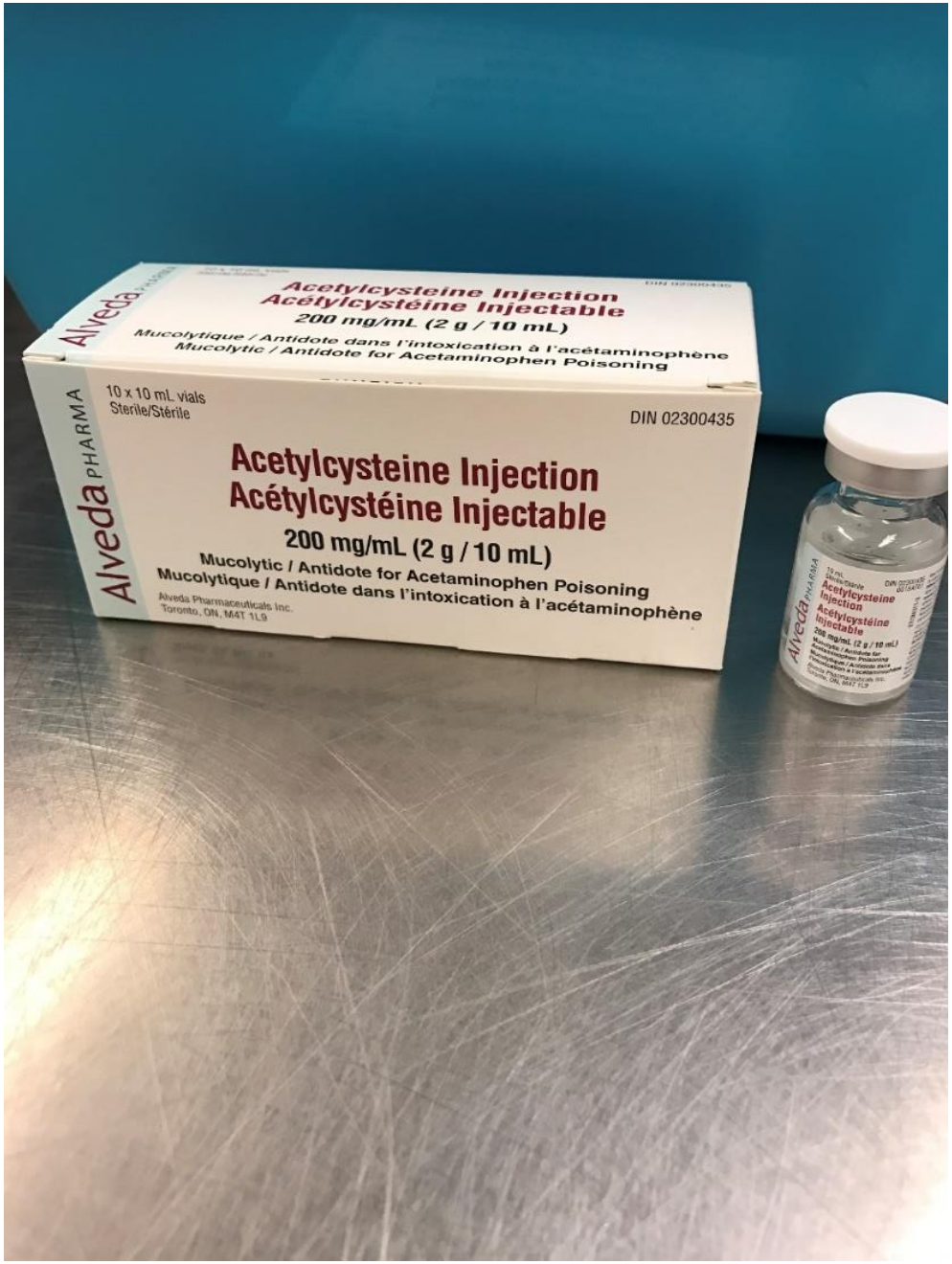
Antidote Kit

- Acetylcysteine
- Atropine
- Calcium Chloride
- Calcium Gluconate
- Cyanide Kit
- Deferoxamine
- Dimercaprol
- Ethyl Alcohol
- Flumazenil
- Fomepizole
- Glucagon
- Lipid Kit
- Methylene Blue
- Naloxone
- Pralidoxime
- Pyridoxine
- Sodium Bicarbonate

ER Fridge

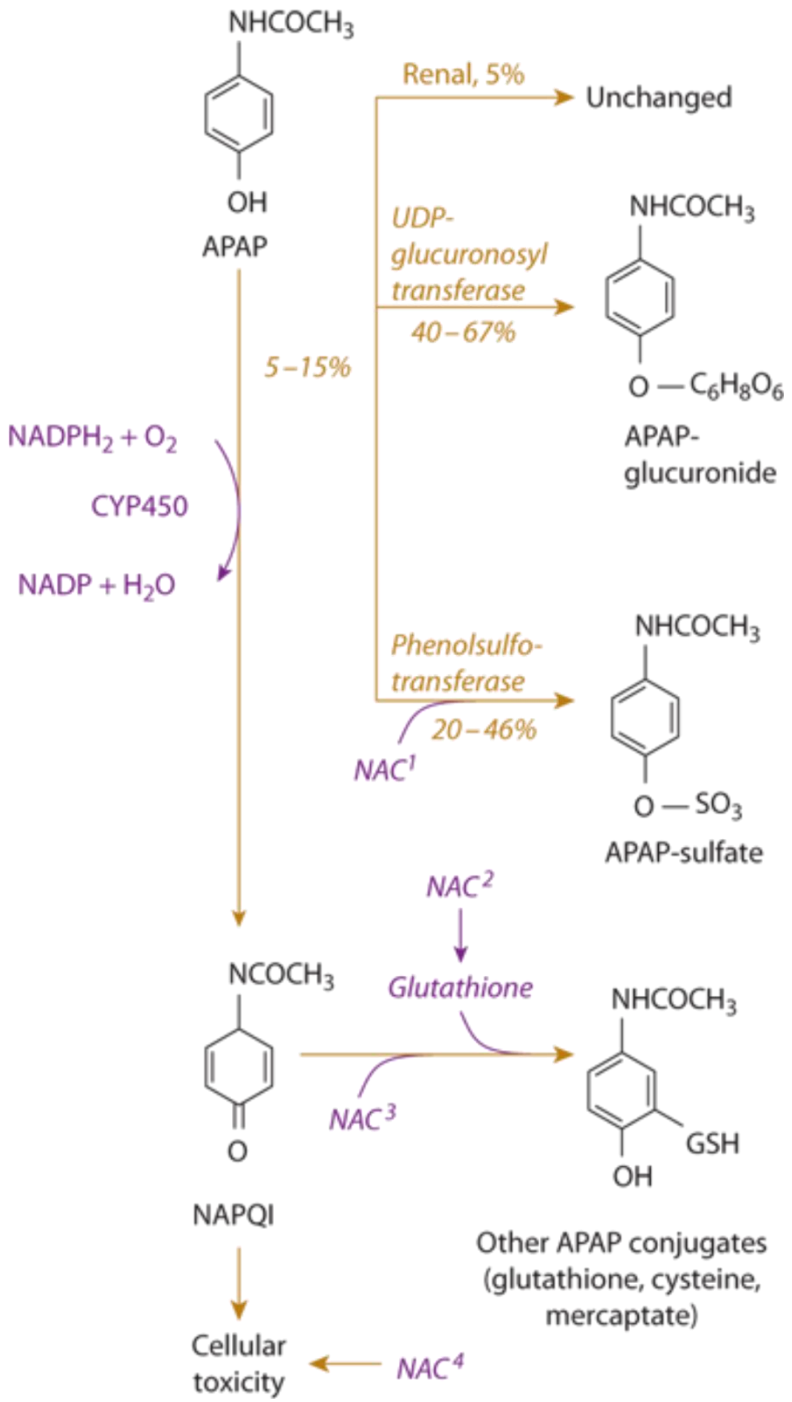
- Digoxin Immune Fab
- Octreotide

Acetylcysteine



Acetylcysteine[1,2]

- **Toxin:** Acetaminophen
- **Dosing & Administration:**
  - *21-hour IV Protocol*: 150 mg/kg in 200 mL D5W over 60 minutes, then 50 mg/kg in 500 mL D5W over 4 hours, followed by 100 mg/kg in 1000 mL D5W over 16 hours
  - Total dose = 300 mg/kg over 21 hours
- **MOA:**
  - Augments glutathione reserves depleted by the metabolism of acetaminophen
- **Onset:**
  - Immediate



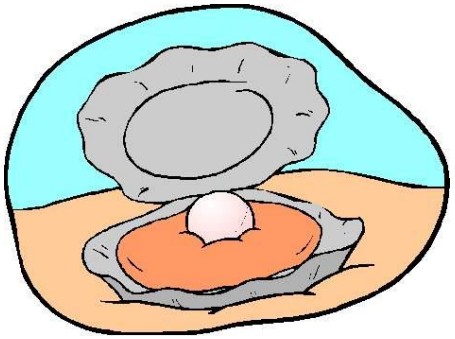
Goldfrank's Toxicologic Emergencies, 10e, 2015 > Acetaminophen
Robert S. Hoffman, Mary Ann Howland, Neal A. Lewin, Lewis S. Nelson, Lewis R. Goldfrank
FIGURE 35–1.

Acetylcysteine[2]

- **Monitoring:**
  - Serum acetaminophen levels, AST, ALT, bilirubin, PT, INR, serum creatinine, BUN, serum glucose, hemoglobin, hematocrit, and electrolytes
  - Obtain first acetaminophen level 4 hours post-ingestion
  - Reassess LFTs for possible hepatotoxicity every 4-6 hours

Acetylcysteine[1,2]

Clinical Pearls



- Best results if given within 8-10 hours of overdose (but may be started within 24 hours)
- Infusing the initial dose of 150 mg/kg over a period of 60 minutes reduces risk of anaphylactoid reactions

Ethanol


30 mL
Dehydrated Alcohol
Alcool déshydraté
Injection USP
100% v/v
SANDOZ

Ethanol[1,3]

- **Toxin:** Methanol (windshield washer fluid), ethylene glycol (antifreeze)
- **Dosing & Administration:**
  - A loading dose is calculated so as to give a blood level of at least 100 mg/dL or 22 mmol/L (42 g/70 kg in adults)
  - 100% ethanol should NOT be used for parenteral administration unless appropriately diluted in NS, D5W, or dextrose-saline to get a **final concentration of 10% v/v**
  - Dehydrated alcohol 100% v/v = 78.9 g/100 mL (or 78.9% w/v)

Ethanol[1]

	Amount of ethanol	Volume of 10% v/v ethanol
Loading dose (over 30 minutes) *	600-800 mg/kg	7.6-10.1 mL/kg
Maintenance dose		
• **non-drinker**	66 mg/kg/hr	0.8 mL/kg/hr
• **moderate drinker**	110 mg/kg/hr	1.4 mL/kg/hr
• **ethanol abuser**	154 mg/kg/hr	2 mL/kg/hr
During hemodialysis		
• **non-drinker**	169 mg/kg/hr	2.1 mL/kg/hr
• **moderate drinker**	213 mg/kg/hr	2.7 mL/kg/hr
• **ethanol abuser**	257 mg/kg/hr	3.3 mL/kg/hr

* assuming initial ethanol concentration is zero.

