

Lecture 1: Introduction to Toxicology

Lecture outlines:

1. Initial approach
2. Toxic Syndromes
3. Decontamination
4. Diagnostic Tests
5. Observation

TOXIDROME

Constellation (group) of physical findings that can be attributed to a specific class of toxins and can provide important clues to narrow the differential diagnosis.

However:

- ❑ Lots of medications have unique effects not easily grouped
- ❑ Polydrug overdoses may result in overlapping and confusing mixed syndromes.

5 basic toxidromes:

Sympathomimetic

Opiate

Cholinergic

Anti
cholinergic

Sedative
hypnotics

❖ Mechanism of action:

Excessive sympathetic stimulation involving epinephrine, norepinephrine and dopamine leading to excessive stimulation of alpha and beta adrenergic system.

❖ MANAGEMENT:

1- Supportive care

- Monitor airway, diagnose ICH, rhabdomyolysis.
- IV fluids for insensible losses and volume repletion

2- **Benzodiazepines** (to control and sedate the patient)

3- BP management if severe

4- **Give BOTH alpha and beta blockers (labetalol).**

>> NEVER GIVE BETA BLOCKERS ONLY because alpha effect will dominate and worsen the symptoms.

* Attention deficit hyperactivity disorder

** Intracerebral hemorrhage

Sympathomimetic

❖ EXAMPLES:

- Cocaine
- Methamphetamine/Amphetamines (Captagon)
 - Ecstasy (MDMA)
 - ADHD* drugs e.g. Ritalin, Adderal
- Ephedrine
- Caffeine (e.g. energy drinks)



Amphetamine



Cocaine



❖ FEATURES:

- Tachycardia +/- arrhythmias
- Mydriasis
- Diaphoresis
- Hypertension +/- ICH**
- Confusion with agitation
- Seizures
- Rhabdomyolysis (due to excess movement) renal failure can result

❖ MANAGEMENT:

* Competitive opioid antagonist:

Naloxone

- Goal of return of spontaneous respirations sufficient to ventilate the patient appropriately
- May have to re-dose as opiates may act longer than antagonist



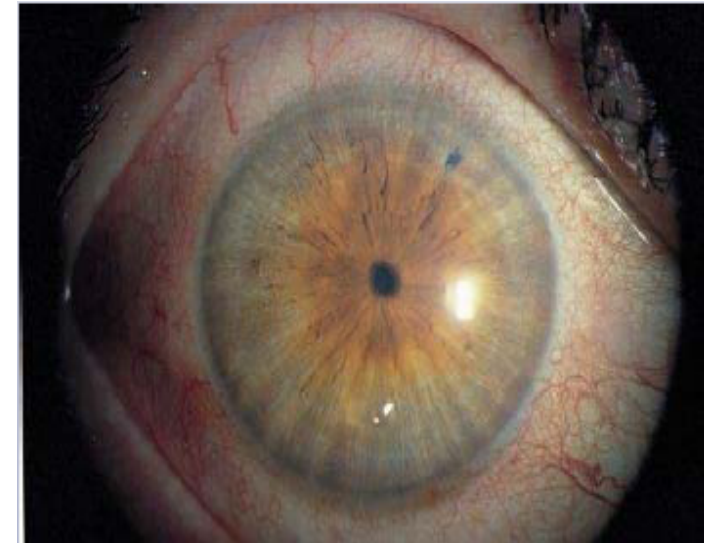
OPIATE

❖ EXAMPLES:

- Morphine and codeine
- Heroin
- Methadone
- Meperidine
- Hydrocodone
- Oxycodone

❖ FEATURES:

- Coma
- Miosis (pin point pupil)
- Respiratory depression (slow shallow breathing)
- Peripheral vasodilation
- Orthostatic hypotension
- Flushing (histamine)
- Bronchospasm
- Pulmonary edema
- Seizures (Meperidine, Propoxyphene)
- Constipation on long run



❖ MANAGEMENT:

1- Supportive care

IVF to replace insensible losses from agitation, hyperthermia

2- Benzodiazepines to stop agitation

3- Physostigmine (cholinomimetic)

- **Induces cholinergic effects**
- Short acting
- May help with uncontrollable delirium
- **Do not** use if ingestion not known
- Danger with TCAs (tricyclic anti depressants)

❖ Mechanism of action:

ANTAGONIZE the effects of endogenous Acetylcholine by blocking the receptors.

❖ EXAMPLES:

- Atropine
- Scopolamine
- Amantadine

***All the following classes have ANTICHOLINERGIC activity:**

- Antihistamines
- Antiparkinsonians
- Antipsychotics
- Antidepressants
- Antispasmodics
- Mydriatics
- Muscle relaxants
- Many plants
(e.g. jimson weed, Amanita muscaria)

Anticholinergic

❖ FEATURES:

➤ CNS muscarinic blockade:

- Confusion
- Agitation
- Myoclonus
- Tremor
- Abnormal speech
- Hallucinations
- Coma

➤ Peripheral muscarinic blockade:

- Mydriasis
- Anhidrosis*
- Tachycardia
- Urinary retention*
- Ileus

*** Distinguishing features of anticholinergic from SYMPATHOMIMETIC.**

❖ Mechanism of action:

Block **acetylcholinesterase** from working (prevent Ach degradation)
=> excess of acetylcholine in **synapses**
=> excess stimulation of **the muscarinic and nicotinic systems**

❖ EXAMPLES:

- Organophosphate and carbamate insecticides.
- Physostigmine
- Edrophonium
- Some mushrooms

Cholinergic



❖ MANAGEMENT:

1- Supportive care

2- Antagonize muscarinic symptoms

=> **Atropine**

3- Stop aging of enzyme blockade

=> **2-PAM (Pralidoxime)**: regenerate AchE.

