PEDIATRIC TOXICOLOGIC MYSTERIES: IT'S A DANGEROUS WORLD

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HOW DO WE BEST RETAIN CLINICAL KNOWLEDGE?

OR

8 AM SUNDAY MORNING

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- A 3 year old child is rushed to your emergency department by his parents who claim that he suffered a ***generalized seizure*** at home
- They describe the seizure as lasting less than 2 minutes

8 AM SUNDAY MORNING

- No fever or intercurrent illness is described. Past medical history is negative for birth trauma, developmental delay, recent trauma, or drug exposure
- There is no family history of seizures

PHYSICAL EXAMINATION

- Vital Signs
  - ***T 39C*, HR 140, RR 20, *BP 140/95***
- General
  - Combative
- HEENT
  - ***Dilated*** pupils, TM clear, Pharynx moist

PHYSICAL EXAMINATION

- Neck
  - Supple
- Chest
  - No murmur, Clear lungs
- Abdomen
  - ***Hyperactive*** bowel sounds
  - No masses

PHYSICAL EXAMINATION

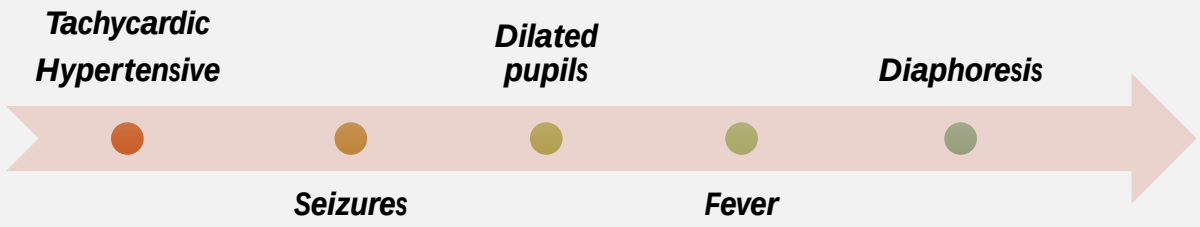
- Pulses
  - Normal
- Extremities
  - Full ROM
- Neurologic
  - Non focal
- Skin
  - ***Diaphoretic***

EXAM 1 HOUR LATER

- Afebrile
- ***HR 140***
- ***BP 120/88***
- ***Pupils still dilated***
- Agitated

IS THIS A SIMPLE FEBRILE CONVULSION?

DEFINE THE SYMPTOM COMPLEX OR TOXIDROME



WHAT ARE SOME OF THE TOXINS THAT CAUSE DILATED PUPILS (A.A.A.S)?

- A
  - Antihistamines
- A
  - Antidepressants
- A
  - Anticholinergics
- S
  - Sympathomimetics

DISTINGUISHING BETWEEN ANTICHOLINERGICS AND SYMPATHOMIMETICS

- ***Shared Findings***
  - Hyperthermia
  - Tachycardia/Hypertension
  - Mydriasis
- Sympathomimetics
  - ***Diaphoresis***
  - Active bowel sounds

COMMON FORMS OF STIMULANT EXPOSURE/ABUSE

- Cocaine (all forms)
- Amphetamines (including ADHD Drugs)
- Weight loss products (PPA, caffeine)
- OTC analeptics (caffeine)
- Bootleg products (theophylline)

COCAINE

MECHANISM OF ACTION

- Inhibition of ***catecholamine reuptake*** and CNS stimulation
- Smoking and IV use produce maximal effects within 1-2 minutes, oral and nasal absorption within 20-30 minutes

