Cardiovascular Drugs overdose

Team Leaders

Khalid Aleedan & Aseel Badukhon

Done by

Abdullah Altwerki
Abdulmajeed Alammar
Mohammed Alyousef
Samar Alqahtani
Muneerah Alzayed

Revised by: Yara & Basel

Objectives

? Not given (:

Some grey text in this lecture is NOT extra; it is from 435 teamwork so please check it out!

NOTES EXTRA BOOK IMPORTANT GOLDEN NOTES

Beta-Blockers

Beta-Blockers (Beta-Sympatholytics)

Mechanism of Action

-Inhibits endogenous catecholamines
-Rapidly absorbed after oral ingestion, and the peak occurs in 1 to 4 hours MCQ If Patient came in this period and no symptoms, then the patient is fine.
-Volume of distribution for various beta-blockers generally exceeds 1 L/kg, meaning tissue concentrations exceed those of serum (Hemodialysis is not effective for most "most but not all (:" beta-blockers)
-Absence of symptoms 4 hours after ingestion implies a low risk for subsequent morbidity unless a delayed-release preparation is involved.
BB has a very high volume of distribution, so the medication will be available intracellular not in the blood.
So the dialysis won't help in case of BB overdose.

Manifestations & complications of Overdose in order to decrease frequency

1. Bradycardia (65/90 cases)
2. Hypotension (64/90)
3. Unconsciousness (50/90)
4. Respiratory arrest or insufficiency (34/90)
5. Hypoglycemia (uncommon in adults)
6. Seizures (common only with propranolol, 16/90) like other Na channel blockers Propranolol may cause severe bradycardia or tachycardia
7. Symptomatic bronchospasm (uncommon)
8. VT or VF (VF, ventricular fibrillation; VT, ventricular tachycardia). (6/90)
9. Mild hyperkalemia (uncommon)
10. Hepatotoxicity, mesenteric ischemia, renal failure (rare or single case reports)

Bradycardia and hypotension are the most important.

Management

-IV fluids the first thing must do, in ER we give crystalloid.
-Oxygen
-Monitoring of card for rhythm and respirations
-Activated Charcoal is unproven treatment
-Multiple-dose charcoal without supporting evidence for an improvement in outcome
The first step in the treatment of BB overdose is:
-Atropine, Glucagon(antidote), Crystalloid fluids.
-Others include (Catecholamines if there is no response with the fluid or Atropine., NaHCO3 if Na blockers if there is a QRS prolongation like with Propranolol overdose., Ca will help the heart to pump the blood., Extracorporeal elimination and circulatory assistance)
Other treatments:
-High-Dose Insulin Euglycemia (HDIE) Therapy Theoretical
-Insulin

Summary of the treatment:

GI Decontamination in BB overdose never work. GI Decontamination you do it if: 1- the patient take a lethal dose. 2- present to you in first one hour.3- you make sure that the airway is protected imp, because if not the patient may aspirate the charcoal and develop chemical pneumonitis, and this may kill the patient. Insulin has inotropic effect, but is given with dextrose to prevent further hypoglycemia.

To summarize: The first step in the treatment of beta-blocker overdose is: 1- atropine 'first line' 2- if fails glucagon ' some inotropic effect, a well known antidote, but not the first because of nausea, vomiting and hyperglycemia. 3- crystalloid fluids 4-Calcium is a good inotrope but only used as a last resort • Note: Some start with 500ml to 1 L fluid, if it didn't work we add another bolus of fluid and atropine.. Others start with atropine immediately .

Don't skip it because it says summary, doctor said he made a question out of it (:

Phase I (Resuscitation)

Boluses of atropine, Glucagon, fluids

Glucagon is the antidote in my slides and in the exam

Phase II (Stabilization)

-Infusions of Glucagon, Insulin-glucose, Catecholamines (epinephrine, norepinephrine, isoproterenol, dobutamine, dopamine, metaraminol)
-Phosphodiesterase Inhibitors (Amrinone)
-Early cardiac pacing if no prompt response to chronotropic or dromotropic drugs
-Peripheral arterial and pulmonary artery catheter monitoring if refractory hypotension
-Consider hemodialysis** of hydrophilic BBs with low protein binding and low V_d * see, not all can't work with dialysis (:"

(* volume of distribution; memories of pharmacology!)