- Doses given above are only guidelines; administration should be adjusted according to blood alcohol levels

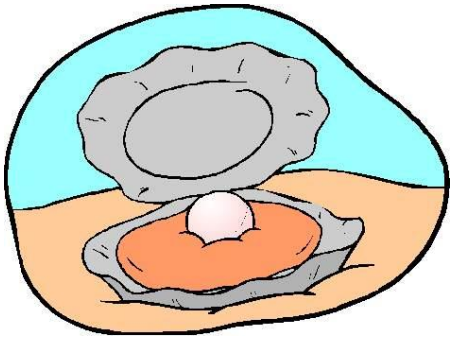
Ethanol[1,3]

- **MOA:**
  - Outcompetes methanol for alcohol dehydrogenase
- **Onset:**
  - Rapid
- **Monitoring:**
  - Electrolytes (including serum magnesium), arterial pH, blood gases, HR, BP
  - Monitor blood glucose and blood alcohol concentrations (aim 22-28 mmol/L) during therapy
  - Continue therapy until methanol or ethylene glycol levels are undetectable

Goldfrank's Toxicologic Emergencies, 10e, 2015 > Toxic Alcohols
Robert S. Hoffman, Mary Ann Howland, Neal A. Lewin, Lewis S. Nelson, Lewis R. Goldfrank
FIGURE 109–1.

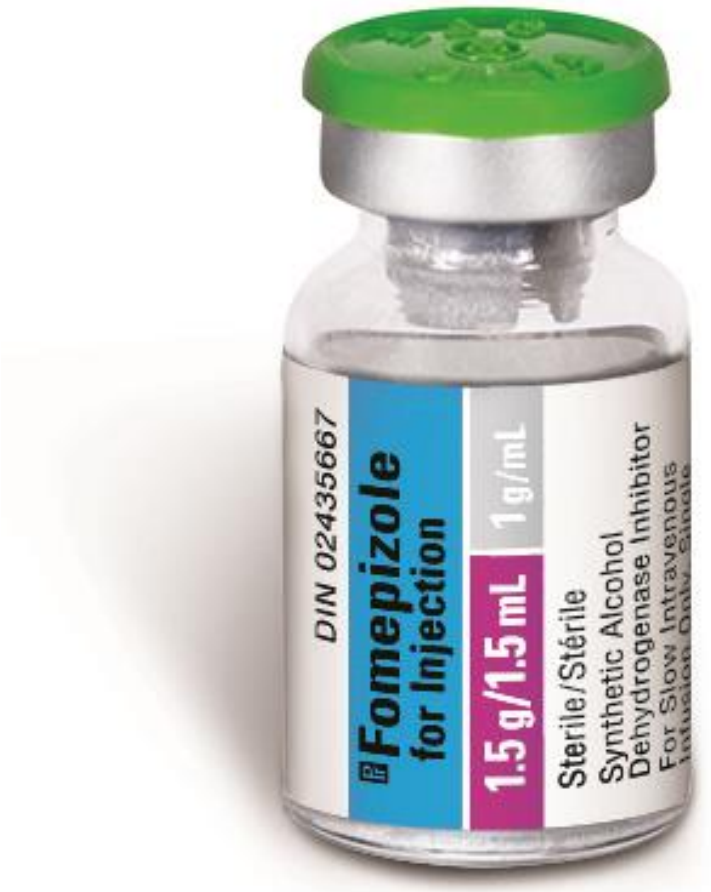
Ethanol[1,3]

Clinical Pearls



- Difficult to obtain, dose, and monitor levels; associated with multiple negative side effects if utilized
- No benefit to adding ethanol therapy to fomepizole therapy in methanol and ethylene glycol-poisoned patients

Fomepizole


DIN 02435667
Fomepizole
for Injection
1.5 g/1.5 mL
1 g/mL
Sterile/Stérile
Synthetic Alcohol
Dehydrogenase Inhibitor
For Slow Intravenous

Fomepizole[1,4]

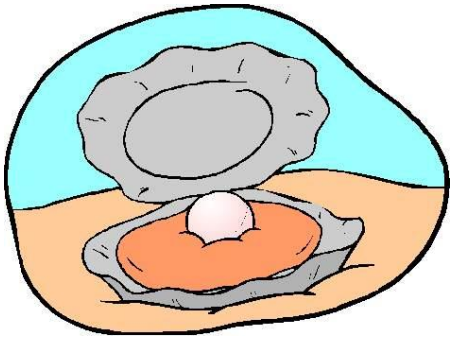
- **Toxins:** Methanol, ethylene glycol
- **Dosing & Administration:**
  - Loading dose 15 mg/kg IV; followed by maintenance doses of 10 mg/kg Q12H for 4 doses
  - If therapy is still needed beyond 48 hours, continue infusion with 15 mg/kg IV Q12H until ethylene glycol or methanol levels are undetectable or below 3.2 mmol/L and 6 mmol/L, respectively
- **MOA:**
  - Competitively inhibits alcohol dehydrogenase

Fomepizole[1,4]

- **Onset:**
  - Immediate
- **Monitoring:**
  - Resolution of clinical signs and symptoms of ethylene glycol or methanol intoxication
  - Plasma/urinary ethylene glycol or methanol levels, urinary oxalate (ethylene glycol), plasma/urinary osmolality
  - Renal/hepatic function
  - Serum electrolytes and ABGs
  - Ideally, fomepizole plasma concentrations should be monitored (generally not available)

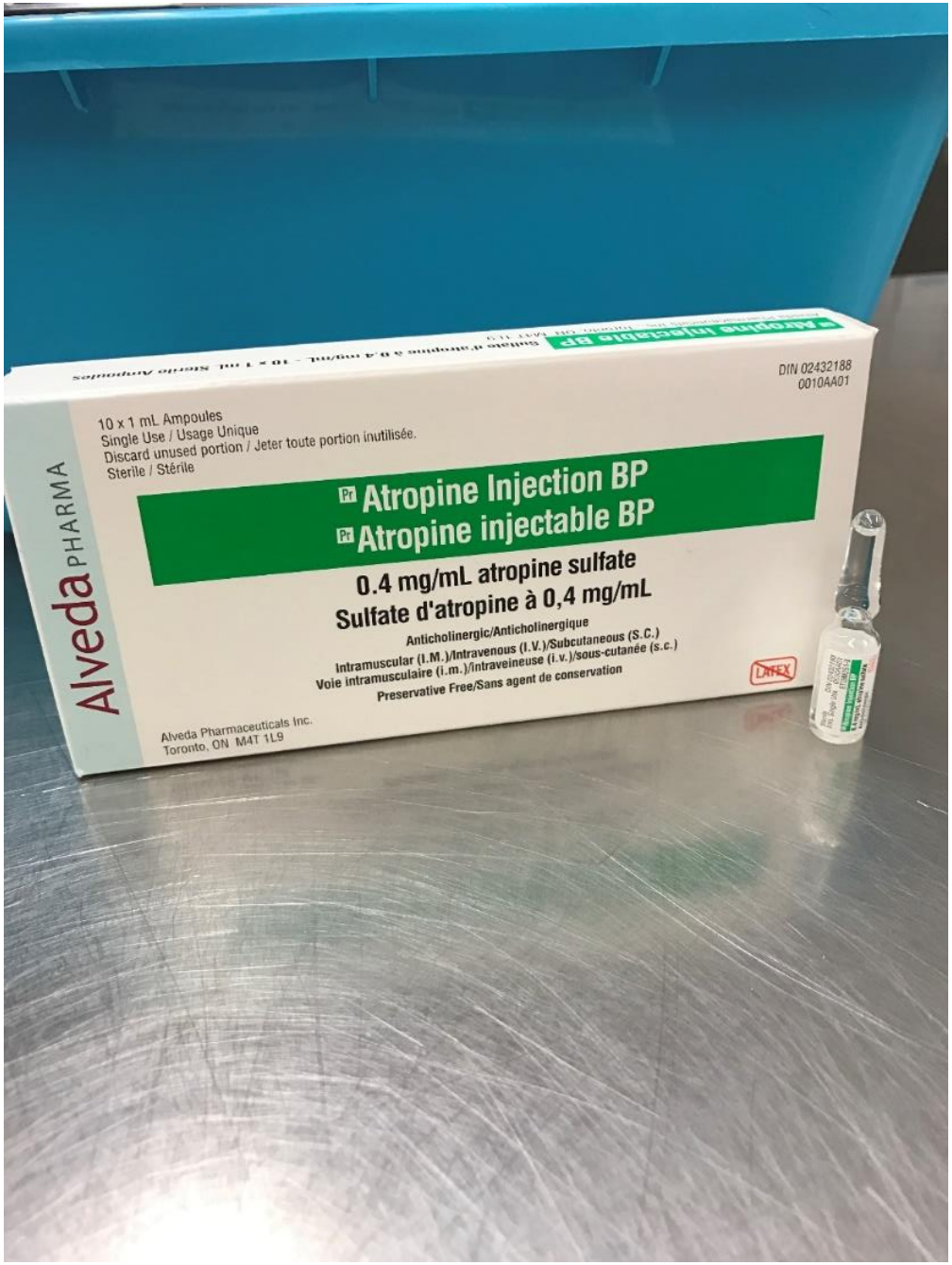
Fomepizole[1,4]

Clinical Pearls



- More convenient and easier to use than ethanol
- Requires dose increase on fifth maintenance dose due to auto-induced metabolism
- Undiluted fomepizole solidifies at temperatures below 25°C
  - Liquefy by warming
  - Solidification does not affect the stability

Atropine


DIN 02432188
0010AA01
10 x 1 mL Ampoules
Single Use / Usage Unique
Discard unused portion / Jeter toute portion inutilisée.
Sterile / Stérile
Pr Atropine Injection BP
Pr Atropine injectable BP
0.4 mg/mL atropine sulfate
Sulfate d'atropine à 0,4 mg/mL
Anticholinergic/Anticholinergique
Intramuscular (I.M.)/Intravenous (I.V.)/Subcutaneous (S.C.)
Voie intramusculaire (i.m.)/intraveineuse (i.v.)/sous-cutanée (s.c.)
Preservative Free/Sans agent de conservation
LATEX
Alveda PHARMA
Alveda Pharmaceuticals Inc.
Toronto, ON M4T 1L9

Atropine[1,5,6]

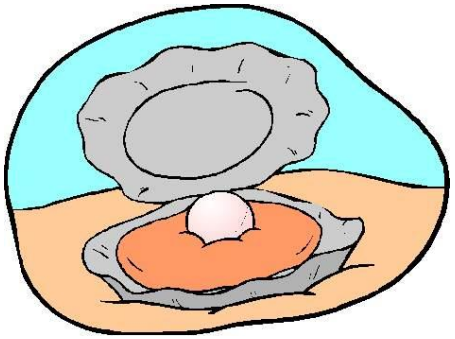
- **Toxins:** Organophosphates and carbamates pesticides, nerve agents, drug/toxin-induced bradycardia
- **Dosing & Administration:**
  - *Pesticide Poisoning:* 1-2 mg IV/IM repeated Q5-60min PRN (in severe cases: 2-6 mg , repeated Q5-60min PRN)
  - *Nerve Gas Exposure*: 2-6 mg IV/IM repeated Q5-10min until secretions are minimal, the skin is dry and ventilation is adequate
  - *Bradycardia*: 0.5-1 mg IV, repeated Q3-5min up to a total dose of 3 mg or 0.04 mg/kg, whichever is less

Atropine[1,5,6]

- **MOA:**
  - Decreases action of the parasympathetic nervous system increasing conduction velocity (dromotropy) and HR (chronotropy)
  - Enhances conduction through the AV junction
- **Onset:**
  - IV: Immediate; IM: Within 15-30 min
- **Monitoring:**
  - HR, BP, pulse, mental status
  - IV dosing requires continuous ECG monitoring
  - Observe for signs of urinary retention

Atropine[1,5,6]

Clinical Pearls



- Should still be considered as initial treatment for symptomatic bradycardia, but failure with this drug may be expected
- Transplanted hearts will not respond to atropine

Pralidoxime

Pralidoxime[1,7]

- **Toxin:** Organophosphate pesticides, anticholinesterase agents used in the treatment of myasthenia gravis (i.e. neostigmine, pyridostigmine), nerve agents

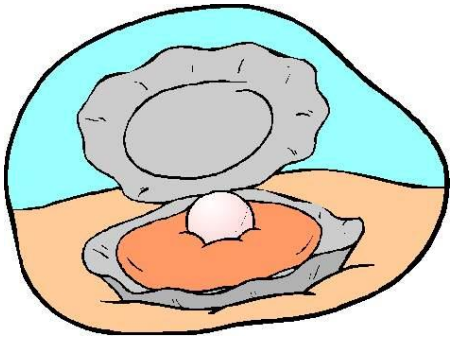
- **Dosing & Administration:**
  - *Pesticide Poisoning*: 1-2 g IV, IM, or SC (may repeat in 60 minutes PRN). Alternatively, a continuous IV infusion of 500 mg/hr.
  - *Anticholinesterase Overdose*: 1-2 g IV followed by 250 mg IV Q5min PRN.
  - *Nerve Gas Exposure*: 1-2 g IV/IM/SC. Repeat in 60 minutes PRN.