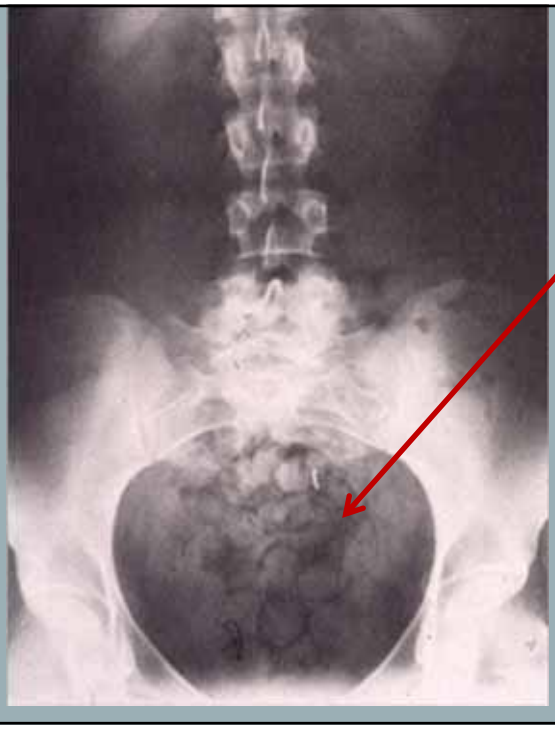
CLASSIC CNS PRESENTATION

- Initial euphoria followed by anxiety, agitation, psychosis, muscle rigidity, or hyperactivity
- Seizures are usually brief and self limited

ASSOCIATED EFFECTS

- Pneumothorax and pneumomediastinum
- Body packers and body stuffers

COCAINE BODY PACKER



COCAINE IN THE PEDIATRIC POPULATION

- Placental transfer
- ***Breast milk contamination***
- Passive exposure to secondary sources

AMPHETAMINES

- Methamphetamine (speed, ice)
- STP (serenity, tranquility, peace)
- MDA (love drug)
- MDMA (ecstacy)
- ADHD Drugs

RESULTS OF ED WORKUP

- Labs normal
- CSF normal
- CT normal
- Urine tox screen ***positive for cocaine***

TOXIN IN THIS CASE

- Exposure to parental cocaine

A GOOD GIRL GONE BAD

HISTORY

A 10 year old girl arrives with her parents who claim that ever since she woke up this morning she has behaved as if she was ***"possessed!"***

She is presently recovering from an active case of ***chicken pox***

She reports no fever, stiff neck, nausea, vomiting, or new rash

PHYSICAL EXAMINATION

Vital Signs

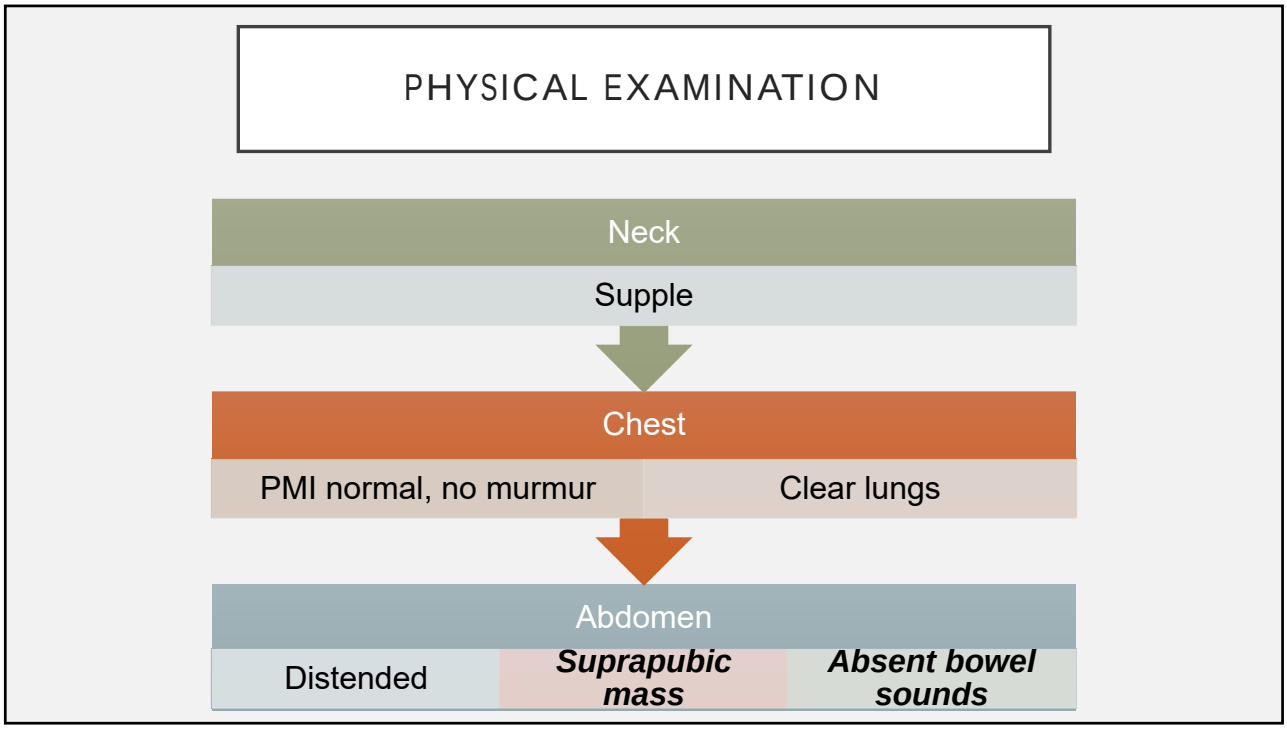
T 40C	***HR 140***	***RR 20***	***BP 140/95***