4- Prevent and terminate seizures

=> **Diazepam**

❖ FEATURES: (SLUDGE syndrome)

Salivation

Lacrimation

Urination

Diaphoresis

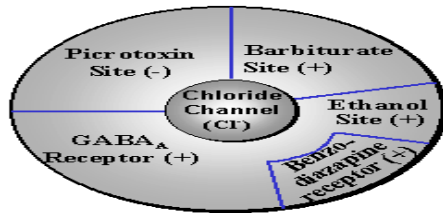
GI upset: Diarrhea, vomiting

Eye: Miosis

❖ Mechanism of action:

- Different agents have different mechanisms
- Many of them interfere in the GABA system: increase GABA stimulation and induce sedation

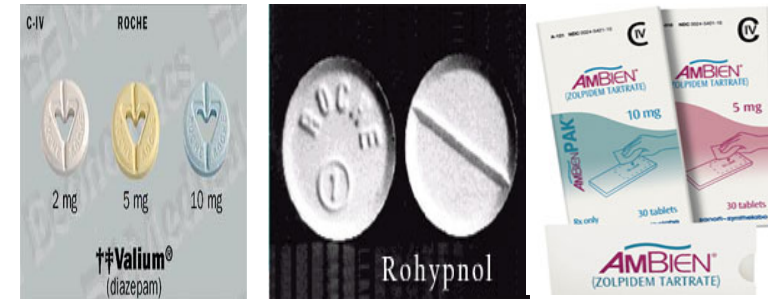
GABA_A Receptor:



SEDATIVE-HYPNOTICS

❖ EXAMPLES:

- Benzodiazepines (e.g. Rohypnol)
- Diazepam
- Zolpidem (Ambien)



❖ MANAGEMENT:

- 1- Supportive care
- 2- Use **benzo antidote "Flumazinil"**
 - It is an antagonist at the benzodiazepines receptor
 - **RARELY INDICATED**
 - If seizures develop either because of benzo withdrawal, a co-ingestant or metabolic derangements, have to use 2nd line agents, barbiturates, for seizure control

❖ FEATURES

- CNS depression, lethargy
- Can induce respiratory depression
- Can produce bradycardia or hypotension

GASTRIC DECONTAMINATION:

☐ METHODS

1. **Ipecac:** Induce vomiting.
2. **Gastric Lavage:** take out pills from the stomach
3. **Charcoal:** Adsorb the toxins in the gut
4. **Whole Bowel:** flush out the system

Why is the vast majority of patients are unlikely to benefit from gastric decontamination ?

- ✓ They have ingested nontoxic substances
- ✓ They have ingested nontoxic amount of toxic substances
- ✓ They present long after decontamination would be expected to be of any benefit!

Who are the Patients who theoretically may benefit from decontamination ?

- ✓ Present early after ingestion (1 hour)
- ✓ Have taken a delayed release products
- ✓ Have taken potentially life-threatening overdose

Ipecac

- Emetine and Cephaeline
- **Induces emesis**
- **DOES NOT HAVE A ROLE IN ED CARE**

Not used anymore because risk of aspiration outweighs vomiting.



GASTRIC LAVAGE

- **Rarely**, if ever indicated
- **Indicated in Life threatening Ingestion that occurred within < 1 hour**
- Airway protection is key
- Lots of complications

NOTE: DO not lavage tylenol, do not lavage an SSRI



Activated Charcoal

- **No proven outcome benefit**, and its use should be carefully weighed against potential complications.

- **Works to adsorb substances to its matrix**

Not effective for metals, caustics, alcohol, alkali, acid, hydrocarbons

- **Contraindications**

Aspiration, ARDS, bowel obstruction

- **Dosing 1 g/kg po dose ± single dose of cathartic.**



If GI decontamination is considered, no matter the method, potential benefit must be weighed against the potential complications.

Diagnostic studies

Acid-base status

Liver Function Test (LFT)

Renal function

Cardiac conduction (ECG)

Drug levels
Based on history or clinical findings

Toxin specific finding
e.g. CK for cocaine

- Other common ingestants may have common diagnostic tests:

1- Paracetamol:

Paracetamol level, LFT, coagulation profile.

