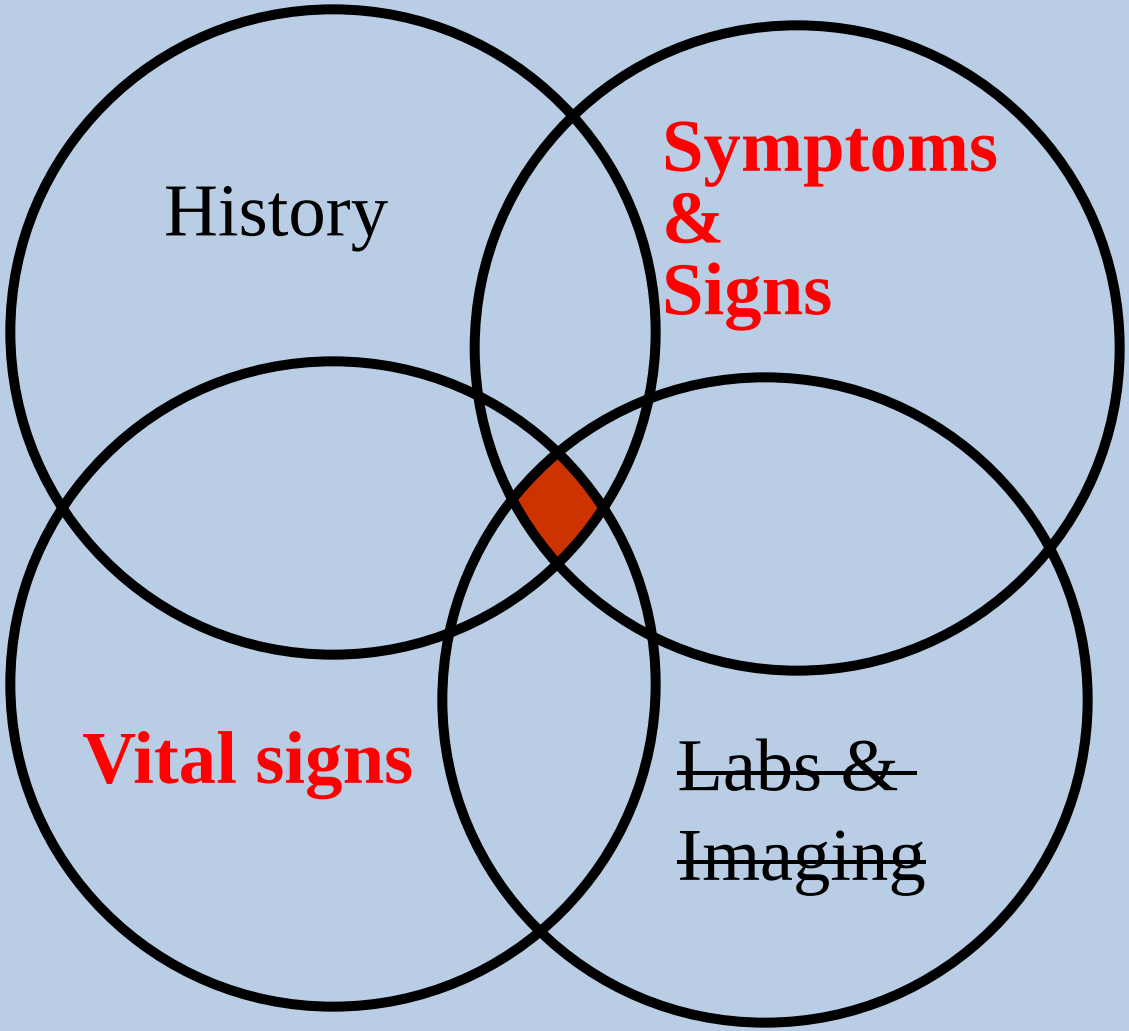
Toxidromes

Toxi-what?

- Toxidrome
  - Portmanteau of “toxic syndrome”
  - It is a constellation of commonly seen features and exam findings that are typical for certain types of poisonings

Toxidrome



OMG! Toxidromes r my fav!