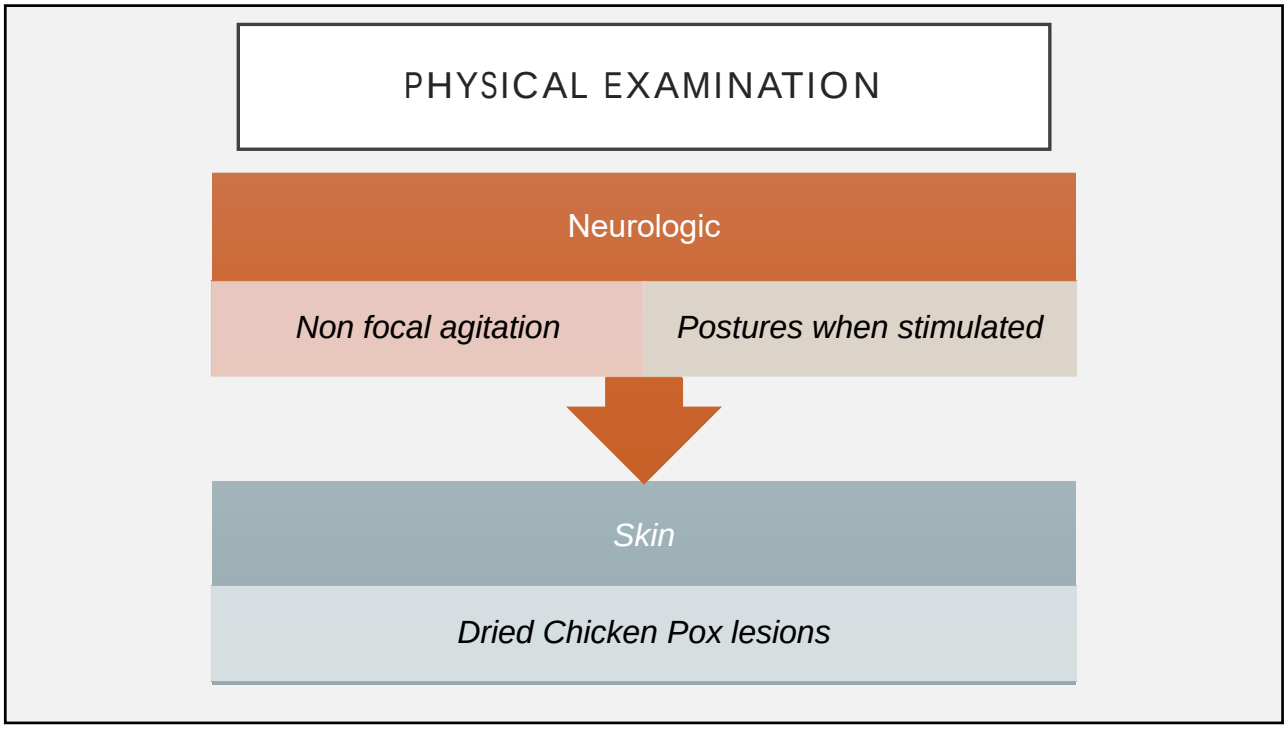
General

Combative, cursing adolescent

HEENT

Dilated, reactive pupils	TM clear	***Pharynx dry***


PHYSICAL EXAMINATION
Neck
Supple
Chest
PMI normal, no murmur
Clear lungs
Abdomen
Distended
Suprapubic mass
Absent bowel sounds