Pralidoxime[1,7]

- **MOA:**
  - Reactivates cholinesterase which have been inactivated by organophosphate pesticides and related compounds
- **Onset:**
  - IV: 5 to 15 minutes; IM: 35 minutes
- **Monitoring:**
  - Vital signs, BP, and respiratory status
  - Continuous ECG and hemodynamic monitoring is necessary
  - With organophosphate poisoning or anticholinesterase overdose, monitor closely for muscle weakness or twitching, reduction in respiratory function, or altered consciousness

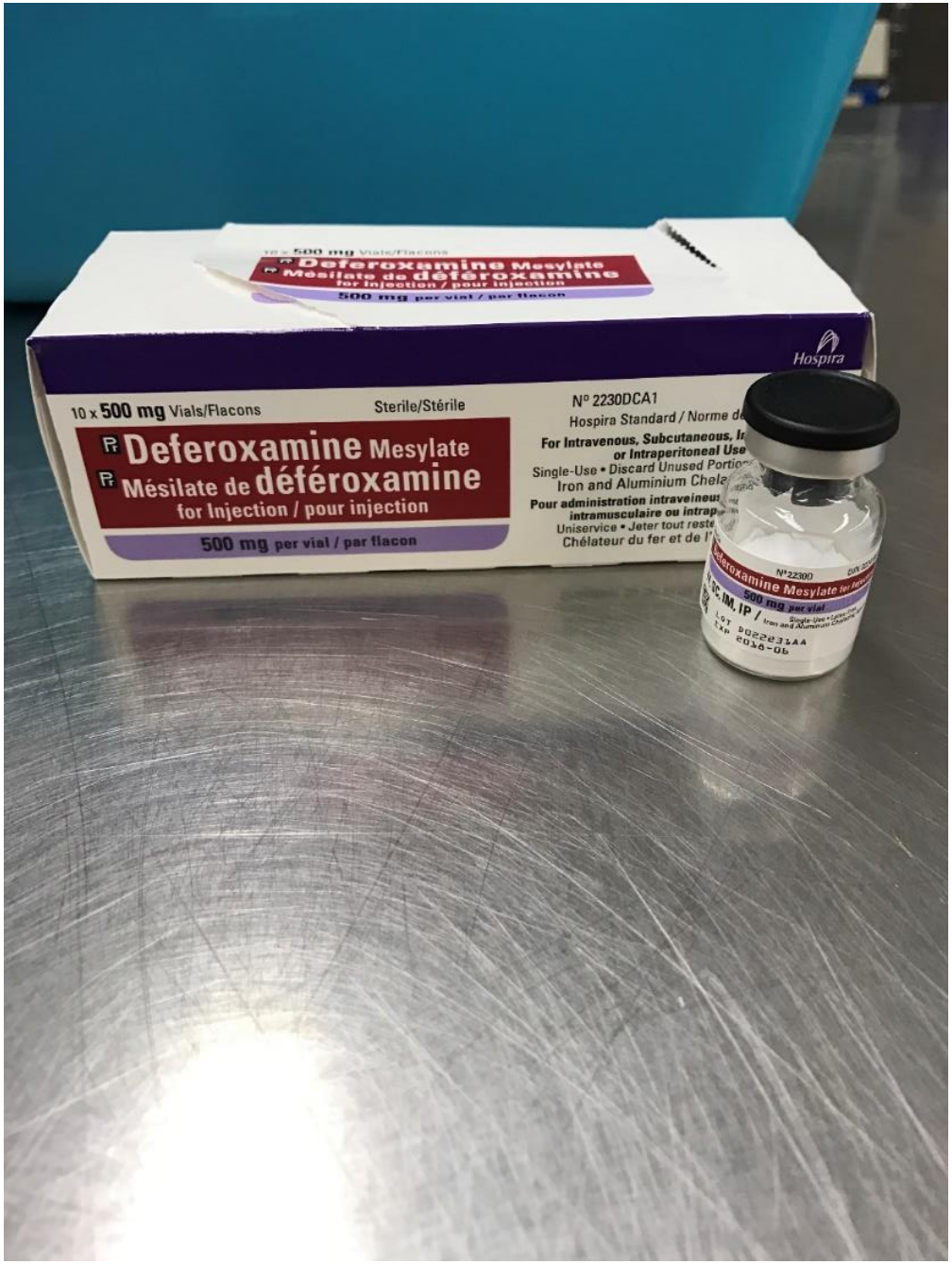
Pralidoxime[1,7]

Clinical Pearls



- No proven benefit in carbamate poisoning
- Reduce dose in renal dysfunction
- Use with atropine in most cases of organophosphate poisoning
  - Atropine administered before pralidoxime
- Patient exposed 2-6 days ago may benefit from treatment

Deferoxamine



Deferoxamine[1,8]

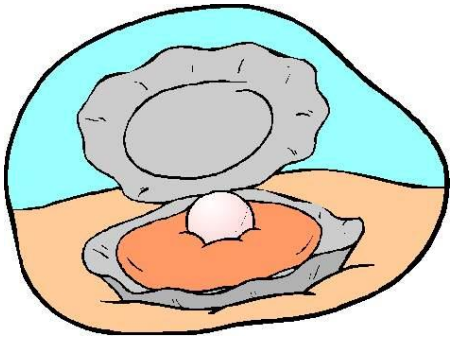
- **Toxin:** Iron salts (acute)
- **Dosing & Administration:**
  - 1 g **IM**/IV followed by 500 mg at 4-hour intervals for 2 doses. Depending on clinical response, subsequent doses of 500 mg may be administered Q4-12H. Maximum dose: 6 g/day.
  - 100 mg of desferoxamine binds 8.5 mg of iron (as the ferric ion)
- **MOA:**
  - Chelating agent that binds free iron creating ferrioxamine which is excreted in the urine

Deferoxamine[1,8]

- **Onset:**
  - Rapid
- **Monitoring:**
  - BP, serum iron, ferritin, TIBC, CBC with differential, serum creatinine, LFTs

Deferoxamine[1,8]

Clinical Pearls



- Not a substitute for standard treatment of iron intoxication
- Urine may become pink
- Deferoxamine challenge test no longer advocated as a method to confirm the ingestion of a toxic iron dose
- Use greater than 24 h has been associated with acute respiratory distress syndrome (ARDS)

Dimercaprol

Dimercaprol[9]

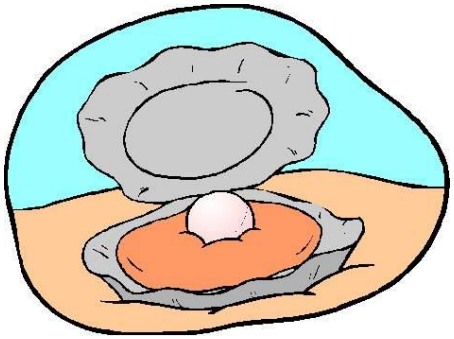
- **Toxins:** Arsenic, gold, mercury, lead
- **Dosing & Administration:**
  - *Arsenic or Gold Poisoning (Mild):* Deep IM: 2.5 mg/kg every 6 hours for 2 days, then every 12 hours for 1 day, followed by once daily for 10 days
  - *Arsenic or Gold Poisoning (Severe):* Deep IM: 3 mg/kg every 4 hours for 2 days, then every 6 hours for 1 day, followed every 12 hours for 10 days
  - *Mercury Poisoning:* Deep IM: 5 mg/kg initially, followed by 2.5 mg/kg 1-2 times/day for 10 days
  - *Lead Poisoning:* Deep IM: 4 mg/kg every 4 hours for 2-7 days

Dimercaprol[9]

- **MOA:**
  - Sulfhydryl group combines with ions of various heavy metals to form nontoxic, soluble chelates which are excreted in urine
- **Onset:**
  - 30 minutes
- **Monitoring:**
  - Renal function, urine pH, infusion-related reactions
  - *Arsenic Poisoning*: Urine arsenic concentration
  - *Lead Poisoning:* Blood lead levels (baseline and 7-21 days after completing therapy); hemoglobin, iron status

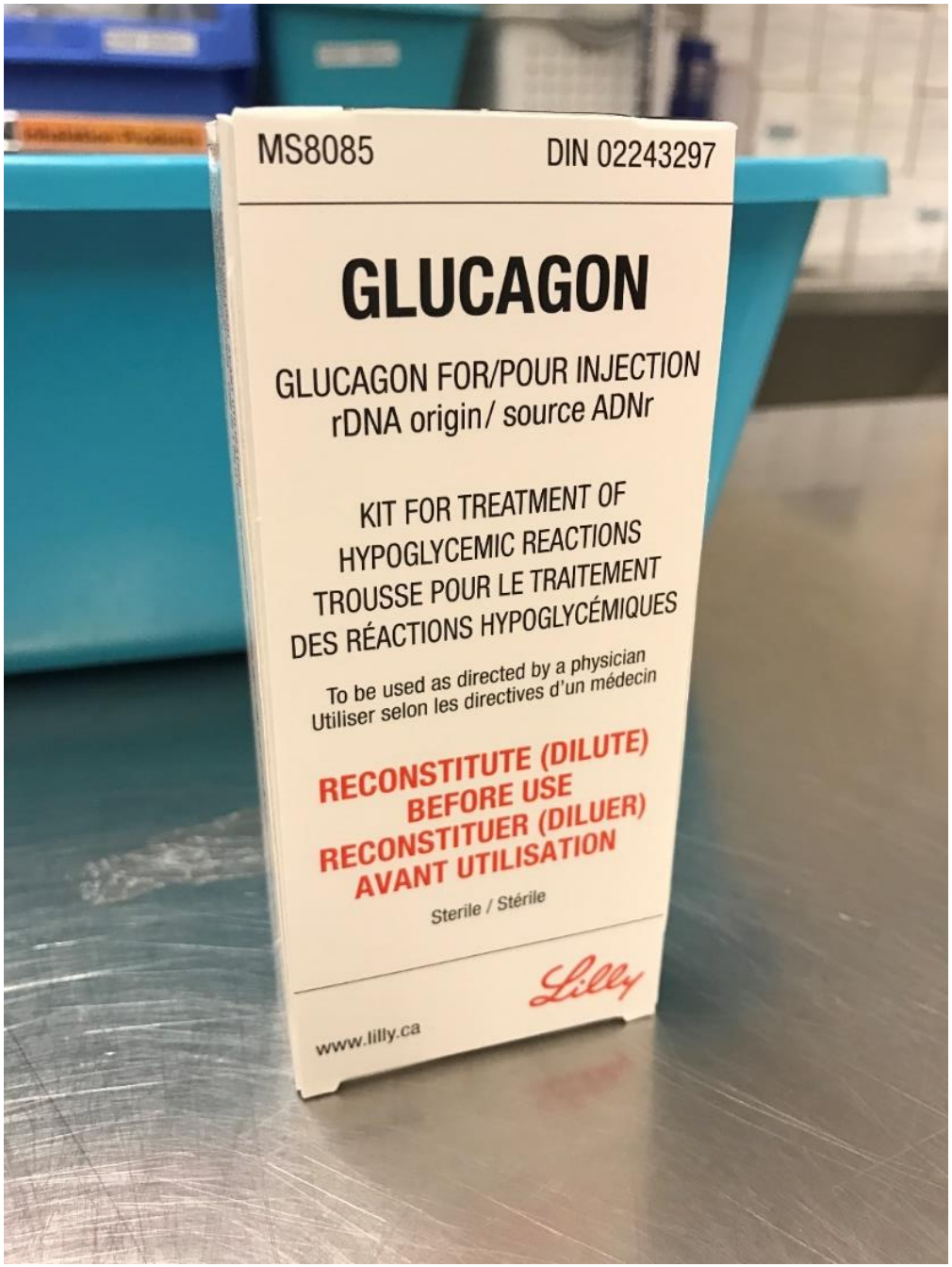
Dimercaprol[9]