- Interesting physical exam findings
- A careful history & physical usually gives enough clues to get the answer
- Don’t require labs, CTs, MRIs, or tricorders


PWR
SYS
DATA
SENSE
ALPHA
BETA
GAMMA
DELTA
LIBRARY
A
B
DEVICE INPUT
GEO
MET
BIO
COM TRANSMISSION
ACPT
POOL
INTRSHP
TRICRDR
EMRG
IMAGE RECORD
FWD
INPUT
RVS
ERASE
LIBRARY
ID
TR-580 TRICORDER VII
STARFLEET R&D-SAN FRANCISCO

Poison versus Medicine

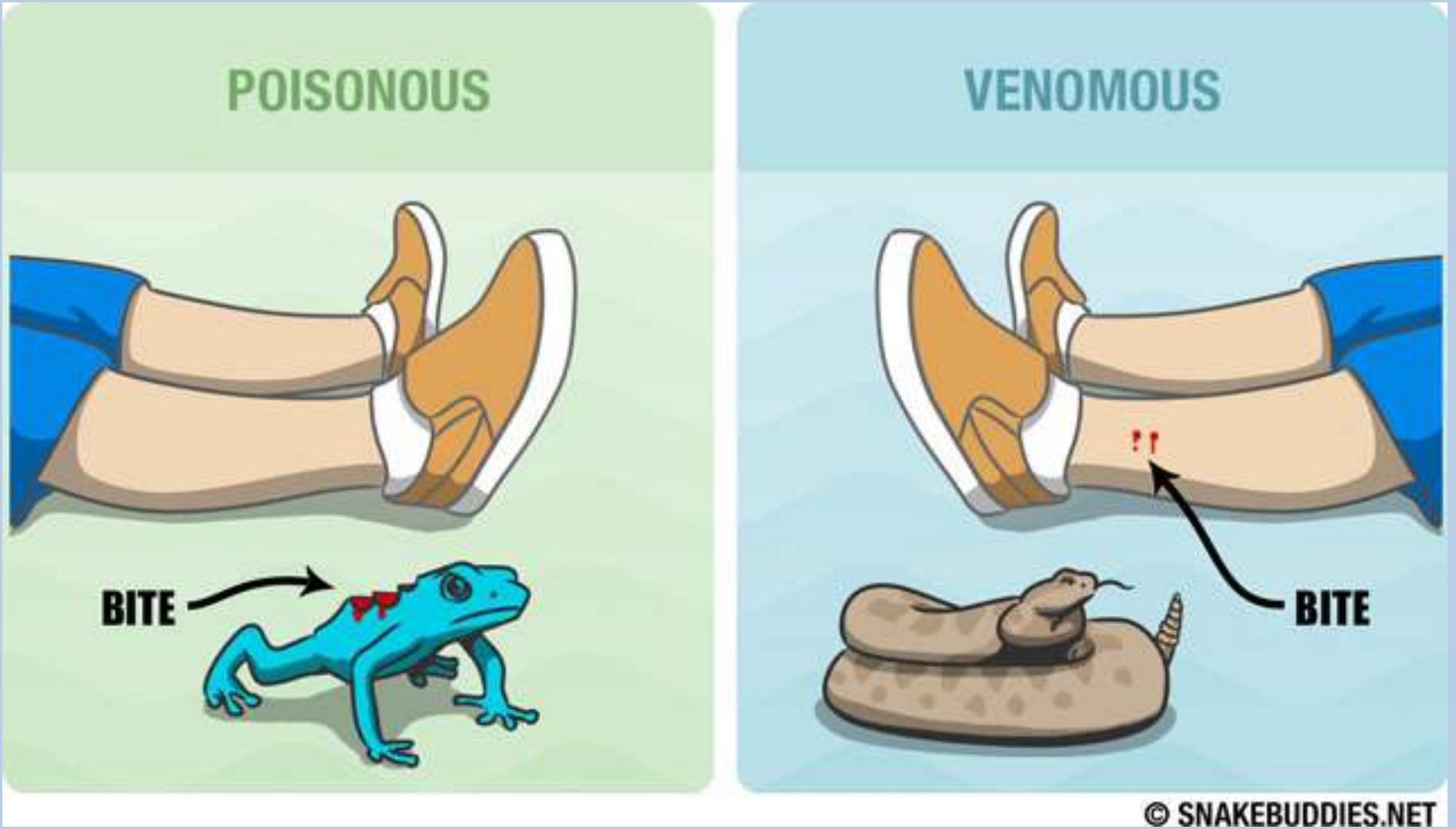
- The dose is the difference…alcohol!