2- Salicylates

ASA level, metabolic acidosis, **respiratory alkalosis**, renal insufficiency, anion gap

3- SSRI:

Prolonged QTc (corrected QT interval)

4- Toxic Alcohols

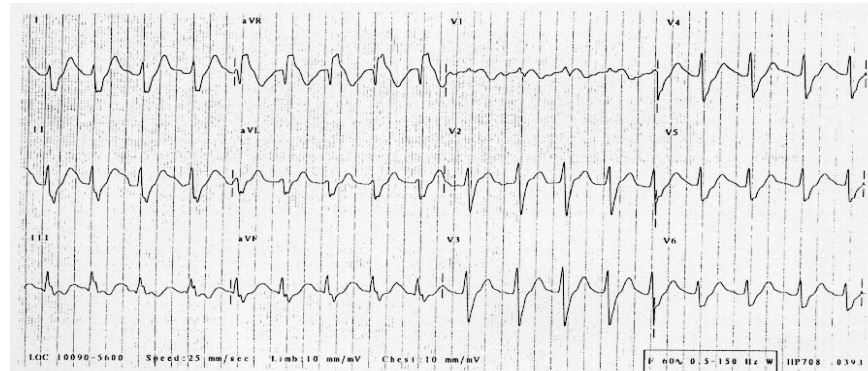
- **Osmolality gap** with ethylene glycol (EG), methanol and isopropyl alcohol
- **Anion gap acidosis** with EG and methanol.

- ECG

- Evaluate:

1. QRS and QTc
2. presence of blocks, rhythm

QTc > 450 and a QRS > 100 can be concerning for toxin induced (e.g. TCAs) cardiac abnormalities

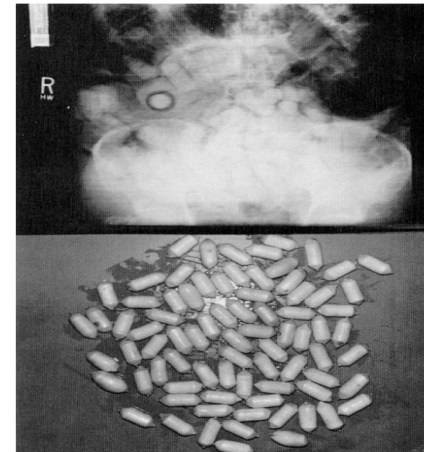


- Radiographs:

- **Limited usefulness**
- Radiodense substances on AXR: (**CHIPES**)

Chloral hydrate, Ca
Hheavy metals
Iron, iodides
Phenothiazines
Enteric coated
Slow release

- Packers/ stuffers
- Aspiration



Observation Period:

1. IF: Normal labs, normal ECG, normal exam, no history of extended release drug
⇒ **Observe for approximately 6 hours.**
2. IF: Extended release medications, oral hypoglycemic involved
⇒ **Observation depending on agent, 12-24 hours**

Case...

› 18 years old man found “down” › EMS transports Reports from scene: “he took something” › No pill bottles on scene, No family with him, Friends that found him are long gone › He is now in your ED, You are never going to know exactly what he took.

- How do I treat him? → Good supportive care, good physical examination
- How do I decontaminate him(if I need to do!)? → A. Charcoal as long as he is not in aspiration risk
- What do I order? → Chem, ASA, Paracetamol, ECG at a minimum
- Do I give him an antidote? → Coma cocktail**, others as indicated by clinical condition & or labs.
- When can he go to psych? → Observe for 6 hours and re-evaluate

**refers to a combination of substances administered in an emergency to comatose individuals, at a time when the cause of the coma in the individual was not yet known.

One combination include : dextrose, flumazenil, naloxone, and thiamine

Match the features in column A to their best answers in column B:

No	A	B
1	Agitated, pupils 8 mm, sweaty, HR 140, BP 230/130	Opiate (2)
2	Unarousable, RR 4, pinpoint pupils	Cholinergic (4)
3	Confused, pupils 8mm, flushed, dry skin, no bowel sounds, 1000 cc output with Foley	Sedative hypnotics (5)
4	Vomiting, urinating uncontrollably, HR 40, Pox 80% from bronchorrhea, pupils 2 mm	Sympathomimetic (1)
5	Lethargic, HR 67, BP 105/70, RR 12, pupils midpoint	Anti cholinergic (3)

MCQs

Q6: Which of the following features distinguish anticholinergic from sympathomimetic?

- A- Dry skin
- B- Accelerated heart rate
- C- Urinary retention
- D- A+C

Q7: In which of the following toxidromes DIAZEPAM is used to terminate seizures?

- A- opiate
- B- Cholinergic
- C- Anticholinergic
- D- Sedatives

Q8: Which of the following is the mechanism of action of sedative-hypnotics?

- A- Stimulate serotonin and induce alert
- B- Stimulate dopamine and depress arousal
- C- Stimulate GABA and induce sedation
- D- Inhibit GABA and induce sedation

Q9: A 5year old child diagnosed with ADHD, he is at risk of developing which of the following toxidromes?

- A- Opiate
- B- Sympathomimetic
- C- Anticholinergic
- D- Organophosphate

Q10: Which of the following is an indication to manage a patient with gastric lavage?

- A- Presented to the ER 1 hour after ingestion
- B- patient have taken nontoxic dose of toxic substance
- C- Ingestion of nontoxic substance
- D- Patient presented with coma.

6: D

7: B

8: C

9: B

10: A



**If you have any questions You can always
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