**(Protein binding varies from 0% for sotalol to 93% for propranolol. But if it is high so it can't be dialyzed easily
Elimination half-lives vary from 8 to 9 minutes for esmolol to as long as 24 hours for nadolol and other.)

{ Beta-Blockers }

Diagnostic strategies: (435 teamwork)

- Depend on the clinical picture. (Toxidrome; you can't diagnose it by toxicology screen; it's diagnosed clinically)
- Hypoglycemia is common in children

Disposition:

Patients who remain completely asymptomatic for 6 hours after an oral overdose of normal-release preparations can be safely referred for psychiatric evaluation if it was a suicidal attempt, with medical consultation for the first 24 hours

(:

Some good stuff from 435:

Please, don't skip!

- What is the most common presentation of b-blockers intoxication ? bradycardia
- What could happen with bradycardia ? hypernatremia (uncommon)
- Propranolol can present with wide complex tachycardia (in the majority of the cases, it is due to propranolol). Treated with sodium bicarbonate
- Why propranolol ? 1-Most fatalities 2- it has different MOA, by blocking sodium channels so it increases the sympathetic drive .. and the NA blockage will lead to prolonged QRS ..
- Both propranolol and TCA present with wide complex tachys and seizure.. how to differentiate? Really we don't need to differentiate since the treatment is the same. 'Supportive' by IV sodium bicarbonate .. drug levels might help in TCA but we don't usually do it.

435 teamwork (:

Beta-Blockers

Non selective Beta-Blockers

Drug	VD (UKG)	ISA	Elimination half life (HR)	Lipophilic	Protein binding (%)	MSE	Comments
Propranolol Has Na+ blocking effect.	4	0	4	+	93	+	most fatalities
Nadolol	4	0	10-20	0	20	0	dialyzable
Timolol	1.9	0	3-5	+	10	0	dialyzable
Pindolol	3-6	+	3-4	+	51	+	
Labetalol	10	0	4-6	0	50	+	Alpha blocker also
Oxprenolol	1.3	+	2	+	78		
Sotalol	1.6-2.4	0	7-18	+	0	0	Class III and class II antidysrhythmic; torsades de pointes; dialyzable
Carvedilol	1.5-2	0	6-10	+	95	0	

Selective Beta-Blockers

Metoprolol	5.5	0	3-4	+	12	0	
Atenolol	0.7	0	5-8	0	5	0	dialyzable
Esmolol	2	0	0.13	0	55	0	
Acebutolol	1.2	+	2-4	+	26	+	QT prolongation, VT
Practolol	1.6	+	10-11	+		0	
Bisoprolol	2.9	0	10-12	0	30	0	
Betaxolol	5-13	0	12-22	0	55	0	

Calcium Channel Blockers

Ca^{+2} Channel Blockers

Perspective

-Most fatalities occur with Verapamil, but severe toxicity and death have been reported for most drugs of this class.

The most toxic CCB drug in overdose is verapamil since it acts centrally unlike nifedipine which acts peripherally.

You have a patient ingestion a large amount of a medication, she came to the ER with hypotension -bradycardia -hyperglycemia. What type of drug she took? CCB

Pathophysiology

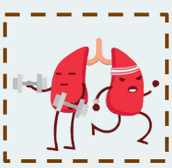
-They block the **slow calcium channels** in the myocardium and vascular smooth muscle, leading to coronary and peripheral vasodilation.
- **Reduce** cardiac contractility, **Depress** SA nodal activity, **Slow** AV conduction.
- Both verapamil and Diltiazem act on the heart and blood vessels, whereas Nifedipine acts on blood vessels, thus primarily causes vasodilation.
- In the pancreas, calcium channel blockade inhibits insulin release, resulting in hyperglycemia. (Remember BBs cause hypoglycemia)
- As with beta-blockers, selectivity is lost in cases of overdose
- All calcium channel blockers are rapidly absorbed
- Onset of action and toxicity ranges from less than 30 minutes to 60 minutes so it is likely that the patient is ok if no symptoms occur in 2 hrs.
- Peak effect of nifedipine can occur as early as 20 minutes after ingestion.

