TOXICOLOGY

432 Team

1

General approach to the Poisoned Patient (An introduction to Toxicology)

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COLOR GUIDE: • Notes • Important • Additional

Objectives

Not given!

TOXIDROMES:

- Constellation of physical findings that can be attributed to a specific class of toxins and can provide important clues to narrow the differential diagnosis.
- 5 Basic Toxidromes:
  1. Sympathomimetic
  2. Opiate
  3. Anticholinergic
  4. Cholinergic
  5. Sedative Hypnotic

Difficulties:

- Not every drug fits into a broad based category
- Lots of meds have unique effects not easily grouped
- Polydrug overdoses may result in overlapping and confusing mixed syndromes.

1. Sympathomimetic:

- Cocaine
- Methamphetamine/Amphetamines =Ceptagone
- Ecstasy (MDMA)
- ADHD meds like ritalin, adderal
- Ephedrine
- Caffeine (e.g. Red Bull)

- Tachycardia +/- arrythmias
- Mydriasis
- Diaphorisis
- Hypertension +/- ICH (intra cranial hemorrhage)
- Confusion with agitation
- Seizures
- Rhabdomyolysis → RF can result

Excessive SYMPATHETIC stimulation involving epinephrine, norepinephrine and dopamine, (both β and α receptors)

What do you do about it?

- **Supportive care**
  - Monitor airway, diagnose ICH, rhabdo
  - IVF for insensible loses and volume repletion
- **Benzos, benzos, benzos, benzos**
- **BP mgmt if severe**
- **NEVER GIVE BETA BLOCKERS.**

Note(s):

› Rhabdomyolysis results from increased ATP demand and eventual exhaustion of muscle stores

2. Opiate:

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

- Coma
- Miosis (pinpoint pubil)
- Respiratory depression
- Peripheral vasodilation
- Orthostatic hypotension
- Flushing (histamine-like effect)
- Bronchospasm
- Pulmonary edema
- Seizures (meperidine, propoxyphene)

What do you do about it?

- **Competitive opioid antagonist: Naloxone.**(can be used as therapeutic or diagnostic)
  - Goal of return of spontaneous respirations sufficient to ventilate the patient appropriately
  - May have to re-dose as opiates may act longer than antagonist.
  - In opiod OD, the Naloxone will wear off before the opiate so can't let patient go

3. Sed-Hypnotic:

- Different agents have different mechanisms
- Many interfere in the GABA system

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

What do you do about it?

- **Supportive care**
  - Be wary of the benzo “antidote” Flumazinil. It is an antagonist at the benzo 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.

4. Anticholinergic: similar to sympathomimetic but NO SWEATING

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

CNS muscarinic blockade:

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

Peripheral muscarinic effects:

- Tachycardia
- Mydriasis
- Anhidrosis (dry skin)
- Urinary retention
- Ileus

By definition, these agents ANTAGONIZE the effects of endogenous Acetylcholine by blocking the receptors.

What do you do about it?

- **Supportive care** → IVF to replace insensible losses from agitation, hyperthermia
- **Benzos to stop agitation**
- **Physostigmine**
  - Induces cholinergic effects
  - Short acting
  - May help with uncontrollable delirium
  - Do not use if ingestion not known
  - Danger with TCAs

Note(s):

Sweat glands have only sympathetic innervation. Anticholinergics have similar effect to sympathomimetic except for sweat glands because they have muscarinic receptors. If u stimulate the sympathetic fibers, that will cause sweating. Also, if you give a muscarinic receptor agonist, that will also cause sweating because the sweat glands have a muscarinic receptor. But anticholinergics block this receptors.

5. Cholinergic: fluids everywhere!

- Organophosphate
- Carbamate insecticides
- Physostigmine
- edrophonium
- Some mushrooms.