PHYSICAL EXAMINATION
Neurologic
Non focal agitation
Postures when stimulated
Skin
Dried Chicken Pox lesions

PRIMARY SURVEY

ABC'S intact

↓

Dextrostix 120

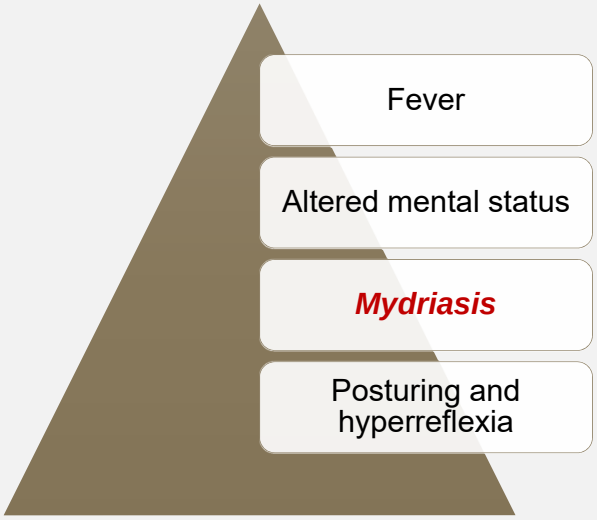
↓

CNS issues

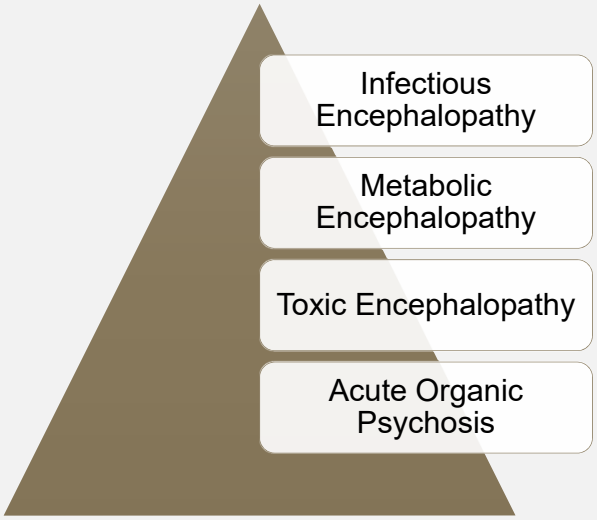
↓

Encephalopathy

INITIAL PROBLEM LIST



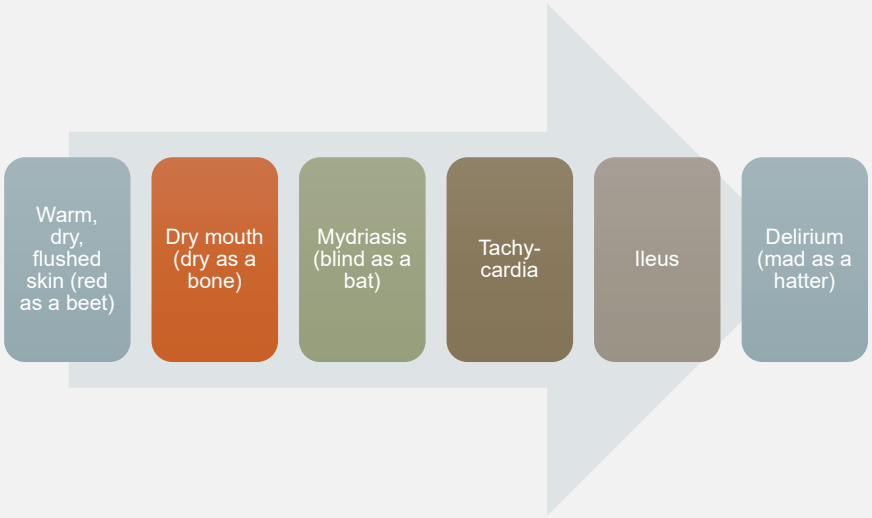
DIFFERENTIAL DIAGNOSIS



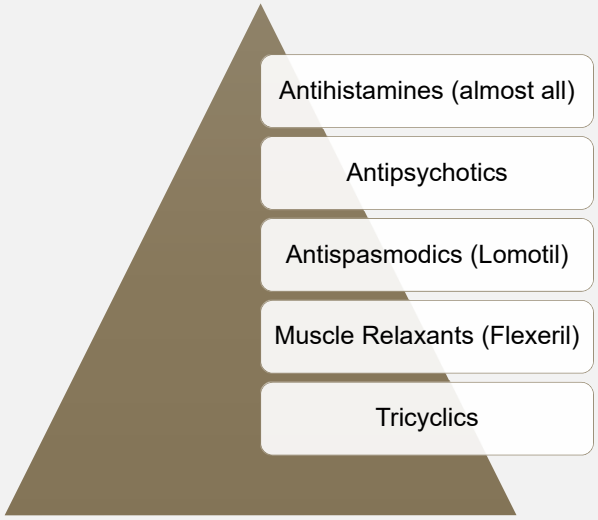
INVESTIGATIONS

- **Normal Labs**
  - CBC, lytes
  - LFT's, ***ammonia***
- **CT/ CSF normal**
  - ***required large amounts of versed to sedate***
- **Tox screen negative**

COULD THIS BE THE CLASSIC ANTICHOLINERGIC SYNDROME?



DRUGS WITH ANTICHOLINERGIC EFFECTS

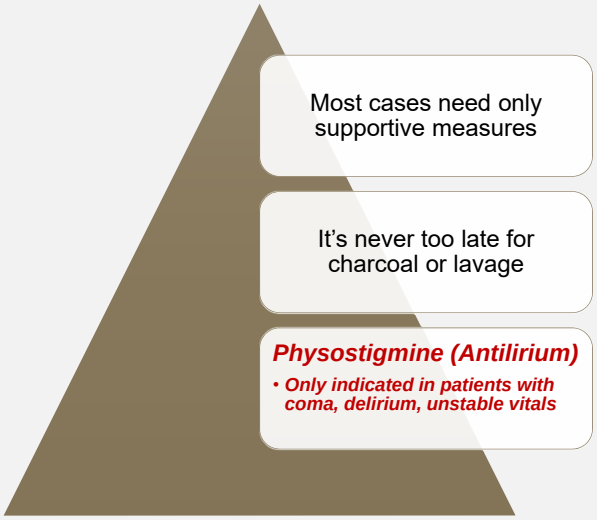


ANTIHISTAMINE OD

- Therapeutic as H1 receptor antagonists
- In OD mimic ***anticholinergic*** poisoning
- In general, toxicity occurs after ingestion of 3-5X usual daily dose
- Children are ***more sensitive to the toxic effects of antihistamines than adults***

A BIT OF HISTORY

TREATMENT OF ANTICHOLINERGIC SYNDROME



CASE PROGRESSION

- Given IV Physostigmine
  - mentation returned to normal

TOXIN IN THIS CASE: TOPICALLY APPLIED BENADRYL

BAD NIGHT TO BE ON CALL

HISTORY

- A 4 month old infant arrives with a chief complaint of ***diarrhea, vomiting, and "looking ill"***
- Well until 3 days PT ED visit, his stools are described as ***frequent*** (15-20/day), foul, green, and mostly water- no blood is noted
- The emesis is sporadic, non bilious
- Others in the home have similar symptoms, but are recovering

HISTORY

- Over the past 12 hours, his activity level has decreased and his parents ***don't like his color***
- Tmax at 38C
- No rash or cough is described
- His urine output is inestimable due to the profuse diarrhea
- Birth and PMH are normal - immunized