Different between CCB and BB? All the manifestations happens faster with CCB because the peak is up to 2 hours

High protein binding and Vd greater than 1 to 2 L/kg make hemodialysis or hemoperfusion ineffective.
Fortunately (except with sustained-release preparations), their half-lives are relatively short, limiting toxicity to 24 to 36 hours

Manifestations & Complications of Ca channel blockers poisoning:

They usually are hyperglycemic.
Seizures and unconsciousness (uncommon)with CCB, it more commonly happens with Propranolol toxicity.
It is difficult to differentiate between CCBs and beta blockers intoxication; the best way is to do it by Hx. Anyways management is almost the same but in CCBs intoxication be more generous in using ca.

Cardiovascular 	Hypotension,sinus bradycardia,sinus arrest,AV block,AV dissociation,junctional rhythm,asystole; ventricular dysrhythmias uncommon except with bepridil	Neurologic 	Lethargy, confusion, slurred speech, coma; seizures (uncommon); cerebral infarction (rare)
Pulmonary 	Respiratory depression,apnea; pulmonary edema; adult respiratory distress syndrome	Metabolic 	Metabolic (lactic) acidosis; hyperglycemia (mild); hyperkalemia (mild)
Gastrointestinal 	Nausea, vomiting, bowel infarction (rare)	Dermatologic 	Flushing, diaphoresis, pallor, peripheral cyanosis

Lactic acidosis and hyperglycemia = you should think of CCB since CCB and beta-blockers have very similar symptoms except for these two symptoms.

Calcium Channel Blockers

Diagnostic strategies:

- Serum levels Ca antagonists are not available.
- Glucose and Electrolytes (including Ca & Mg)
- Hyperglycemia secondary to insulin inhibition occurs occasionally but mild and short-lived no treatment is needed
- Lactic Acidosis occurs with hypotension and hypoperfusion
- ECG: a prolonged QRS or QT interval suggest bepridil or a co-ingested cardiac toxin such as TCA

Management:

CCBs intoxication management is the same as beta blockers management, except in CCBs we give calcium salts and that is being in form of Ca chloride and and Ca gluconate. Ca+ is the antidote

IV first step in management.

O_2

Cardiac monitoring

No evidence for activated charcoal

Vomiting is a powerful vagal stimulus that can exacerbate bradycardia and heart block.If you wanna intubate the pt, make sure to sedate him, because intubating him will stimulate the vagus and result in severe nausea and vomiting

If there is hypotension and bradycardia:
-Atropine
-IV Ca
-Epinephrine, Norepinephrine and Dobutamine have also led to successful outcomes "catecholamines"
-Glucagon has been used for its ionotropic and chronotropic effects
-Insulin

[If symptomatic bradycardia or heart block persists, the next step is a pacemaker (435 teamwork)]

Other treatment: High-Dose Insulin Euglycemia (HDIE) Therapy

{ Calcium Channel Blockers }

Summary of the treatment:

Don't skip it because it says summary, doctor said he made a question out of it (;

PHASE I

Boluses of:

- ❏ Atropine
- ❏ Calcium
- ❏ Fluids

PHASE II

- ❏ Catecholamines infusions
- ❏ Calcium infusion
- ❏ Insulin glucose infusion
- ❏ Glucagon infusion
- ❏ Phosphodiesterase infusion
- ❏ Transcutaneous or transvenous cardiac pacing
- ❏ Invasive monitoring

PHASE III

Consider intra-aortic balloon counterpulsation, cardiac bypass

Disposition:

Because the peak effect occurs in 90 minutes to 6 hours, patients who are totally asymptomatic for 6 hours can be safely discharged.
For delayed-release preparations should be admitted for at least 24 hours of continuous cardiac monitoring