- Nearly all medications are poisons that are sometimes helpful at a very low dose
  - Diphenhydramine (Benadryl) – anti-cholinergic
  - Aspirin – blocks the COX enzyme, poisons platelets

Philip Theophrastus Bombast von Hohenheim
aka PARACELSUS (1493-1541)

"What is there that is not poison? All things are poison and nothing [is] without poison. It is only the dose determines whether something is or is not a poison."

Poison versus Venom



Taipan Snake

Goals

- Overview of the most common toxidromes
- Excited Delirium
- Diagnostic pitfalls of toxidromes
- Working as a team for patient care
  - History
  - Vitals
  - Treatment

Anticholinergic Syndrome

Cholinergic Syndrome

Sympathomimetic Syndrome

Opioid / Ethanol / Sedative Toxidrome

First Case – Rave Gone Bad

20ish year old female brought in by ambulance from a party/rave. No eyewitnesses to events (they all fled). Patient is very confused and all of her muscles are rigid.

PMH/PSH: Unknown
Meds: Unknown
Allergies: Unknown
All other questions:
Unknown

Case 1: Physical Exam

VS: **T 41.4** HR 180 BP 196/130

HEENT: Pupils dilated and unreactive. Upper left deviated gaze, copious oral secretions

Lungs: symmetric bilateral chronic

Heart: Tachycardic

Abd: Normal, nontender

Neuro: Appears to be rigid, tonic seizures?

Skin: Piloerection

Case 1

- Patient though to be in status epilepticus
- Valium 30mg, Ativan 20mg, intubated, sedated
- Cooling protocol initiated
- Propofol drip for status epilepticus
- Mother arrives and tells us that the patient was 16-years old when she went her first party

What Did This Patient Take?

- Methamphetamines?
- Ecstasy?
- Cocaine?
- Ma-huang?
- All of the Above?

