Morning report A4

Sidra Ilyas, MD
Tomas Murphy, MD

Chief complaint

66 year old man who lives in a AFC home presented to the emergency department with the chief complaint of generalized weakness, fatigue, and somnolence

HPI

- Barely arousable on presentation, unable to answer questions
- Initial history gathered from AFC home
- Patient had been feeling tired and fatigued for the past few days prior to presentation but now is not responding to them other than with pain/discomfort; has never happened previously to patient
- Decreased fluid intake, no air conditioning in the AFC
- Is given his medications regularly by the AFC
- No known trauma/falls, illicit substance use, change in medications, use of other residents' medications
- No strange behaviors or movements at AFC
- No fevers, chills, rashes, or known sick contacts

Histories

PMH: Hypertension, Schizophrenia, COPD

PSH: Hernia repair

Social History: Smoker (unclear about the amount - EMR says 1-1.5 PPD since the age of 15). Denies alcohol, IVDU, or other illicit drug use (past record indicates marijuana and opiate use). Used to drink 0.5 pint/day

Family History: unknown

Meds: Valproic acid 750 mg qAM and 1000 mg qHS, quetiapine 400 mg TID, Trazodone 100 mg qHS, albuterol inhaler, Breo, Amlodipine 10 mg, lisinopril 40 mg

ROS

Unable to obtain due to patient’s clinical status

History by Chart Review

- Multiple past admissions for hypoxic, hypercapnic respiratory failure
  - Most recently admitted in May, 2018 with hypoxic respiratory failure requiring intubation
  - Attributed to COPD exacerbation
  - UDS positive for benzodiazepines, THC, and opiates at that time
- Past inpatient psych admissions with aggressive behavior

Illness Script

Middle aged man with history of schizophrenia on multiple medications, presenting with acute onset of weakness, fatigue, and encephalopathy.

Vitals

BP: 103/66

Heart rate: 92

Respiratory rate: 16

Temperature: 36.5

SpO2: 99

Physical exam

General: Patient is somnolent, but groans and spontaneously moving all 4 extremities, not oriented to time, place and person.

Eye: Pupils are equal, round and reactive to light

HENT: Normocephalic, Atraumatic, Oral mucosa is somewhat dry, No pharyngeal erythema, Ear canals patent, No sinus tenderness, No nasal discharge, a non tender - mobile swelling on the left posterior parietal area with no erythema

Respiratory: Lungs CTA bilaterally, No wheeze, Respirations are non-labored, Breath sounds are equal.

Cardiovascular: Regular rate, Regular rhythm, S1 auscultated, S2 auscultated, No click, No rub, Good pulses equal in all extremities, Normal peripheral perfusion, No edema.

Gastrointestinal: Soft, Non-tender, Non-distended, Normal bowel sounds.

Neurologic: Patient is in altered sensorium and responds to verbal commands, Symmetric facies, DTRs intact (no hyperreflexia) proximally and distally, No rigidity, No clonus, No repetitive movements

Motor: Moving all four limbs spontaneously. Plantar reflexes down-going bilaterally

CN: Light reflex present, pupils equal and reactive, rest could not be assessed.

Sensations: Pain perception is present.

Differential Diagnoses?

Differential Diagnosis for AMS

- Brain disorders
- Infectious causes
- Metabolic causes
- Electrolyte imbalances
- Psychiatric illness
- Drugs/toxins
  - Intoxication/Overdose
  - Withdrawal

Studies?

Studies?

CBC

CMP

Ammonia level

CT Head

Troponin

ABG

UA

UDS

Valproic acid level

CBC:

WBC: 5.5 (40% N, 46% L, 9% M, 3%E)

Hemoglobin: 13.9

Hematocrit: 44.3

Platelets: 134

MCV: 96.1

CMP

NA 144

K 4

Cl 106

CO2 31

BUN 20

Cr 0.7

Glucose 84

ALT 4

AST 8

Bilirubin total 0.4

Calcium 8.3

Albumin 3.3

Total protein 5.7

Alkaline phosphatase 53

Ammonia level

112

CT head

No acute intracranial hemorrhage or mass effect.

troponin

<0.04

ABG

Ph 7.35

Pco2 56

P02 60.9

HCo3 31.4

Base excess 4.5

O2 Sat: 92%

UDS

Negative for opiates, BZD, cocaine, methadone

UA

Clear, yellow

Glucose negative

Bilirubin negative

Ketones negative

Sp. gr. = 1.016

pH = 7.5

Blood negative

Protein negative

NItrite negative

LE negative

Valproic acid level

143

(Normal range 50-100)

Your plan of action?