Again, 435 teamwork

435 teamwork (:

Calcium Channel Blockers

Ca Channel Blockers

Drug	VD (UKG)	Half Life (HR)	Protein binding (%)	Comments
Verapamil	4	3-12	90	90 Most fatalities; impairs contractility and cardiac conduction more than most other calcium antagonists
Diltiazem	1.5-5.3	3-7.9	70-80	Suppression of atrioventricular node similar to verapamil; myocardial depression otherwise less
Nifedipine	1.4-2.2	1-5	92-98	Vasodilation greatest effect
Nicardipine	0.64	8-9	95	Vasodilation
Nimodipine	0.94-2.3	1-2	95	No reports of oral overdose (2005 PDR)
Amlodipine	21	30-50	98	Vasodilation
Bepridil	8	33-42	99	99 Class I as well as class IV antidysrhythmic; prolongs QT: torsades de pointes
Felodipine	10	10	99	vasodilation
Isradipine	3	1.9-16	95	Vasodilation
Nisoldipine	4-5	7-12	99	Vasodilation

Nitrates & Nitrites

Nitrates & Nitrites

Mechanism of action

-They are widely used as vasodilators in the treatment of heart failure and ischemic heart disease.
-They augment coronary blood flow as well as reduce myocardial oxygen consumption by **reducing afterload**.
- At lower doses nitrates primarily dilate **veins**
- At higher doses they also dilate **arteries**

-Nitrites are also **oxidizing agents** that convert hemoglobin to methemoglobin, impairing oxygen delivery

Always ask the patient if he take PDE inhibitors (viagra) in the last 4 hrs before giving nitrates in the ER.

Pathophysiology

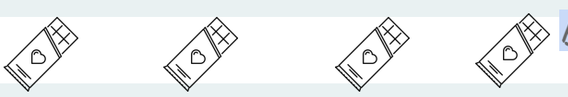
-Hypotension is a common complication, but usually responds to supine positioning, IV fluids and reduction of the dose
-Hypotension is usually transient
-Low-dose pressors are occasionally needed, but it is best to avoid them in the setting of acute coronary syndromes
-Nitrates toxicity is usually iatrogenic

Before give any patient in the ER Nitrates make sure that the patient doesn't use any Nitrates or Nitrates derivative.

Methemoglobinemia & Management:

IV fluid. usually good response
If a patient comes with MI and he is taking Viagra (phosphodiesterase PDE inhibitor)..NEVER give nitrates !! It might kill the patient. If you gave accidentally then give I.V fluids and if no response then give vasopressors in low doses.

- When methemoglobin levels exceed 15%, a venous blood sample appears chocolate brown, and the skin appears blue even while patients look remarkably comfortable
- Unlike most cases of cyanosis, supplemental oxygen even with 100% O_2 doesn't improve patient's color (they have abnormal Hb)
- Pulse oximetry is not reliable What can cause hypotension, methemoglobinemia, tachycardia = Nitrates.



Blue as smurfs and brown as a chocolate!

Treatment:

→ IV methylene blue, but this antidote is usually not needed unless methemoglobinemia approaches 30% Doc says 15% we give them.
→ The usual dose of methylene blue in adults is 1 to 2 mg IV over 5 minutes

Digitalis

Digitalis

Therapeutic dose

-In therapeutic doses, it has two effects:
1-Increasing the force of myocardial contraction
2-Decreasing AV[1] conduction to slow the ventricular rate in AFib[2]
-It inhibits membrane Na-K ATPase[3] which increases intracellular Na and Ca and increases extracellular K.
-Indirectly increases vagal activity and decreases sympathetic activity
low therapeutic window = frequent intoxication

1-Atrioventricular
2-Atrial fibrillation
3-Adenosine triphosphatase

Toxic dose

-With toxic levels, digitalis paralyzes the Na-K pump, K can't be transported into cells "Hyperkalemia >> Arrhythmia!" 13.5 mEq/L
-Directly halts the generation of impulses in SA node, depresses conduction through AV node, and increases the sensitivity of the SA & AV nodes to catecholamines.
-Digitalis can produce virtually any dysrhythmia or conduction block, and bradycardias are as common as tachycardias. (435 teamwork)
Tachy and brady

Hyperkalemia and Hypomagnesemia exacerbate the toxicity

- The significant protein binding and large volume of distribution suggest that hemodialysis, hemoperfusion, and exchange transfusion are ineffective

When dialysis can be effective? Low protein binding rate, low molecular weight, low volume of distribution, hydrophilic.