PHYSICAL EXAMINATION

Vital Signs
- T 38C
  HR 140
  RR 30
  BP 80/46
- ***OSAT 88%***

General
- ***Tired, lethargic infant***

Chest
- PMI normal, ***no murmur***
- ***Clear lungs***

PHYSICAL EXAMINATION

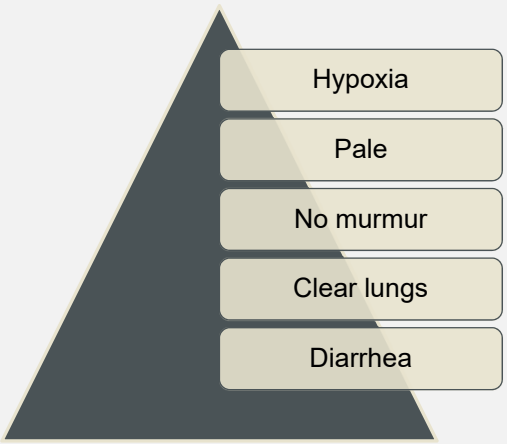
Pulses
- *Fair*

Extremities
- Full ROM

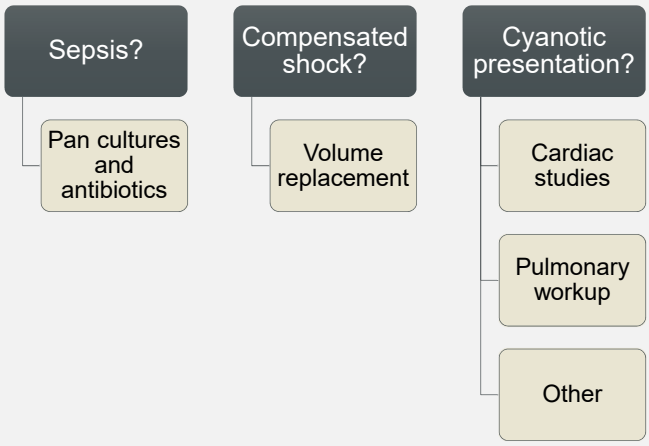
Neurologic
- Non focal lethargy

Skin
- ***Normal Cap Refill***

DEFINE THE SYMPTOM COMPLEX



ESTABLISH A FRAMEWORK FOR INVESTIGATION



INTERVENTION/RESPONSE

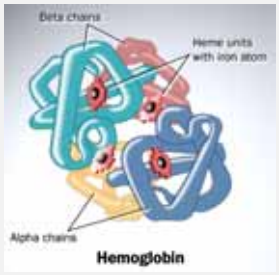
- ***OSAT 87% in room air***
  - ***87% in 100% O2***
- CXR normal
- ABG in 100% O2
  - pH 7.33 pCO2 35 ***pO2 300 (OSAT 88%)***

CAN DISSOLVE IT **CAN'T CARRY IT**

BLOOD ON THE TRACKS

WHAT IS METHEMOGLOBINEMIA?

- The conversion (oxidation) of iron in the heme moiety from ***ferrous to ferric state, rendering it incapable of binding oxygen***
- Fe++ → Fe+++



ETIOLOGIES OF METHEMOGLOBINEMIA

- Nitrates
  - Amyl Nitrate
  - Nitroglycerin
  - ***Infectious Diarrhea***
- Benzocaine
  Lidocaine
- Quinone
- Sulfonamides
- Napthalene

TREATMENT

Mild cases:
Remove offending agents + supplemental oxygen

Level >30%:
Methylene blue

Intravenous: 1-2 mg/kg over 5 minutes	May repeat dose within one hour	*Contraindicated* in G6PD Deficiency

CASE PROGRESSION

- Methemoglobin level = 30
- Received methylene blue over 8 hours
- ***Stool grew rotavirus***

The mechanism of methemoglobinemia in infants with bacterial overgrowth most probably involves the endogenous production of nitrates in the gastrointestinal tract by the altered gastrointestinal flora

WHO HAS THE BREATH MINTS?

HISTORY

- A 3 year old presents with a three day history of ***fever, progressive sleepiness, and respiratory distress***
- Previously healthy, his parents report that he developed a fever (101) at first, for which they gave Tylenol

HISTORY

- His behavior has become that of a lethargic and irritable child, with what the parents describe as a ***"funny, fast breathing pattern"***
- No rash, URI, nausea, vomiting or diarrhea is described

PHYSICAL EXAMINATION

- Vital Signs
  - ***T 40C, HR 140, RR 70 and deep, BP 140/70***
- General
  - Sleepy toddler, responding to mother's voice
- HEENT
  - Normal pupils, Pharynx dry
- Neck
  - Supple

PHYSICAL EXAMINATION

- Chest
  - PMI normal, no murmur
  - Clear lungs
- Abdomen
  - Soft, No mass
  - Bowel sounds normal