- S - Salivation
- L - Lacrimation
- U - Urination
- D - Diaphoresis
- G - Gasterointestinal upset → vomiting, diarrhea
- E - Eye → miosis

Block acetylcholinesterase from working → End up with excess of acetylcholine in synapses → Leads to excess stimulation of the muscarinic and nicotinic systems

What do you do about it?

- **Antagonize muscarinic symptoms** → Atropine
- **Stop aging of enzyme blockade** → 2-PAM (Pralidoxime)
- **Prevent and terminate seizures** → Diazepam
- **Supportive care**

Note(s):

The attachment of the agent to the enzyme is permanent (unless removed by therapy). The agent can be removed from the enzyme and the enzyme "reactivated" by several types of compounds, the most useful of which are the oximes. If the agent-enzyme complex has not "aged," oximes are useful therapeutically. Aging is a biochemical process by which the agent-enzyme complex becomes refractory to oxime reactivation of the enzyme

ED approach:

- **Airway, breathing, circulation**
- **Establish IV, O_2 and cardiac monitor**
- **Consider coma cocktail**
  - Thiamine, D50, Narcan
- **Evaluate history and a thorough physical exam**
  - Look at vitals, pupils, neuro, skin, bowel sounds, and sweat.
  - Gives you hints regarding the general class of toxins
  - Guides your supportive care
- **Draw blood / urine for testing**
- **Time to consider decontamination options**

Gastric Decontamination Overview:

- **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!
- **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
- **No prospective studies have demonstrated outcome benefit with gastric decontamination.**
- **If GI decontamination is considered, no matter the method, potential benefit must be weighed against the potential complications.**

Ipecac	Lavage	Charcoal	Whole Bowel
Induce vomiting	Take out pills from the stomach	Adsorb the toxins in the gut	Flush out the system
• Emetine and Cephaeline • Induces emesis • DOES NOT HAVE A ROLE IN ED CARE	• Rarely, if ever, indicated • Life threatening ingestions that occurred within < 1 hour • Airway protection is key • Lots of complications	• No proven outcome benefit and its use should be carefully weighed against potential complications. • If the patient presents early (before absorption) • Works to adsorb substances to its matrix - Not for metals, caustics, alcohol, alkali, acid, hydrocarbons • contraindications - Aspiration, ARDS, bowel obstruction • Dosing 1 g/kg po dose, +/- single dose of cathartic	

diagnostic studies

- **Acid base status, Renal function, Liver function, ABG**
  Cardiac conduction "ECG": Evaluate QRS and QTC, presence of blocks, rhythm
  - QTc > 450 and a QRS > 100 can be concerning for toxin induced cardiac abnormalities (eg TCAs).
- **Drug levels :** Based on history or clinical findings

- **Any toxin specific findings** : CK for cocaine, …etc.
  - common ingestants may have common dx test abnormalities:

Paracetamol	Salicylates	SSRI	Toxic Alcohols
› Paracetamol level, › LFT, › coags	› ASA level, › metabolic acidosis, respiratory alkalosis, › renal insufficiency, › anion gap	› Prolonged QTc	› Osmolal. gap with ethylene glycol, methanol and isopropyl alcohol › Anion gap acidosis with EG and methanol

- **Radiographs:**
  - Limited usefulness
  - CHIPES (radiopaque)
    - Chloral hydrate, Ca
    - Heavy metals,Iron, iodides
    - Phenothiazines
    - Enteric coated
    - Slow release
  - Packers/ stuffers
  - Aspiration

Observation Period

- Normal labs, normal ECG, normal exam, no history of extended release drug → Approximately 6 hours
- If self-harm and suicidal→ psychiatry
- Extended release medications, oral hypoglycemics involved → 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.

What to do?

- **Start with the basics**
  - Airway, breathing, circulation

s with all patients, the initial survey begins with the ABC's. If the patient is unstable, then the history and physical must be performed while simultaneously performing resuscitation.