Digitalis Intoxication:

Cardiac "Dysrhythmia"

- Nonspecific
- More specific but not pathognomonic

Noncardiac

- General
- Gastrointestinal
- Ophthalmologic
- Neurologic

A very wide spectrum. Most important effects are GI (nausea and vomiting) and blurred or colored vision, as well as neurological symptoms.

Digitalis Intoxication

Dysrhythmias associated with Digitalis Toxicity "Cardiac"

Nonspecific

-PVCs, especially bigeminal and multiform
-First-, second (Wenckebach's), and third-degree AV block
-Sinus bradycardia
-Sinus tachycardia
-Sinoatrial block or arrest
-Atrial fibrillation with slow ventricular response
-Atrial tachycardia
-Junctional (escape) rhythm
-AV dissociation

-Ventricular bigeminy and trigeminy
-Ventricular tachycardia
-Torsade's de pointes
-Ventricular fibrillation

More Specific, but Not Pathognomonic

-Atrial fibrillation with slow, regular ventricular rate (AV dissociation)
-Nonparoxysmal junctional tachycardia (rate 70-130 beats./min)
-Atrial tachycardia with block (atrial rate usually 150-200 beats/min)
-Bidirectional ventricular tachycardia

Which medication might give multi types of arrhythmias?
Digitalis

Noncardiac Symptoms in adults and children

Neurologic

Dizziness, Headache, (Confusion, disorientation, delirium), (Visual and auditory hallucinations), (Paranoid ideation, acute psychosis), Somnolence, Abnormal dreams, (Paresthesias and neuralgia), Aphasia, Seizures

Ophthalmologic

Blurred or snowy vision, Photophobia, Yellow-green chromatopsia (also, red, blue and brown), (Transient amblyopia, diplopia, scotomata, blindness)

General

Weakness
Fatigue
Malaise

Gastrointestinal

Nausea and vomiting
Anorexia
Abdominal pain
Diarrhea

Digitalis

Diagnostic Strategies:

Serum digoxin levels:

The only drug in this lecture that we depends on its level.

Peak levels after an oral dose of digoxin occur in 1.5 to 2 hours, with a range of 0.5 to 6 hours

Steady-state serum concentrations are not achieved until after distribution, or 6 to 8 hours after dose or overdose, and may be only ¼ to ⅛ of the peak level

-The ideal serum digoxin concentration for patients with heart failure is 0.7 to 1.1 ng/mL.
-In acute poisoning, serum potassium may begin to rise rapidly within 1 to 2 hours of ingestion, potassium should be withheld, even if mild hypokalemia is measured initially. i.e. even if there was hypokalemia we don't give K because it's trapped inside the cells, unless very severe.

435 teamwork

Management:

First thing is you give is fluid,and check for K level

There is no evidence to support:

- Gastric emptying
- Activated charcoal
- Multidose charcoal has no proven benefit

1	Atropine	Supportive (avoid inotropes as much as you can) "435 teamwork"	We use the lower energy because the heart is already irritable and it may cause malignant arrhythmia .
2	Pacing	Cardioversion and defibrillation can cause asystole after attempt to treat tachydysrhythmias	Lower energy settings, such as 25 to 50 J, may be less hazardous
3	Electrolytes correction	A-K:Raising the serum potassium to 3.5 to 4 mEq/L is an important early treatment. Level >5 mEq/L warrants consideration of digitalis antibody (Fab fragment) treatment	B-Mg: For significant magnesium depletion
4	Fab Fragments	Digifab or Digibind (These are antibodies) "Next slide for further details"	severe hyperkalemia is indication for treatment with antidote