Clinical Pearls



- Premedication with a histamine H_1 antagonist (eg, diphenhydramine) is recommended
- Administer all injections deep IM at different sites; **not** for IV administration
- Not indicated for treatment of iron, cadmium, or selenium poisoning
  - Use may result in the production of a toxic dimercaprol-metal complex

Glucagon


MS8085
DIN 02243297
GLUCAGON
GLUCAGON FOR/POUR INJECTION
rDNA origin/ source ADNr
KIT FOR TREATMENT OF
HYPOGLYCEMIC REACTIONS
TROUSSE POUR LE TRAITEMENT
DES RÉACTIONS HYPOGLYCÉMIQUES
To be used as directed by a physician
Utiliser selon les directives d'un médecin
RECONSTITUTE (DILUTE)
BEFORE USE
RECONSTITUER (DILUER)
AVANT UTILISATION
Sterile / Stérile
Lilly
www.lilly.ca

Glucagon[1,10,11]

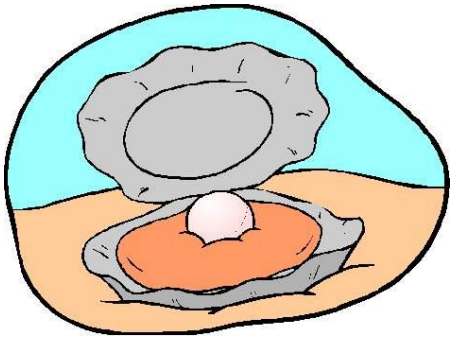
- **Toxins:** β blockers, calcium channel blockers
- **Dosing & Administration:**
  - 3-10 mg IV over 3-5 minutes
  - Follow with a continuous infusion of 1-5 mg/hr (maximum: 10 mg/hour)
  - May require up to 50 mg over a 24-hour period

Glucagon[1,10,11]

- **MOA:**
  - Possesses inotropic and chronotropic actions
- **Onset:**
  - 10-15 minutes
- **Monitoring:**
  - Blood glucose levels, BP, HR, ECG, signs or symptoms of a hypersensitivity reaction

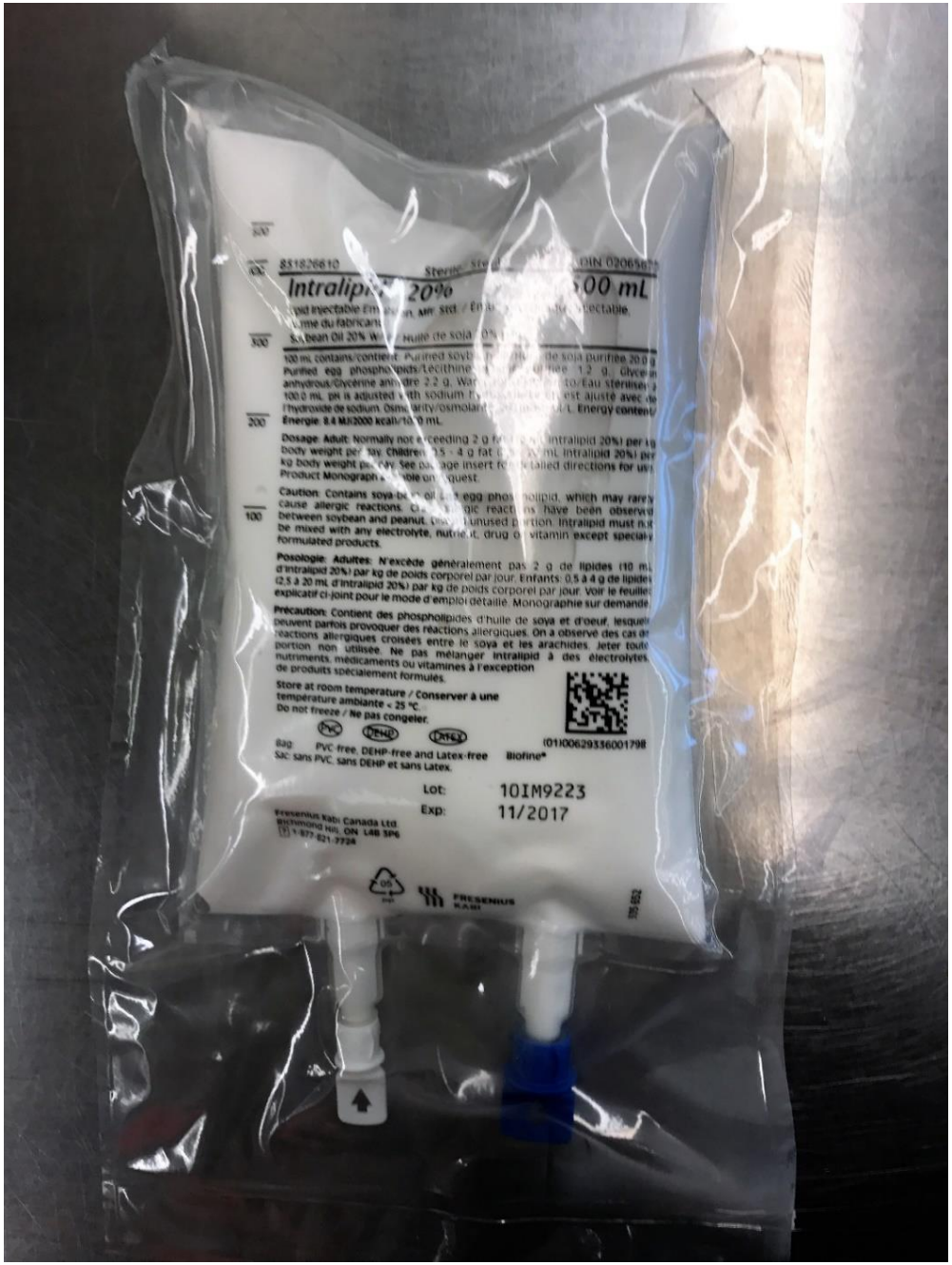
Glucagon[1,10,11]

Clinical Pearls



- Nausea and vomiting common; caution in patients with decreased LOC and unprotected airway
- Variable effects reported with CCB overdoses
  - Offers no pharmacologic advantage over alternative agents

Lipid Kit


Intralipid 20%
Soybean Oil 20%
Lot: 10IM9223
Exp: 11/2017
Fresenius Kabi Canada Ltd.
Richmond Hill, ON L4B 3P6
1-877-821-7724
Bag: PVC free, DEHP-free and Latex-free
Sac: sans PVC, sans DEHP et sans Latex.
Biofine®
Store at room temperature / Conserver à une température ambiante < 25 °C.
Do not freeze / Ne pas congeler.
Caution: Contains soya-bean oil and egg phosphatide, which may rarely cause allergic reactions.
Dosage: Adult: Normally not exceeding 2 g fat per kg body weight per day.
Précaution: Contient des phosphatides d'huile de soya et d'oeuf, lesquels peuvent parfois provoquer des réactions allergiques.
Posologie: Adultes: N'excède généralement pas 2 g de lipides (10 mL d'Intralipid 20%) par kg de poids corporel par jour.

Lipid Kit[1,12]

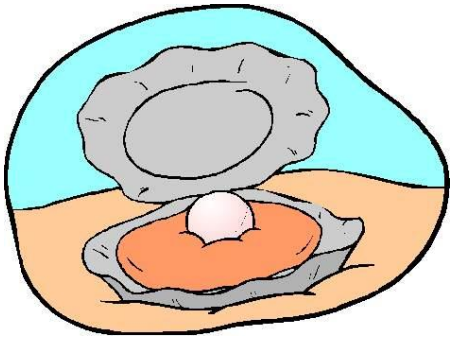
- **Toxins:** Lipid-soluble cardiotoxic medications (local anesthetics, β blockers, CCBs, TCAs)
- **Dosing & Administration:**
  - 1.5 mL/kg as an initial IV bolus over 1 minute, followed by a continuous infusion of 0.25 mL/kg/min IV for 30-60 minutes
  - May repeat bolus once or twice in patients with persistent cardiovascular collapse
  - May increase rate of the continuous infusion to 0.5 mL/kg/min if BP decreases; continue the infusion for at least 10 minutes after hemodynamic stability has been attained
  - Maximum of 10 mL/kg over the first 30 minutes

Lipid Kit[1,12]

- **MOA:**
  - Exogenous lipids provide an alternative source of binding of lipid-soluble drugs, commonly known as the "lipid sink" effect
  - Fatty acids provide the myocardium with a ready energy source, thereby improving cardiac function
- **Onset:**
  - 3-5 minutes
- **Monitoring:**
  - BP, HR, and other hemodynamic parameters should be recorded at least Q15min during the infusion

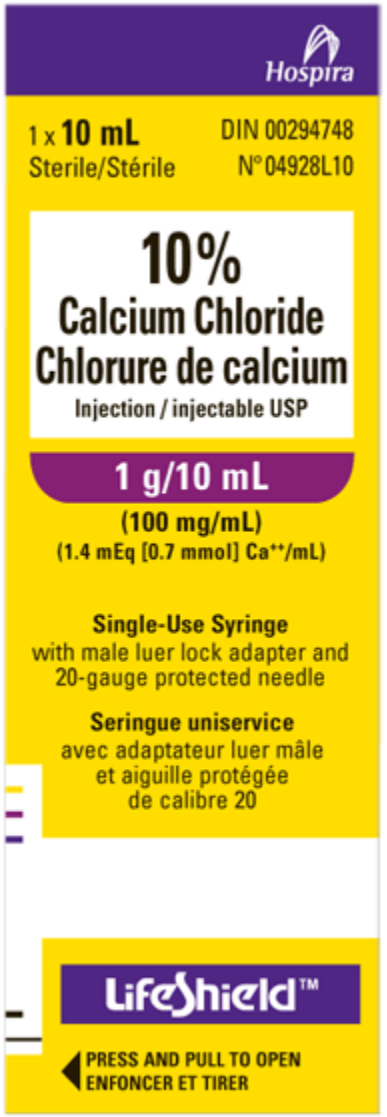
Lipid Kit[1,12]

Clinical Pearls



- Where possible, lipid resuscitation therapy should be terminated after 1 hour or less
- Contraindicated in severe egg or legume (soybean) allergies
- High dose epinephrine should be avoided
  - If necessary, use doses <1 mcg/kg
- Collect blood samples for lab values before administration as blood becomes lipemic