Hypotension: IV fluids

Hyperammonemia: Carnitine

Respiratory and mental status: supportive care

Hospital Course

On initial encounter with the overnight resident, the patient was lying in bed, somnolent, and barely arousable. They were unable to elicit much history. His valproic acid levels came back elevated at 143 and he was started on L-carnitine and IV fluids. On subsequent encounter during rounds (after 1st dose of L-carnitine) patient was seen to be sitting up in the bed, was able to converse and follow commands. He received two doses of L-carnitine 6 hours apart until clinical improvement was seen. He was seen by psychiatry who recommended discontinuing all his psych medications and having him follow up with Psychiatrist outpatient. He was instructed to maintain good hydration.

Learning Objectives

- Work up of AMS secondary to drugs/overdose
    - Recognize classic toxidromes
- Mechanism of valproate toxicity
- Carnitine Mechanism

AMS Differentials

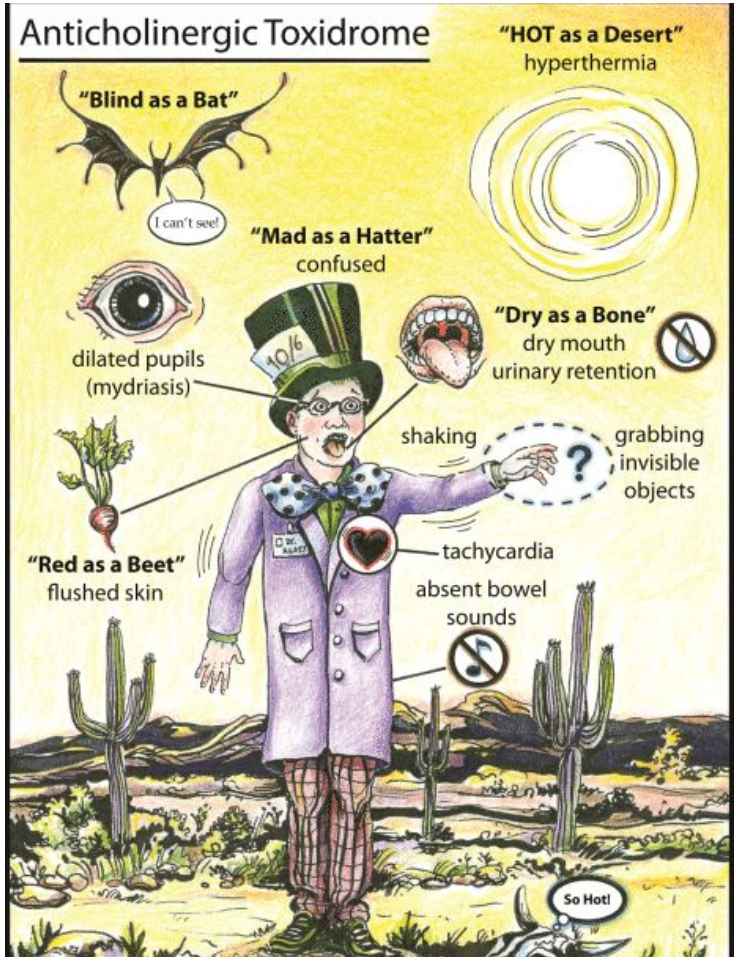
- Drugs/Toxins
- Infections
- Metabolic derangements
- Brain disorders
- Systemic organ failures
- Physical disorders

AMS Drug/Overdose Evaluation

- Starts with thorough history taking
- Often requires calling family members, caregivers, nursing homes, or friends
- In suspected medication/overdose etiology:
  - Identify name of drug(s) with dose and formulation (ER vs IR)
  - Number/quantity of drug
  - Time of ingestion
  - Chronic home med vs other person’s med