PHYSICAL EXAMINATION

- Pulses
  - Normal
- Extremities
  - Full ROM
- Neurologic
  - Non focal lethargy
- Skin
  - ***Medicinal smell***

PRIMARY AND SECONDARY SURVEY

- ABC's intact
- Chemstrip 100
- ***Nonfocal lethargy***
- Pupils normal
- Supple neck
- Clear chest
- Negative PMH, medications, allergies

INITIAL PROBLEM LIST

- Fever
- Lethargy
- ***Hyperpnea***

INITIAL DIFFERENTIAL

- Sepsis
- ***Pneumonia***
- Meningitis

INVESTIGATIONS

- CBC/diff normal
- Electrolytes = ***Anion Gap 30***
- CXR normal
- ABG (room air)
  - ***pH 7.50 pCO2 20 pO2 100 BE -15***

PRIMARY RESPIRATORY ALKALOSIS **PRIMARY METABOLIC ACIDOSIS**

TOXINS THAT CAUSE ANION GAP ACIDOSIS

- M Methanol
- U Uremia
- D DKA
- P Phen (met) formin
- I Iron, INH
- L Lactate
- E Ethanol, Ethylene glycol
- S Salicylates

LAB RESULTS

- Serum Osmolarity= 280
- Calculated Osmolarity= 288
- Ethanol= 0
- BUN= 8
- ***Salicylates = 66mg/dL***

SALICYLATES

- ***Central stimulation*** of the respiratory center= ***primary respiratory alkalosis*** and insensible fluid losses
- Uncouples oxidative phosphorylation and interrupts glucose metabolism ***(primary metabolic acidosis)***
- Alter platelet function and bleeding time

TOXIC DOSE

- Therapeutic dose = 10-15 mg/kg
- Toxic acute dose is > 140 mg/kg
- Severe intoxication seen with 300-500 mg/kg

CLINICAL MANIFESTATIONS

- Vomiting, ***hyperpnea***, tinnitus, and lethargy
- Severe intoxication
  - coma
  - seizures
  - hypoglycemia
  - hyperthermia
  - pulmonary edema

DIAGNOSIS

- History and ASA level
- Anion gap metabolic acidosis
- Initial respiratory alkalosis, dissipates with general clinical deterioration
- Abdominal xrays may demonstrate *radiopaque* enteric-coated or sustained-release tablets

SODIUM BICARBONATE

- ***Increases urine pH, ion trapping ASA***
- Initial dose at 1-2 meq/kg
- Drip of 3 amps in 850 cc D5W at 1.5 - 2 times maintenance
- Attempt to keep urine pH over 7.5
- ***Hemodialysis*** is also very effective

DIAGNOSIS

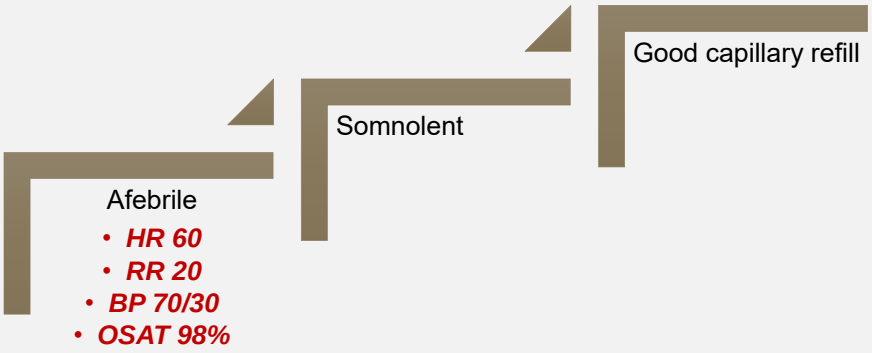
- Oil of Wintergreen Liament
  - ***30 grams ASA/15cc***

HOW SLOW CAN YOU GO?