Calcium Chloride 10%

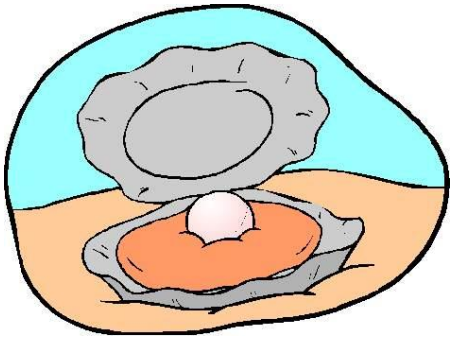


Calcium Chloride 10%[1,13,14,15]

- **Toxins:** Calcium channel blockers, β blockers
- **Dosing & Administration:**
  - Bolus: 10-20 mL (or 1-2 g) Q10-20min PRN; or
  - Infusion: 0.2-0.4 mL/kg/h
- **MOA:**
  - Moderates nerve and muscle performance via AP excitation threshold regulation
- **Onset:**
  - Immediate
- **Monitoring:**
  - Infusion site, ECG, serum calcium and ionized calcium, albumin, serum phosphate, magnesium

Calcium Chloride[13]

Clinical Pearls



- Should be given through central IV due to vascular irritating properties
- Tends to improve conduction disturbances more than hypotension in symptomatic CCB toxicity

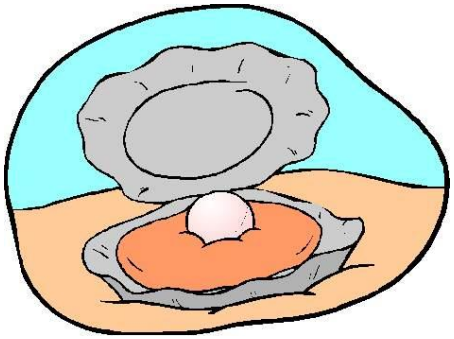
Calcium Gluconate 10%

Calcium Gluconate 10%[1,13,16,17]

- **Toxins:** Calcium channel blockers, β blockers
- **Dosing & Administration:**
  - Bolus: 30-60 mL (or 3-6 g) Q10-20min PRN; or
  - Infusion: 0.6-1.2 mL/kg/h
- **MOA:**
  - Moderates nerve and muscle performance via AP excitation threshold regulation
- **Onset:**
  - Immediate
- **Monitoring:**
  - Infusion site, ECG, serum calcium and ionized calcium, albumin, serum phosphate, magnesium

Calcium Gluconate[13]

Clinical Pearls



- Should not be used in critically ill patients or patients in cardiac arrest as it requires metabolism to release calcium salts
- Tends to improve conduction disturbances more than hypotension in symptomatic CCB toxicity

Methylene Blue

Methylene Blue[1,18]

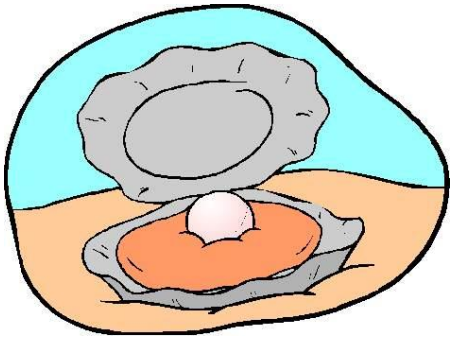
- **Toxin:** Idiopathic/drug-induced methemoglobinemia (i.e. dapsone, topical anesthetics)
- **Dosing & Administration:**
  - 1 to 2 mg/kg IV over five minutes; the dose may be repeated in one hour PRN
- **MOA:**
  - Provides an artificial electron transporter for the ultimate reduction of methemoglobin

Methylene Blue[1,18]

- **Onset:**
  - 10-60 minutes
- **Monitoring:**
  - Serial measurements of methemoglobin levels following treatment with MB
  - Cyanosis

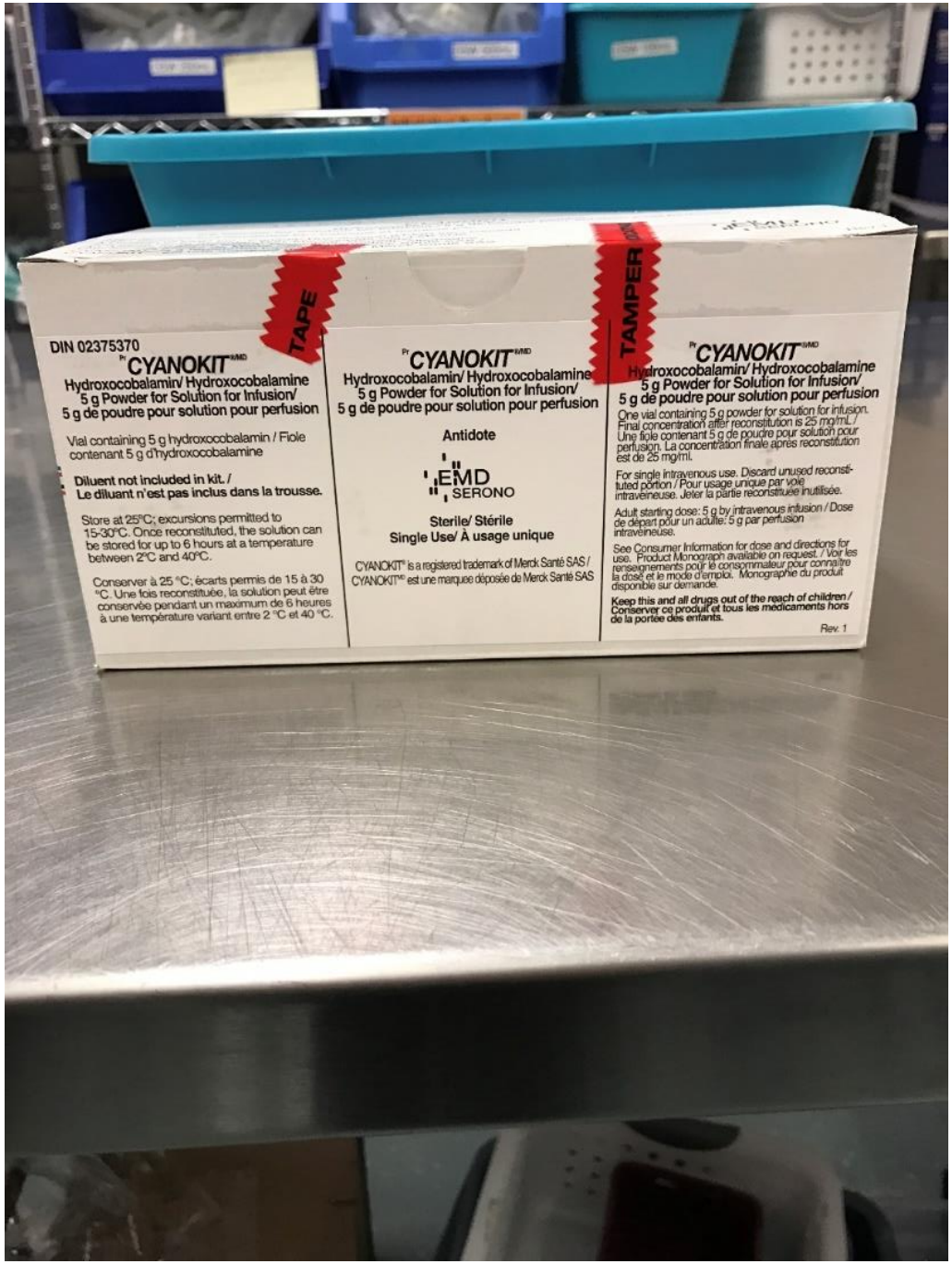
Methylene Blue[1,18]

Clinical Pearls



- Contraindicated in patients with G6PD deficiency as hemolysis may result
- If patient is taking drugs with serotonin reuptake inhibition properties, consider stopping them to avoid a serotonin syndrome reaction
- Patients who rapidly improve clinically do not need to have their methemoglobin rechecked
  - Standard pulse oximeter measurements of methemoglobin are unreliable in the presence of MB

Cyanokit (Hydroxocobalamin)



Cyanokit (Hydroxocobalamin)[1,19]

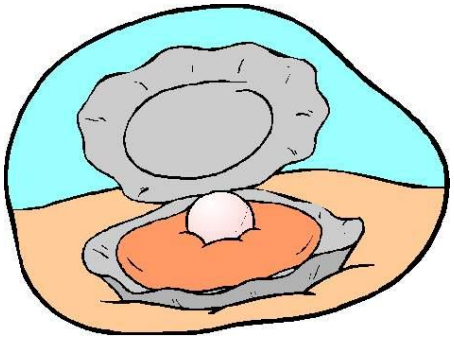
- **Toxins:** Cyanide
- **Dosing & Administration:**
  - 5 g IV, repeat the dose if required. Maximum total dose is 10 g.
  - 5 g of hydroxocobalamin neutralizes ~40 micromole/L (1.04 mg/L) of cyanide in the blood
- **MOA:**
  - Contains a cobalt moiety that binds to intracellular cyanide forming cyanocobalamin, which is excreted in the urine

Cyanokit (Hydroxocobalamin)[1,19]

- **Onset:**
  - 2-15 minutes
- **Monitoring:**
  - BP and HR during and after infusion, serum lactate levels, venous-arterial PO_2 gradient
  - Pretreatment cyanide levels may be useful as post infusion levels may be inaccurate

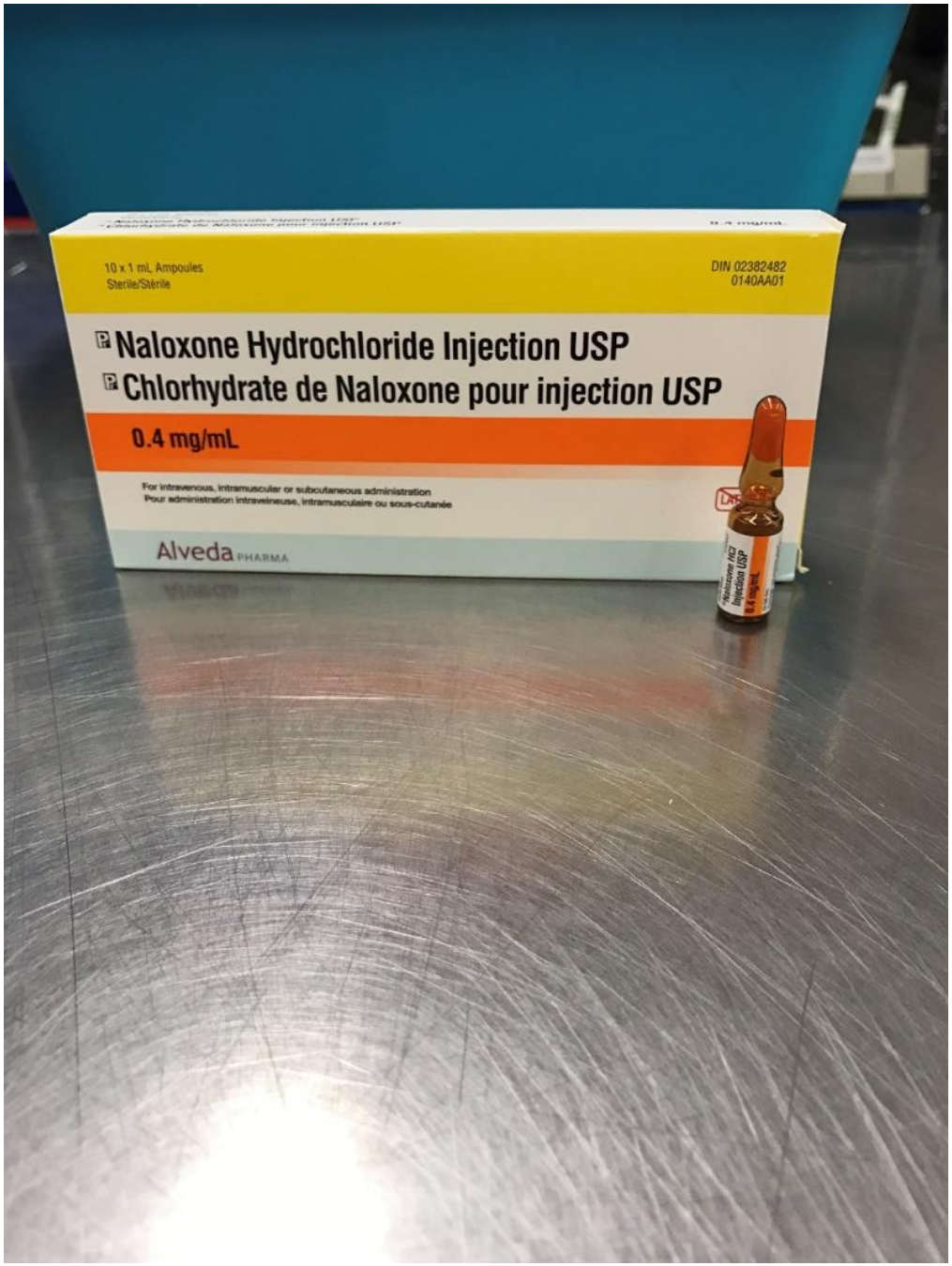
Cyanokit (Hydroxocobalamin)[1,19]