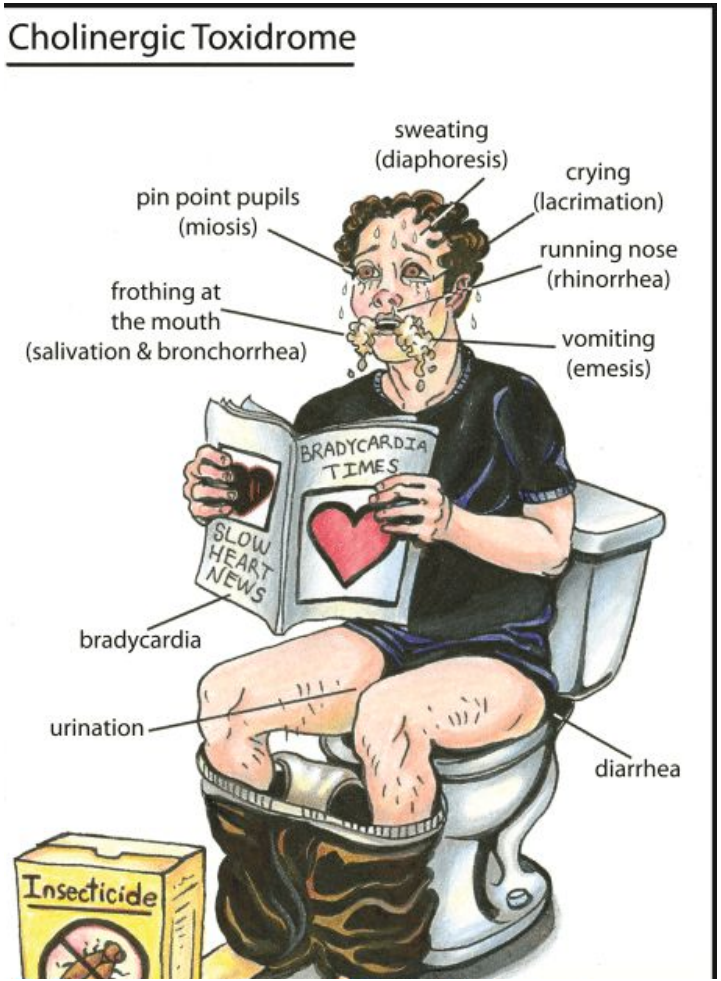
Anticholinergic

- Also HTN, tachycardic, and hyperthermic
- Antihistamines, psychotics, antidepressants, and antiparkinsonian medications



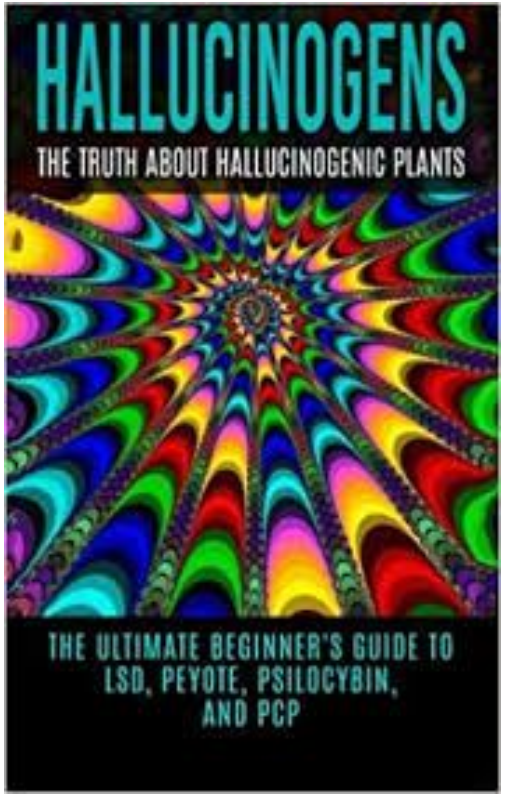
Cholinergic

- Also bradycardia, hypothermia, and tachypnea
- Organophosphates, mushrooms, and carbamates



Hallucinogenic

- Disorientation, hallucinations, hyperactive bowel sounds, panic, and seizures
- HTN, tachycardic, and tachypneic
- Designer amphetamines (Ecstasy), cocaine, PCP, LSD