Digitalis

Management:

Recommendations for administration of Digitalis antibody fragments in adults and children: Just know that we give it in high conc of digoxin and if there is organ damage or high K+

In adults

1. Severe ventricular dysrhythmias
2. Progressive and hemodynamically significant bradydysrhythmias unresponsive to atropine
3. Serum potassium > 5 mEq/L
4. Rapidly progressive rhythm disturbances or rising serum potassium level

5. Co-ingestion of cardiotoxic drugs such as beta-blockers, Ca channel blockers, or TCA
6. Ingestion of plant known to contain cardiac glycosides plus severe dysrhythmias (rare)
7. Acute ingestion > 10 mg plus any one of factors 1 through 6 above
8. Steady-state serum digoxin > 6 ng/mL plus any one of factors 1 through 6 above

In children

1. Ingestion of > 0.1 - 0.3 mg/kg or steady-state digoxin > 5 ng/mL plus rapidly progressive symptoms or signs of digitalis intoxication or potentially life-threatening dysrhythmias or conduction blocks or serum K > 6 mEq/L
2. Co-ingestion of other cardiotoxic drugs with additive or synergistic toxicity
3. Ingestion of plant known to contain cardiac glycosides plus severe dysrhythmias (rare)

{ Summary I }

	mechanism of action	manifestations & complications	diagnostic strategies	management
beta blockers	- Inhibits endogenous catecholamines. - Rapidly absorbed and the peak occurs in 1 to 4 hours.	1. Bradycardia 2. Hypotension 3.Unconsciousness 4. Respiratory arrest or insufficiency. 5. Hypoglycemia (uncommon in adults) 6. Seizures (common only with **propranolol**)	- clinical picture. - Hypoglycemia is common in children	**I** :Boluses of atropine, Glucagon, fluids. **II**: Catecholamines infusions, Insulin glucose infusion Glucagon infusion, Phosphodiesterase infusion, Transcutaneous or transvenous cardiac pacing,Invasive monitoring for BB: hemodialysis of hydrophilic BBs with low protein binding and low V_d for CCB: Calcium infusion
Ca^{+2} channel blockers	- block the slow calcium channels leading to vasodilation. - Reduce cardiac contractility, Depress SA nodal activity, Slow AV conduction. - inhibits insulin release, resulting in hyperglycemia. - rapidly absorbed. - verapamil and Diltiazem act on the heart and blood vessels. - Nifedipine acts on blood vessels.	Hypotension, sinus bradycardia, sinus arrest, AV block, AV dissociation, junctional rhythm, asystole. -Respiratory depression, apnea,pulmonary edema, adult respiratory distress syndrome - Lethargy, confusion, slurred speech, coma -Metabolic (lactic) acidosis, hyperglycemia (mild), hyperkalemia (mild). - Flushing, diaphoresis, pallor, peripheral cyanosis.	- Glucose and Electrolytes (Ca & Mg) - Hyperglycemia. - Lactic Acidosis with hypotension and hypoperfusion - ECG: a prolonged QRS or QT interval suggest bedpril or a co-ingested cardiac toxin such as TCA	

{ Summary II }

	mechanism of action	manifestations & complications	diagnostic strategies	management
digitalis	**Toxic Dose** - paralyzes the Na-K pump, K can't be transported into cells - Directly halts the generation of impulses in SA node, depresses conduction through AV node, and increases the sensitivity of the SA & AV nodes to catecholamines.	cardiac:can give any type of arrhythmia non cardiac symptoms : neurologic, Ophthalmologic , general, gastrointestinal	Serum digoxin levels (peak in 1.5 to 2 hours)	supportive (avoid inotropes as much as you can) 2- Antidote: digibind (Fab Fragments). 3- pacing 4- electrolyte correction
Nitrates & Nitrites	- vasodilators - augment coronary blood flow ,reducing afterload. - At lower doses nitrates primarily dilate veins - At higher doses they also dilate arteries - oxidizing agents that convert hemoglobin to methemoglobin, impairing oxygen delivery	Hypotension usually transient and responds to supine		- IV methylene blue, but this antidote is usually not needed unless methemoglobinemia approaches 30%. - Unlike most cases of cyanosis, supplemental oxygen doesn't improve patient's color