Clinical Pearls



- Deep red colour of hydroxocobalamin interferes with many clinical laboratory tests and possibly HD machines
- May cause reversible red colouration of the skin and mucous membranes that may last up to 15 days & dark red colouration of urine that may last up to 35 days
  - Advise patient to avoid direct sun while skin discoloured

Naloxone


10 x 1 mL Ampoules
Sterile/Stérile
DIN 02382482
0140AA01
Naloxone Hydrochloride Injection USP
Chlorhydrate de Naloxone pour injection USP
0.4 mg/mL
For intravenous, intramuscular or subcutaneous administration
Pour administration intraveineuse, intramusculaire ou sous-cutanée
Alveda PHARMA

Naloxone[1,20,21]

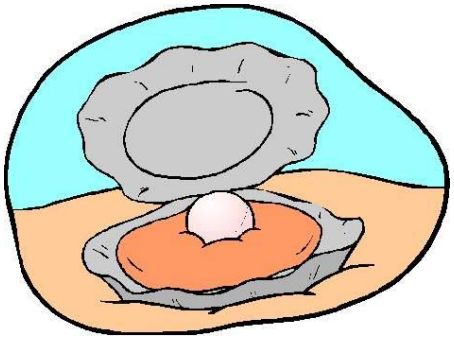
- **Toxins:** Narcotic drugs, other opioid derivatives
- **Dosing & Administration:**
  - 0.4-2 mg IV initially; repeat as 2-3 minute intervals PRN to a maximum of 10 mg
  - If intermittent IV PRN fails, consider continuous IV infusion initially at 0.4 mg/hr, titrate according to patient response
- **MOA:**
  - A specific antagonist of opioids

Naloxone[1,20,21]

- **Onset:**
  - 2-10 minutes
- **Monitoring:**
  - Assess patient for opioid dependency
  - RR, HR, BP, temperature, LOC, ABGs or pulse oximetry

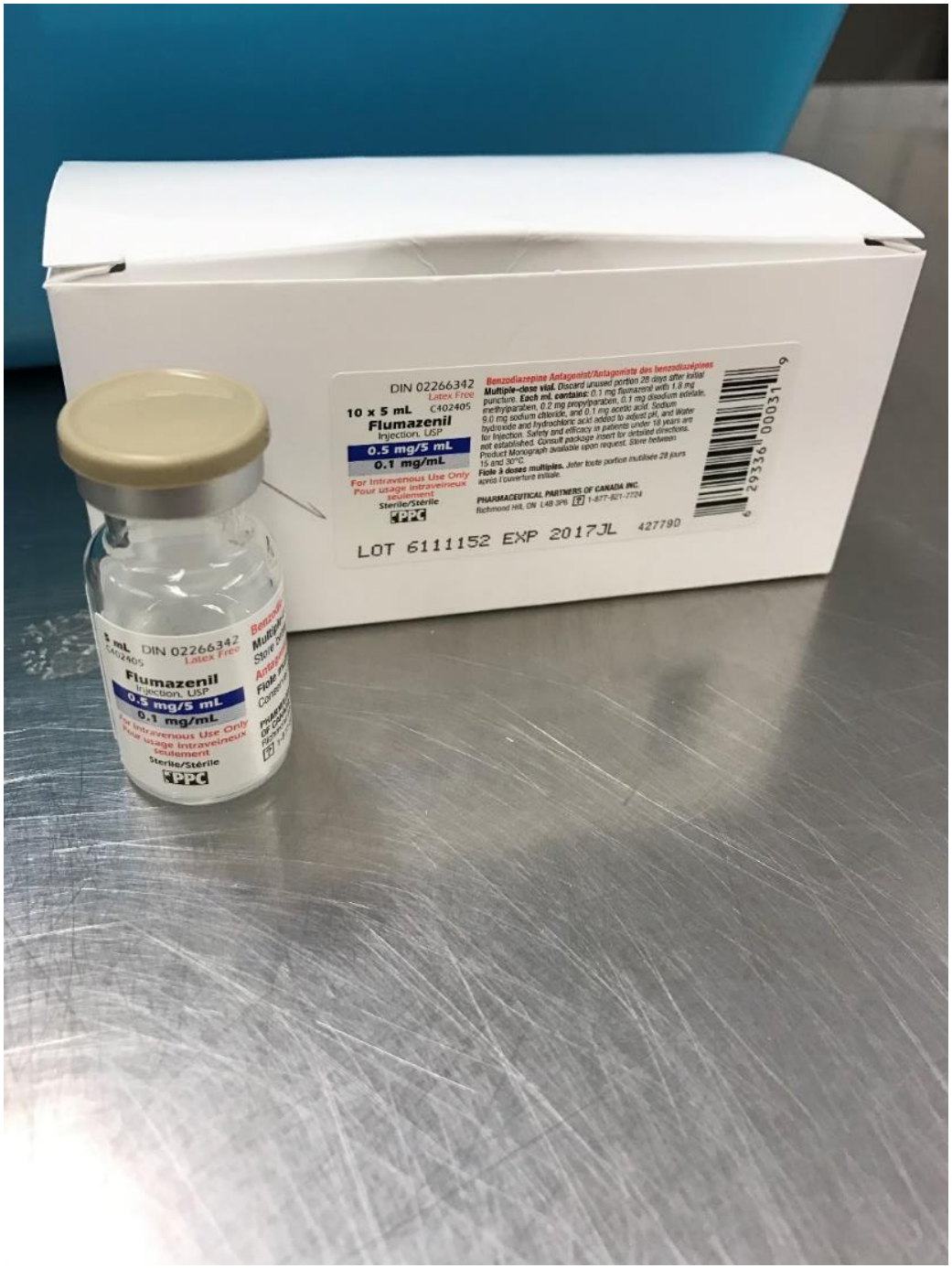
Naloxone[1,20,21]

Clinical Pearls



- Duration of action may be significantly shorter than that of the opioid being antagonized
- Larger doses may be needed to reverse the effects of overdose with fentanyl derivatives

Flumazenil


DIN 02266342
Latex Free
10 x 5 mL C402405
Flumazenil
Injection, USP
0.5 mg/5 mL
0.1 mg/mL
For Intravenous Use Only
Pour usage intraveineux seulement
Sterile/Stérile
PPC
Benzodiazepine Antagonist/Antagoniste des benzodiazépines
Multiple-dose vial. Discard unused portion 28 days after initial puncture. Each mL contains: 0.1 mg flumazenil with 1.8 mg methylparaben, 0.2 mg propylparaben, 0.1 mg disodium edetate, 9.0 mg sodium chloride, and 0.1 mg acetic acid. Sodium hydroxide and hydrochloric acid added to adjust pH, and Water for Injection. Safety and efficacy in patients under 18 years are not established. Consult package insert for detailed directions. Product Monograph available upon request. Store between 15 and 30°C.
Fiole à doses multiples. Jeter toute portion inutilisée 28 jours après l'ouverture initiale.
PHARMACEUTICAL PARTNERS OF CANADA INC.
Richmond Hill, ON L4B 3P6 1-877-821-7724
LOT 6111152 EXP 2017JL 427790
0 29336 00031 9
5 mL DIN 02266342
C402405 Latex Free
Flumazenil
Injection, USP
0.5 mg/5 mL
0.1 mg/mL
For Intravenous Use Only
Pour usage intraveineux seulement
Sterile/Stérile
PPC

Flumazenil[1,22,23]

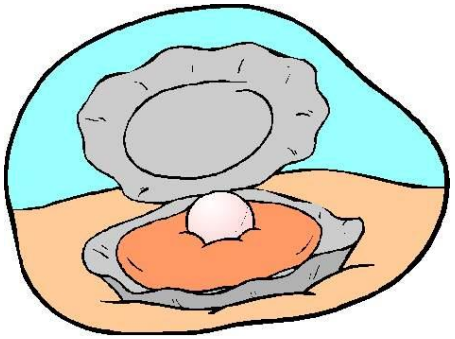
- **Toxin:** Benzodiazepines
- **Dosing & Administration:**
  - Initial dose of 0.3 mg IV over 30 seconds followed by additional 0.3 mg injections, each administered over 30 seconds, at 60 second intervals to a maximum total dose of 2 mg
  - If sedation recurs, may use an infusion of 0.1-0.4 mg/hr

Flumazenil[1,22,23]

- **MOA:**
  - Competitively inhibits the activity at the benzodiazepine receptor site on the GABA/benzodiazepine receptor complex
- **Onset:**
  - 1-2 minutes; 80% response within 3 minutes
- **Monitoring:**
  - Resedation, respiratory depression, seizure activity, HR, BP

Flumazenil[1,22,23]

Clinical Pearls



- Do not give to patients with seizures, benzodiazepine dependence, or tricyclic overdose
- As flumazenil has a short duration of action, patients should be monitored for 2 or more hours for recurrence of sedation after injection
- Although flumazenil can reverse benzodiazepine-induced sedation, it has variable effects on benzodiazepine-induced respiratory depression

Pyridoxine

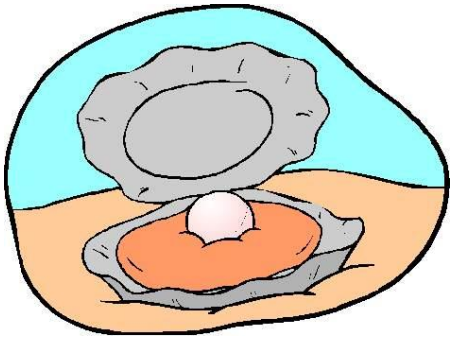

DIN 02245215
Pyridoxine Hydrochloride
Injection, USP
3 g/30 mL
100 mg/mL
Latex free
Contains a preservative
For intramuscular or intravenous use
Sterile
Mylan
1 x 30 mL Multi-Dose Vial

Pyridoxine[1,24]

- **Toxin:** Isoniazid, hydrazines
- **Dosing & Administration:**
  - *Isoniazid overdose*: Dose equal to amount of isoniazid ingested; 1-4 g IV followed by 1 g IM Q30min until entire dose given
  - *Hydrazine overdose:* 25 mg/kg; give 1/3 dose IM and rest by IV infusion over 3 hours
- **MOA:**
  - Isoniazid and hydrazines are associated with vitamin B6 deficiency because they interfere with pyridoxine metabolism
- **Monitoring:**
  - BP, HR, RR
  - Anion gap, ABGs, electrolytes, neurological exam, seizure activity for isoniazid toxicity