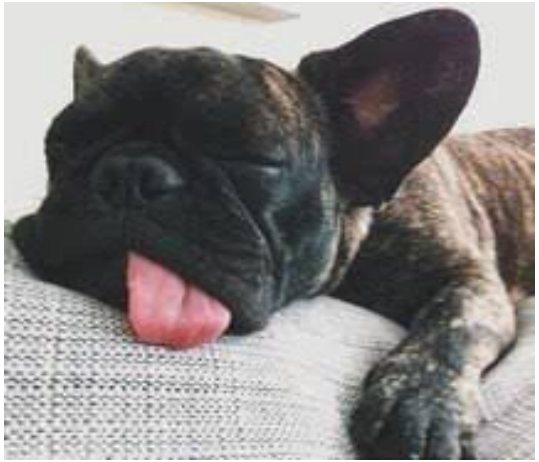


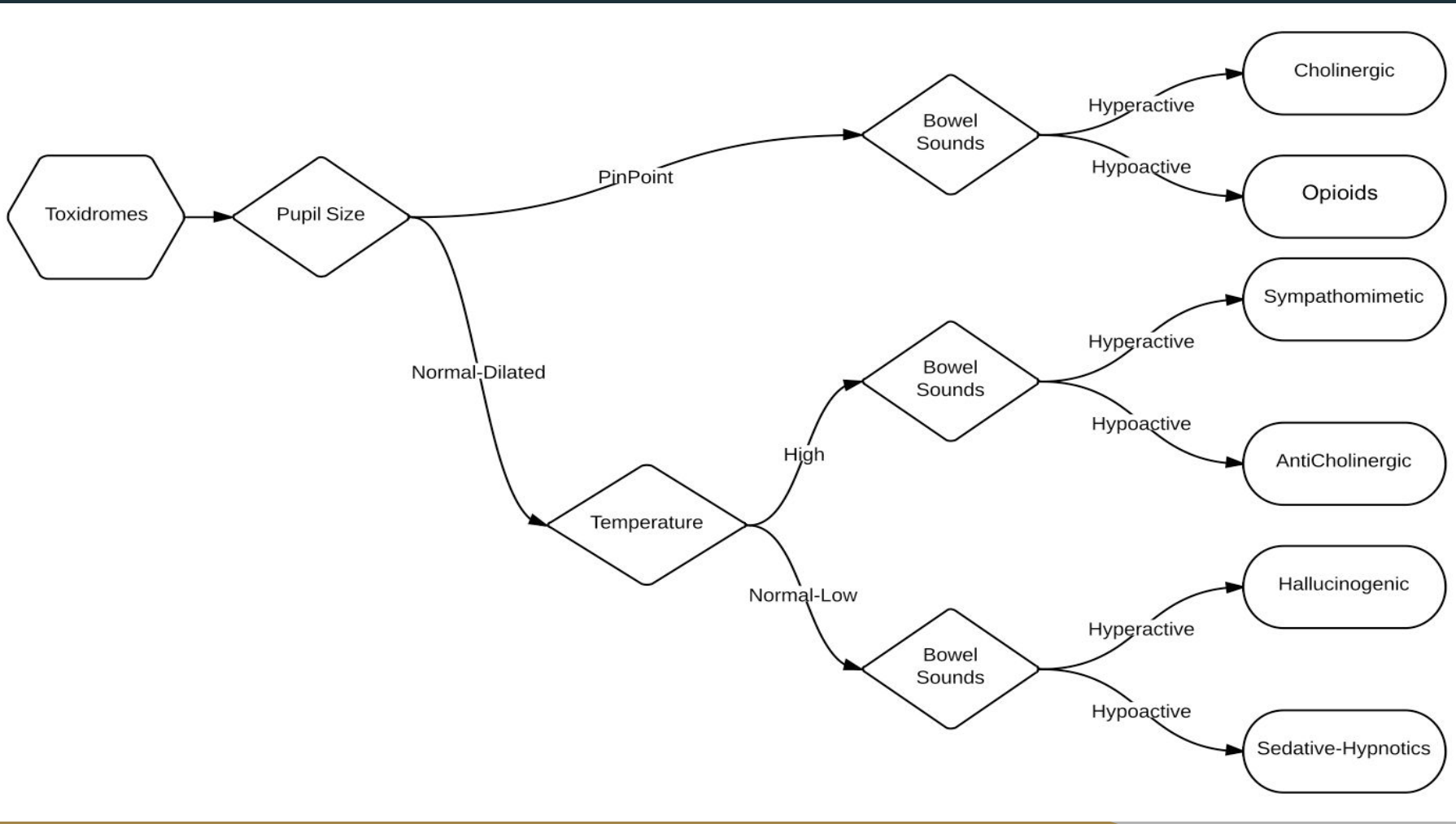
Sympathomimetic

- Anxiety, delusions, diaphoresis, hyperreflexia, mydriasis, paranoia, piloerection, and seizures
- HTN and tachycardia
- Similar to anticholinergic **BUT** has hyperactive bowel sounds and sweating
- Amphetamines, cocaine, ephedrine, pseudoephedrine, caffeine

Sedative/Hypnotic

- Ataxia, blurred vision, coma, confusion, delirium, sedation, slurred speech, hallucinations
- Can cause apnea
- Anticonvulsants, barbiturates, benzos, EtOH




Toxidromes
Pupil Size
PinPoint
Bowel Sounds
Hyperactive
Cholinergic
Hypoactive
Opioids
Normal-Dilated
Temperature
High
Bowel Sounds
Hyperactive
Sympathomimetic
Hypoactive
AntiCholinergic
Normal-Low
Bowel Sounds
Hyperactive
Hallucinogenic
Hypoactive
Sedative-Hypnotics