CASE HISTORY

- A 2 year old accidentally gets into ***Grandpa's heart medications***
- The only open bottle found is ***Verapamil SR***
- The Poison Center is called, and the child is brought in within 45 minutes

CASE PHYSICAL



CALCIUM CHANNEL BLOCKER OVERDOSE

- Pharmacologic effects
  - ***Myocardial depression***
  - ***Peripheral vasodilation***
  - ***Bradycardia***
  - ***Hypotension***
  - ***Heart block***
- Children may be stable initially, but ***progress rapidly to full cardiovascular collapse***

THERAPY

- ***Gastrointestinal decontamination*** is a critical intervention
- Induced emesis should be avoided because CCB-poisoned patients can ***rapidly deteriorate and become severely hypotensive***
- Establish 2 IV Lines, PICU admission

DRUG THERAPY

- Atropine
  - ***the drug of choice for patients with symptomatic bradycardia***
  - clinical experience demonstrates it to be ***largely ineffective*** in improving heart rate in severe CCB-poisoned patients

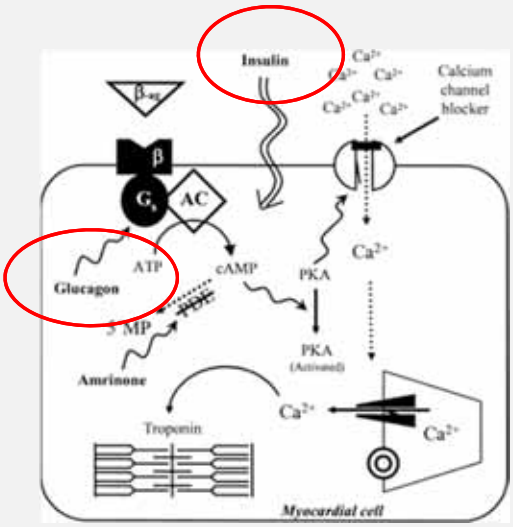
DRUG THERAPY

- Calcium Chloride
  - Appears to be a logical choice
  - Tends to ***improve blood pressure more than it does the heart rate***
  - Exact mechanism is unclear, boluses of Ca2+ increase the extracellular Ca2+ concentration, increase the intracellular concentration gradient through unaffected calcium channels
  - Unfortunately, ***this effect is often short-lived*** and more severely poisoned patients may not improve significantly with calcium salt administration

DRUG THERAPY

- Catecholamines
  - next line of therapy
  - numerous case reports describe the success or failure of a wide variety of vasopressors, including epinephrine, norepinephrine, dopamine, isoproterenol, dobutamine, and vasopressin

SO WHAT ELSE CAN WE TRY?



GLUCAGON

- Endogenous hormone secreted by the pancreatic α cells in response to hypoglycemia and catecholamines
- Has significant ***inotropic and chronotropic effects***
- Glucagon is a ***therapy of choice for β-adrenergic antagonist and calcium channel blocker poisoning*** because of its ability to bypass the β-adrenergic receptor and activate adenylate cyclase in the myocardium

INSULIN AND GLUCOSE (HIE)

- The most promising treatment for patients who are severely poisoned with CCBs may be ***hyperinsulinemia/euglycemia therapy (HIE)***
- ***High-dose insulin has positive inotropic effects***
- Although some indirect evidence suggests that increased Ca2+ entry may be involved, there is growing support for the hypothesis that improved myocardial use of carbohydrates is responsible for clinical improvement

INSULIN AND GLUCOSE (HIE)

- Dosing
  - if the serum glucose is <250 mg/dL an initial bolus of 25-50 g of dextrose (0.5-1 g/kg), should be followed by a dextrose infusion of 0.25-0.5 g/kg/h
  - administer an initial insulin bolus of 1 unit/kg bolus, followed by an insulin infusion at a rate of 0.5-1.0 unit/kg/h, which should be increased if there is no hemodynamic response within 60 minutes

CASE RESOLUTION

- HR soon dropped to 50, BP 60/40
- Given volume and atropine, ***transient*** improvement
- Given calcium chloride, ***transient*** improvement
- Glucagon administered, good clinical effect for 1 hour
- HIE started in PICU, maintained for 30 hours
- VS stable, discharged in 2 days

SUMMARY

- Sympathomimetic presentations may be exogenous
- Drug induced encephalopathy may respond to ***physostigmine***
- Hypoxemia resistant to supplemental oxygen in the absence of cardiopulmonary disease may be ***methemoglobinemia***
- Consider ***pyridoxine*** in refractory status epilepticus
- ***Glucagon and HIE*** are current new therapies for Beta blocker and Calcium Channel Blocker overdoses

THANKS!