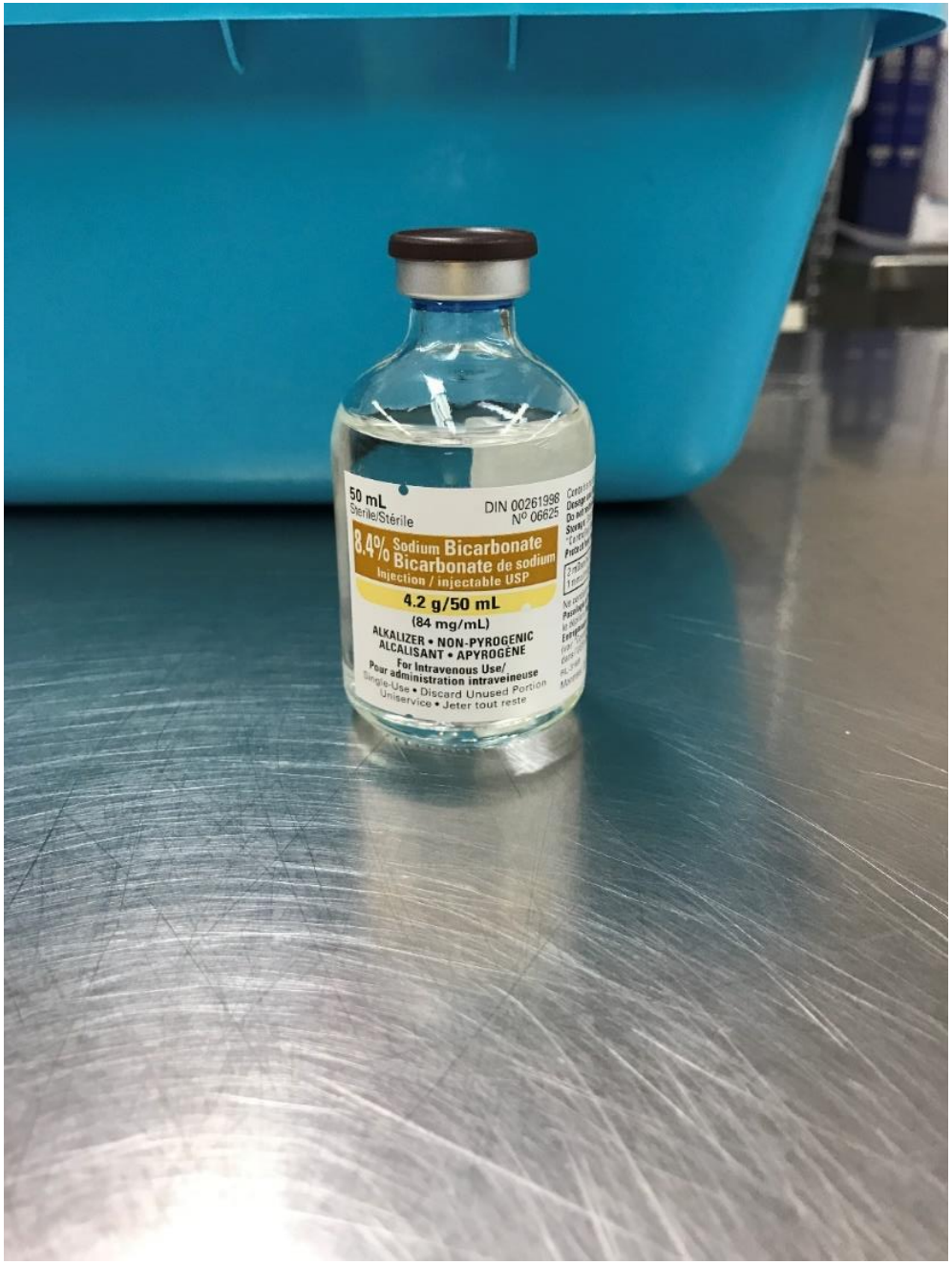
Pyridoxine[1,24]

Clinical Pearls



- Severe, permanent peripheral neuropathies have been reported; neurotoxicity is more common with long-term administration of large doses (>2 g/day)

Sodium Bicarbonate



Sodium Bicarbonate[25]

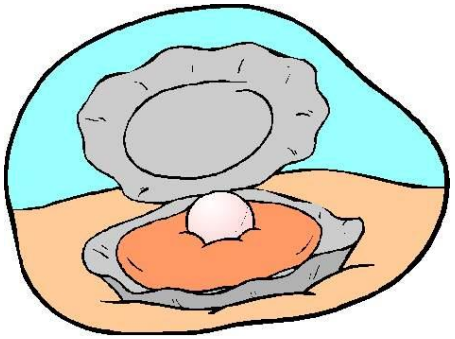
- **Toxin:** Agents producing wide QRS, urine, or serum alkalization (Tricyclic antidepressants)
- **Dosing & Administration:**
  - 1 to 2 mEq/kg, given as a rapid IV push through a large bore IV catheter; may repeat bolus dose if no response after 5 min
  - Following bolus therapy, begin a continuous IV infusion by mixing 150 mEq of sodium bicarbonate in 1 L of 5 percent dextrose (D5W), and infusing at 250 mL/hour
- **MOA:**
  - Increases serum pH thereby favoring the non-ionized form of the drug, making it less available to bind to sodium channels

Sodium Bicarbonate[25]

- **Onset:**
  - 15 minutes
- **Monitoring:**
  - Arterial blood pH & serum potassium hourly until it is the therapeutic range and stable
  - ABGs, electrolytes
  - Useful to run a continuous 12-lead ECG during the infusion to demonstrate the presence (or absence) of narrowing of the QRS complex, a decrease in the R wave amplitude in lead AVR, or resolution of any arrhythmia

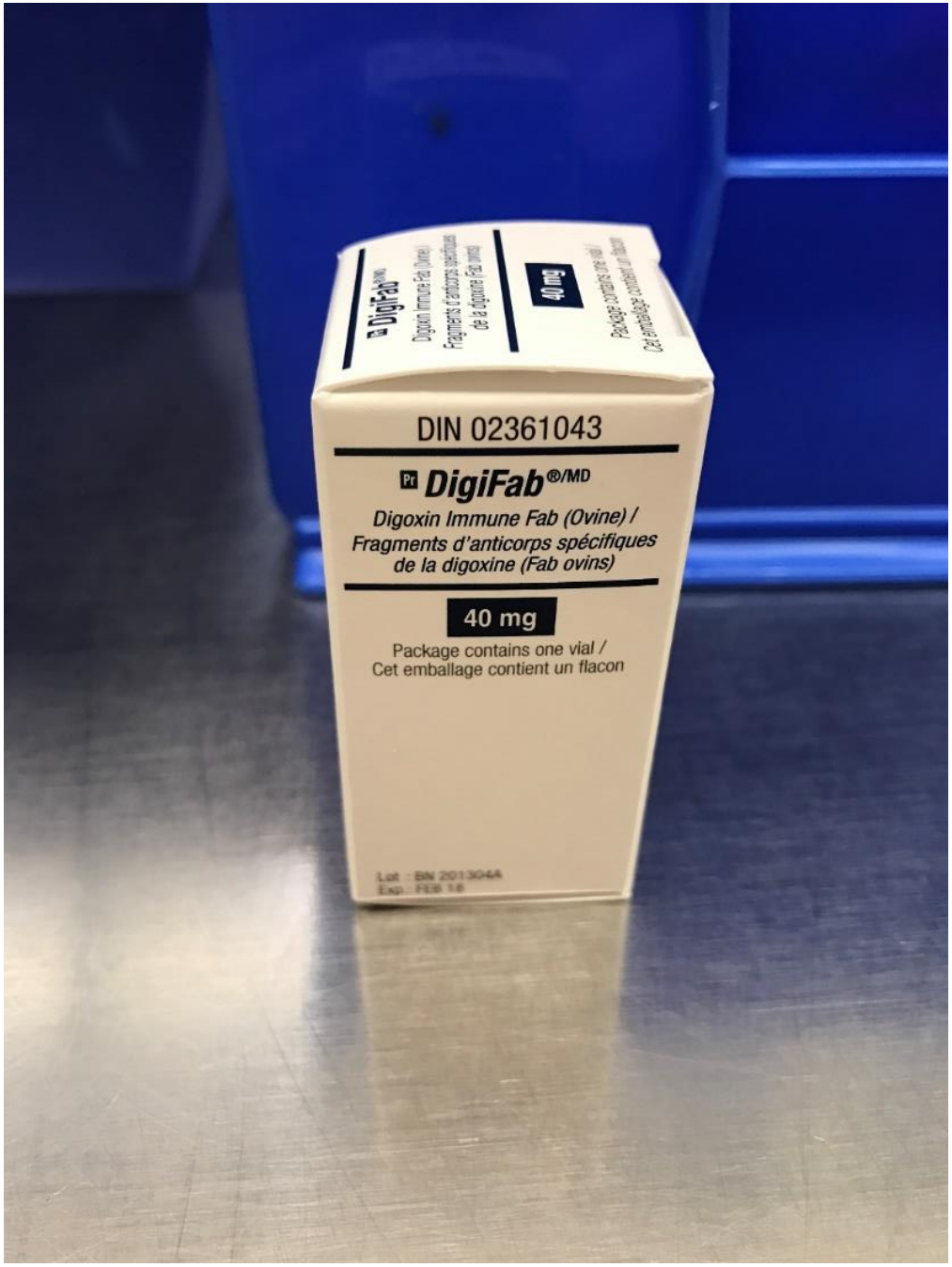
Sodium Bicarbonate[25]

Clinical Pearls



- Most patients with TCA-induced QRS interval prolongation appear to respond to bicarbonate therapy:
  - 80% of patients demonstrate a decrease in QRS interval
  - 90% of hypotensive patients increase their BP

Digoxin Immune Fab



Digoxin Immune Fab[1]

- **Toxins:** Digoxin and related cardiac glycosides
- **Dosing & Administration:**
  - One vial binds 0.5 mg digoxin
  - Indications include serious arrhythmias, hyperkalemia or end-organ dysfunction

Calculating the Dose[26]

Method 1: Neither digoxin level nor amount ingested known

- Empiric treatment consists of 10 vials which should be repeated if clinical response is inadequate

Calculating the Dose[26]

Method 2: Amount of digoxin ingested is known but concentration is unknown

STEP 1: Calculate the Total Body Load (TBL)

TBL for digoxin = Dose (in mg) ingested x 0.8

STEP 2: Calculate the Number of Vials Needed

Number of vials = TBL/0.5

The number of vials should be rounded up!

Calculating the Dose[26]

Method 3: Steady state concentration is known

STEP 1: Convert Serum Digoxin Concentration

Serum Digoxin Concentration in ng/mL = Serum Digoxin Concentration in nmol/L **x 0.78**

STEP 2: Calculate Number of Vials

$$\text{Number of vials} = \frac{\left[\left(\text{serum digoxin concentration in } \frac{\text{ng}}{\text{mL}}\right)(\text{patient's weight in kg})\right]}{100}$$

The number of vials should be rounded up!