How toxic is your knowledge

Q1) 40-year-old male was brought to the hospital and his wife reports that he took about 40 tablets of immediate-release Metoprolol three hours ago in an attempt to end his life. He is lethargic but arousable. His blood pressure is 90/45 mmHg, his heart rate is 45 beats/minute. Which therapy will you try first?
A. Start him on activated charcoal
B. Insert transvenous pacemaker
C. IV atropine
D. IV fluid with dextrose

Q2) which of the following make calcium channel blockers considered as the most likely diagnosis ?
A. diarrhea with nausea and vomiting
B. hypotension ,bradycardia and lethargy
C. dry skin and tachycardia
D. extrapyramidal involuntary movement

Q3) What is the most effective treatment modality in digoxin toxicity?
A. Activated charcoal
B. Potassium replacement
C. Fab fragments
D. Catecholamine

Q4) which of the following has the highest fatality rate among beta blocker overdose ?
A. Sotalol
B. Metoprolol
C. Propranolol
D. Atenolol

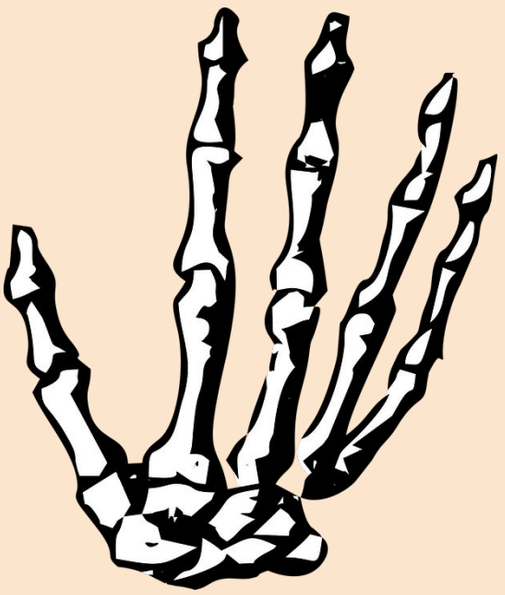
Q5) What is the most common presentation of nitrate intoxication?
A. Severe bradycardia
B. Carboxyhemoglobinemia
C. Hypotension
D. Seizures

Q6) One of the complications of BB is hypoglycemia, which one of the following patient groups are at high risk for this complication?
A- Adults
B-Children
C-Men over 70 year of age
D-Women over 60 year of age

Q7) Which of the following is the appropriate antidote for beta-blocker overdose?
A. Glucagon
B. IV potassium
C. IV magnesium
D. Metoprolol

1-C
2-B
3-C
4-C
5-C
6-B
7-A

Thank you and good luck!



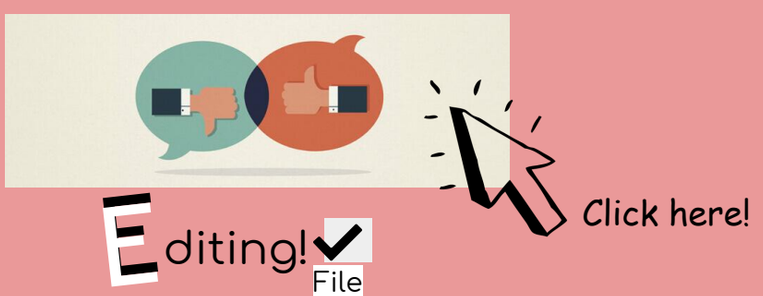
Very Toxic but you are gonna do it!

A+ is yours (:

- Email us at:

436toxicology@gmail.com

How well do you think we have done? We are waiting for your feedback!



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