Symptoms	BP	HR	RR	Temp	Pupil size	Bowel sounds	Diaphoresis
anticholinergic	~	up	~	up	up	down	down
cholinergic	~	~	~	~	down	up	up
hallucinogenic	up	up	up	~	up	up	~
sympathomimetic	up	up	up	up	up	up	up
sedative-hypnotic	down	down	down	down	~	down	down

Valproic Acid

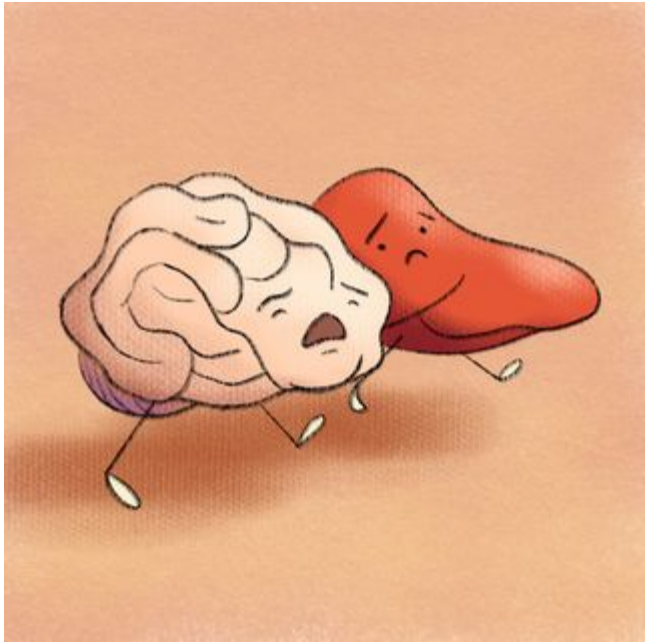
- Used to treat partial and generalized seizures, as well as acute mania, bipolar disorder, and migraines
- Increases GABA through inhibition of GABA transaminases and stimulation of GAD
  - Blocks Na channels at high doses and T-type Ca channels in thalamic region
- Typical therapeutic dosing
  - 500 mg-2 gm in adults
  - 15-60 mg/kg in childrens
- Peak concentrations occur after 1-4 hours for non-enteric and 4-5 hours in enteric coated formulations
- Therapeutic concentration ~50-100 mg/L
- Metabolized by liver by glucuronic acid conjugation and beta and omega oxidation
- Half-life ranges from 5-20 hours (mean 11 hours)

Valproate Toxicity

- CNS dysfunction is primary side effect
  - Ranges from mild drowsiness to coma or fatal cerebral edema
  - Onset and progression typically rapid
- Serum concentrations >180 mg/L usually causes CNS depression
- VS:
  - Respiratory depression, hypotension, tachycardia, hyperthermia
- Metabolic
  - Hyperammonemia, AGMA, hyperosmolality, hypernatremia, hypocalcemia
- GI:
  - N/V/D, mild toxic hepatitis
- Neuro:
  - Miosis, agitation, tremors, myoclonus

VPA Hyperammonemia

- May occur after acute overdose or chronic use
- Not always associated with abnormal LFTs
- Does not necessarily lead to clinical encephalopathy
  - Asymptomatic in ½ cases
- Likely related to propionic acid (VPA metabolite) which inhibits mitochondrial carbamoyl phosphate synthetase (enzyme required for ammonia elimination in urea cycle)
- May also interact with carnitine (cofactor for mitochondrial long-chain fatty acid metabolism)
  - With relative carnitine deficiency, VPA metabolism increases by omega oxidation
  - These products also inhibit carbamoyl phosphate synthetase
- Typical ammonia levels in VPA-associated encephalopathy range from 127-482 mcg/dL



Treatment

- GI decontamination
  - Single dose activated charcoal (1 g/kg; max 50 g)
- Supportive care
  - Airway protection, volume resuscitation
- Carnitine
  - 100 mg/kg IV over 30 minutes (max dose 6 gm)
  - Then 50 mg/kg IV (max 3 gm) q 8 hours

Carnitine

- May give for patient with coma, severe hepatotoxicity, VPA serum concentration >450 mcg/mL, or VPA related hyperammonemic encephalopathy
- Continue treatment until clinic signs of severe poisoning resolve

Take Aways

- Use physical exam and detailed history to determine toxidromes
- Recognize hyperammonemic encephalopathy in patients taking valproic acid
- Consider carnitine for valproic acid toxicities

Thank you