Calculating the Dose

Method 3: Steady state concentration is known

EXAMPLE

STEP 1: Convert Serum Digoxin Concentration

Serum Digoxin Concentration in ng/mL

= 4.2 nmol/L **x 0.78** = 3.276

STEP 2: Calculate Number of Vials

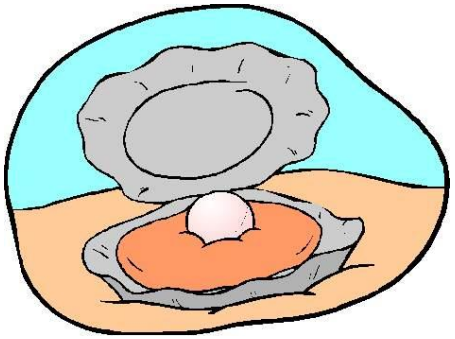
$$\text{Number of vials} = \frac{[(3.276)(63.5)]}{100} = 2.08 = 3 \text{ vials}$$

Digoxin Immune Fab[1,26,27]

- **MOA:**
  - Antibody fragments bind free digoxin
  - As the level of free digoxin in plasma falls, the resulting concentration gradient facilitates dissociation of digoxin from the sodium-potassium ATPase
- **Onset:**
  - Improvement may be seen within 20-90 minutes
- **Monitoring:**
  - Prior to first dose, measure serum K, serum digoxin concentration and serum creatinine
  - Closely monitor serum K (i.e. hourly for 4-6 hours; at least daily thereafter)
  - Temp, BP, ECG

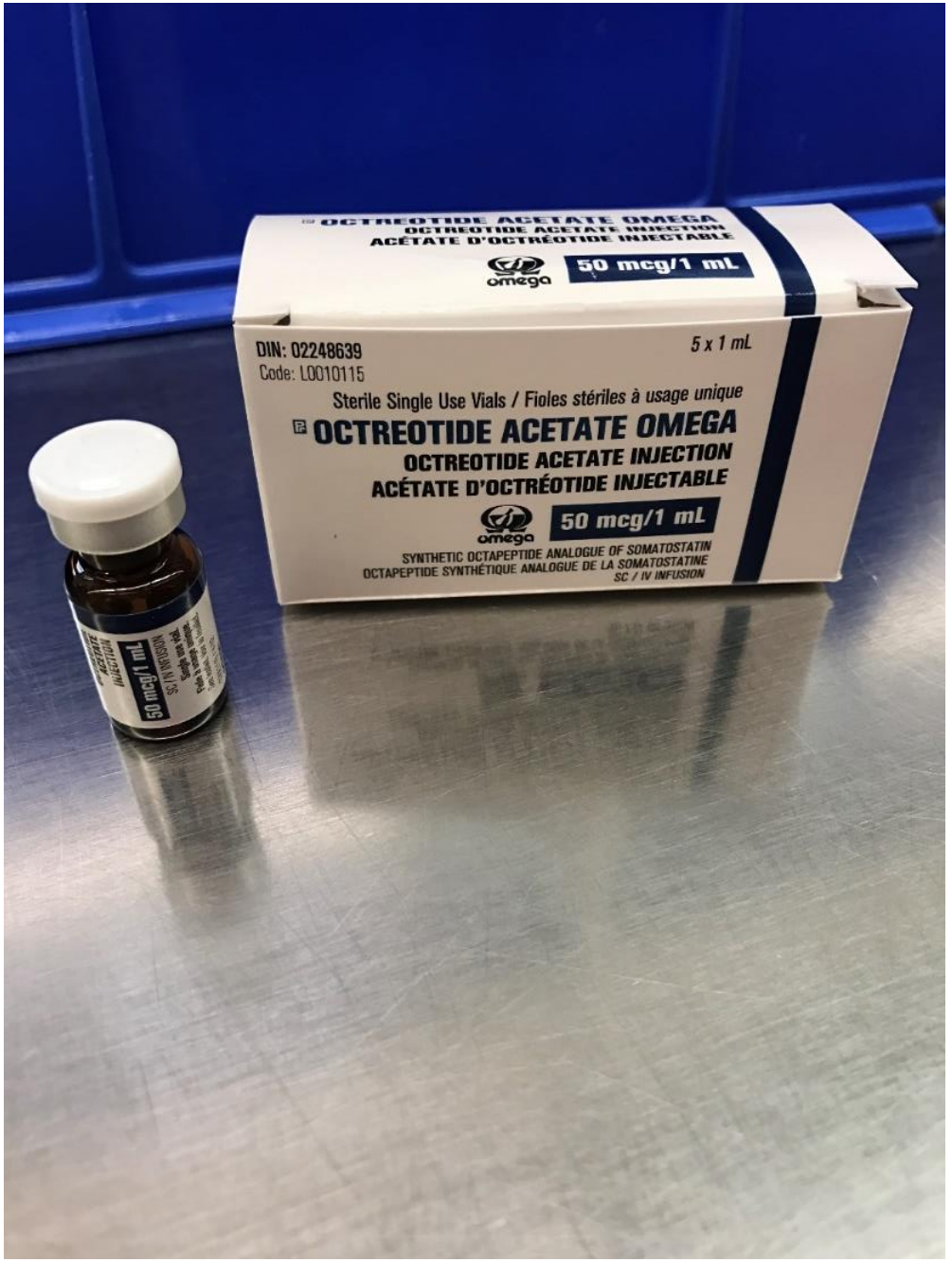
Digoxin Immune Fab[26,27]

Clinical Pearls



- For digoxin levels, draw blood samples just prior to a dose or at least 6-8 h after the last dose
- Fab treatment frequently causes an elevation in the measured digoxin concentration despite a free digoxin level approaching zero
- To convert serum digoxin concentration from nanomol/L to nanogram/mL **multiply by 0.78**
- Stored in fridge

Octreotide

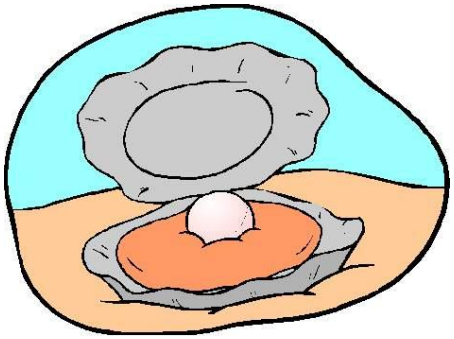

OCTREOTIDE ACETATE OMEGA
OCTREOTIDE ACETATE INJECTION
ACÉTATE D'OCTRÉOTIDE INJECTABLE
omega
50 mcg/1 mL
DIN: 02248639
Code: L0010115
5 x 1 mL
Sterile Single Use Vials / Fioles stériles à usage unique
OCTREOTIDE ACETATE OMEGA
OCTREOTIDE ACETATE INJECTION
ACÉTATE D'OCTRÉOTIDE INJECTABLE
omega
50 mcg/1 mL
SYNTHETIC OCTAPEPTIDE ANALOGUE OF SOMATOSTATIN
OCTAPEPTIDE SYNTHÉTIQUE ANALOGUE DE LA SOMATOSTATINE
SC / IV INFUSION
50 mcg/1 mL

Octreotide[1,28,29]

- **Toxin:** Oral sulfonylurea-induced hypoglycemia
- **Dosing & Administration:**
  - 50-75 micrograms subQ Q6H for 24 hours
- **MOA:**
  - Somatostatin analog that inhibits insulin release from pancreatic beta-islet cells
- **Onset:**
  - 1 hour
- **Monitoring:**
  - Serum glucose to identify any recurrence of hypoglycemia

Octreotide[1,28,29]

Clinical Pearls



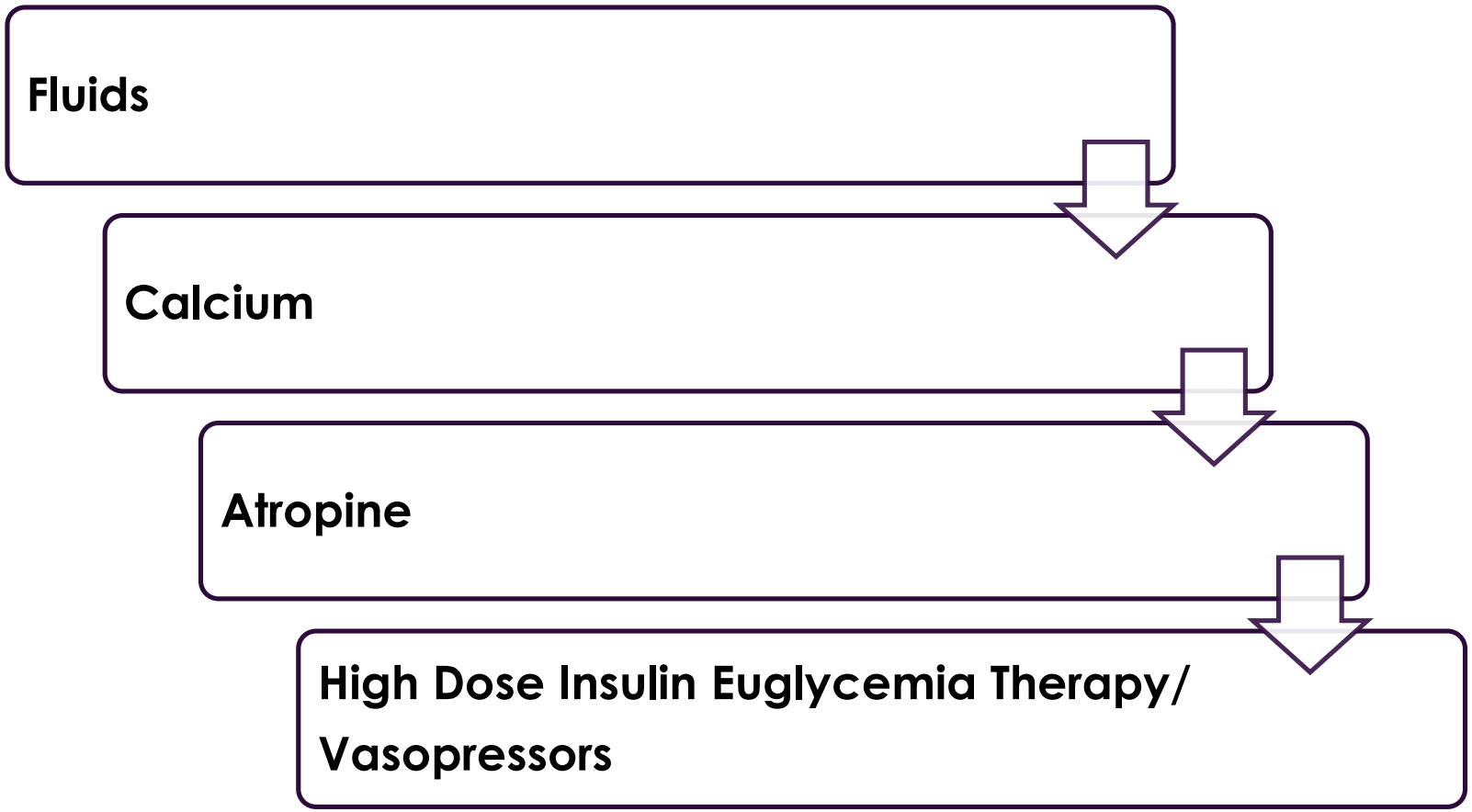
- May also be given as an IV bolus or continuous IV infusion
  - However, in almost all cases, subQ dosing is sufficient to maintain normoglycemia
- Administer octreotide between meals and at bedtime to decrease GI side effects
- Stored in fridge

Case Study Revisited

Acetaminophen Overdose

- Assumed more than 8 hours since acetaminophen ingestion at the time of her blood draw
- Started 21-hour acetylcysteine protocol
- Experienced minimal elevation in AST and ALT which normalized

Calcium Channel Blocker Overdose[13]



Beta Blocker Overdose

- Given a bolus dose of glucagon in the ER
- Also received calcium gluconate, epinephrine, high-dose insulin, and lipid emulsion therapy

SSRI Overdose

- No evidence of serotonin syndrome

Zopiclone & BZD Overdose

- Airway protected
- Patient monitored for respiratory depression

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