Depending on the ingestions, a poisoned patient may present obtunded. An unresponsive patient has lost his or her airway reflexes and is at risk for airway obstruction as well as aspiration. Faced with an unresponsive patient with a history of overdose, one must think of a few reversible possibilities while preparing to control the patient's airway. These reversible causes have been come to be known as the "coma cocktail". In this setting, the following should be considered:

Hypoxia: Place on 100% O2 nonrebreather (also useful prior to intubation)
Hypoglycemia: obtain a point of care fingerstick blood glucose
Opiods: administer Narcan 0.4 to 2mg IV to reverse opiates

With an unresponsive patient, if these measures do not reverse the patient's symptoms, then intubation should be performed.

Once the airway is controlled, attention may turn to breathing. Many toxins can affect the respiratory status and cause a variety of symptoms including frank respiratory failure, hypoxia, flash pulmonary edema, and bronchospasm. These should all be treated with standard therapies and in some cases specific antidotes.

Circulation can be compromised as well. A multitude of toxins can affect hemodynamics including heart rate and blood pressure (hyper or hypotension) as well as cardiac rhythm and intervals. Each of these symptoms can give a clue to what toxin has been ingested.

- **Get a better history from many sources**!
  - Get EMS to get pill bottles, tell you what they do know (found outside, inside, garage…)
  - Call friends, family, neighbors
  - Check Medical charts to see what he is on regularly.
- **Establish a pattern to his symptoms.**
  - Toxic syndrome (TOXIDROM)
- **How do I treat him** → Good supportive care, good physical examination
- **How do I decontaminate him (if I need to do!)** → 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

SUMMARY

1. **Toxidromes are group pf physical findings that can provide important clues to narrow the differential diagnosis.**
   - Agitated, pupils 8 mm, sweaty, HR 140's, BP 230/130 → Sympathomimetic
   - Unarousable, RR 4, pupils pinpoint → Opiate
   - Confused, pupils 8mm, flushed, dry skin, no bowel sounds, 1000 cc output with Foley → Anticholinergic
   - Vomiting, urinating uncontr ollably, HR 40, Pox 80% from bronchorrhea, pupils 2 mm → Cholinergic
   - Lethargic, HR 67, BP 105/70, RR 12, pupils midpoint → Sedative Hypnotic

2. **The vast majority of patients are unlikely to benefit from gastric decontamination.**
   - Activated Charcoal: Given orally. Toxins bind to the charcoal and are excreted without being digested. It is most efficacious if given within the first hour post ingestion. Charcoal does not bind metals (such as iron), alcohols or hydrocarbons. It should be avoided in patients with risk of aspiration
   - Whole bowel irrigation involves the administration of an osmotically balanced polyethylene glycol electrolyte solution to flush the bowel to prevent the absorption of ingested toxins. It is used in cases where charcoal is not effective, with certain sustained release products
   - Gastric Lavage is rarely used and carries significant risks with questionable benefit.
   - Ipecac was universally promoted as a decontamination method. It was used many years ago but this agent should not be used for many reasons. First, it is not effective in removing toxin. Moreover, it has side effects that can cause lethargy and can delay the administration or reduce the effectiveness of other more useful decontamination methods as well as treatments.

Questions

1) A young college student is brought in by EMS after becoming combative at a concert. He is very agitated and altered and requires restraints. His vitals are as follows: pulse 138, respiratory rate 24, blood pressure 154/92, Temp 101.2, Sat 98% on room air. Physical Exam reveals mydriasis, flushed skin, sweating and agitation. An overdose of which of the following agents has caused his symptoms?
   a. Sympathomimetic
   b. Opiate
   c. Cholinergic
   d. Anticholinergic

2) Friends bring in a young man who is apneic and unresponsive. They tell you they were just partying a little and their friend collapsed. His vitals are as follows: pulse 128, Respiratory rate 4, blood pressure 100/70, temp 98F and sat 82% on room air. Which of the following antidote should be used?
   a. Physostigmine
   b. **Benzos**
   c. **Naloxone**
   d. Flumazinil

Answers:

1st Questions: a 2nd Questions: c :