Anticholinergic Syndrome

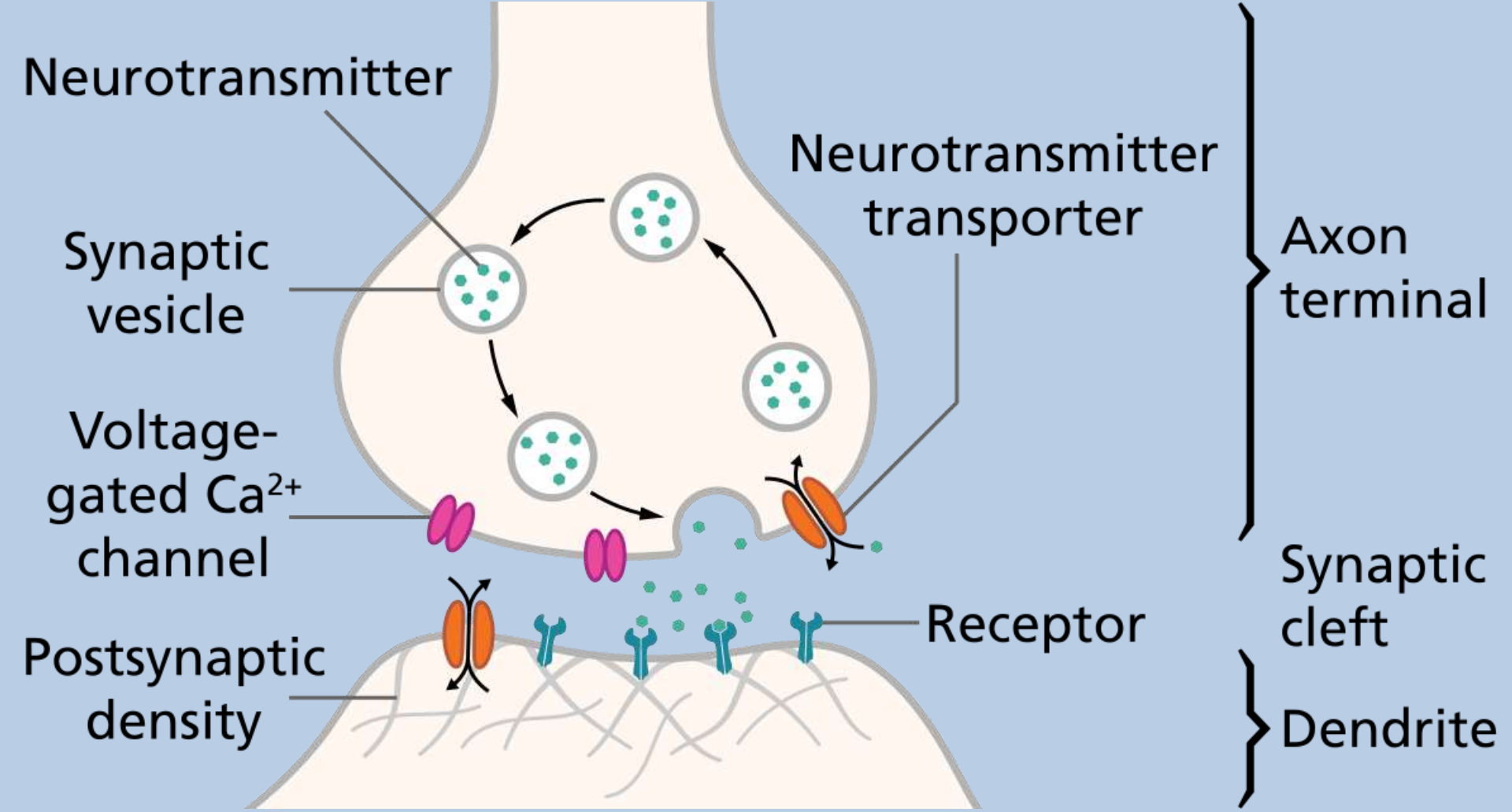
Cholinergic Syndrome

Sympathomimetic Syndrome

Opioid / Ethanol /
Sedative Toxidrome

Effects of Amphetamines

- Increase neurotransmission in central noradrenaline, dopamine and serotonin systems
- Effect varies by particular drug (e.g. increased serotonin causes increased hallucinogenic effect)



Schematic of Neuronal Synapse

Signs and Symptoms of Sympathomimetics

- Mild
  - Euphoria
  - Incr alertness
  - **Bruxism**
  - AMS
  - Tachycardia
  - Hypertension
  - Hyper-reflexia
  - Tremors
- Moderate
  - Agitation
  - Paranoia
  - Hallucination
  - **Diaphoresis**
  - Vomiting
  - Abd pain
  - Palpitations
  - Chest pain

Signs and Symptoms of Sympathomimetics

- Severe
  - **Hyperthermia**
  - Ischemia/vascular rupture
  - Metabolic acidosis
  - Rhabdomyolysis
  - Hyperkalemia
  - Acute Renal Failure
  - Coma
  - Death

Case 1 – Further History

An acquaintance calls the mother and states that patient took hit after hit of a combination of “speed” and “X” because she wasn’t noting an effect.

What are their names?

- Amphetamine
- Methamphetamine (“P” = “pure” crystal meth
- MDMA, Ecstasy, XTC
- MDA, Love Drug
- MDEA, Eve
- PMA
- MBDB
- TMA-2
- DOM/STP, Serenity, Peace, Tranquility
- DOB
- 2CB, MFT
- Khat, cat, quat, gat, jeff
- Ephedrine

Plant-derived Stimulants

- Khat (Catha edulis)
  - Cathine (norpseudoephedrine)

- Ma-huang (Ephedra ma-huang)

- Peyote cactus (Lophophora williamsii)
  - Mescaline

Pitfalls of Sympathomimetics

Patient's presentation can appear to be due to mental illness rather than sympathomimetic.

Consider restraints for safety of patient & staff.

Vital signs are vital; they are crucial in determining severity of overdose and toxicity.

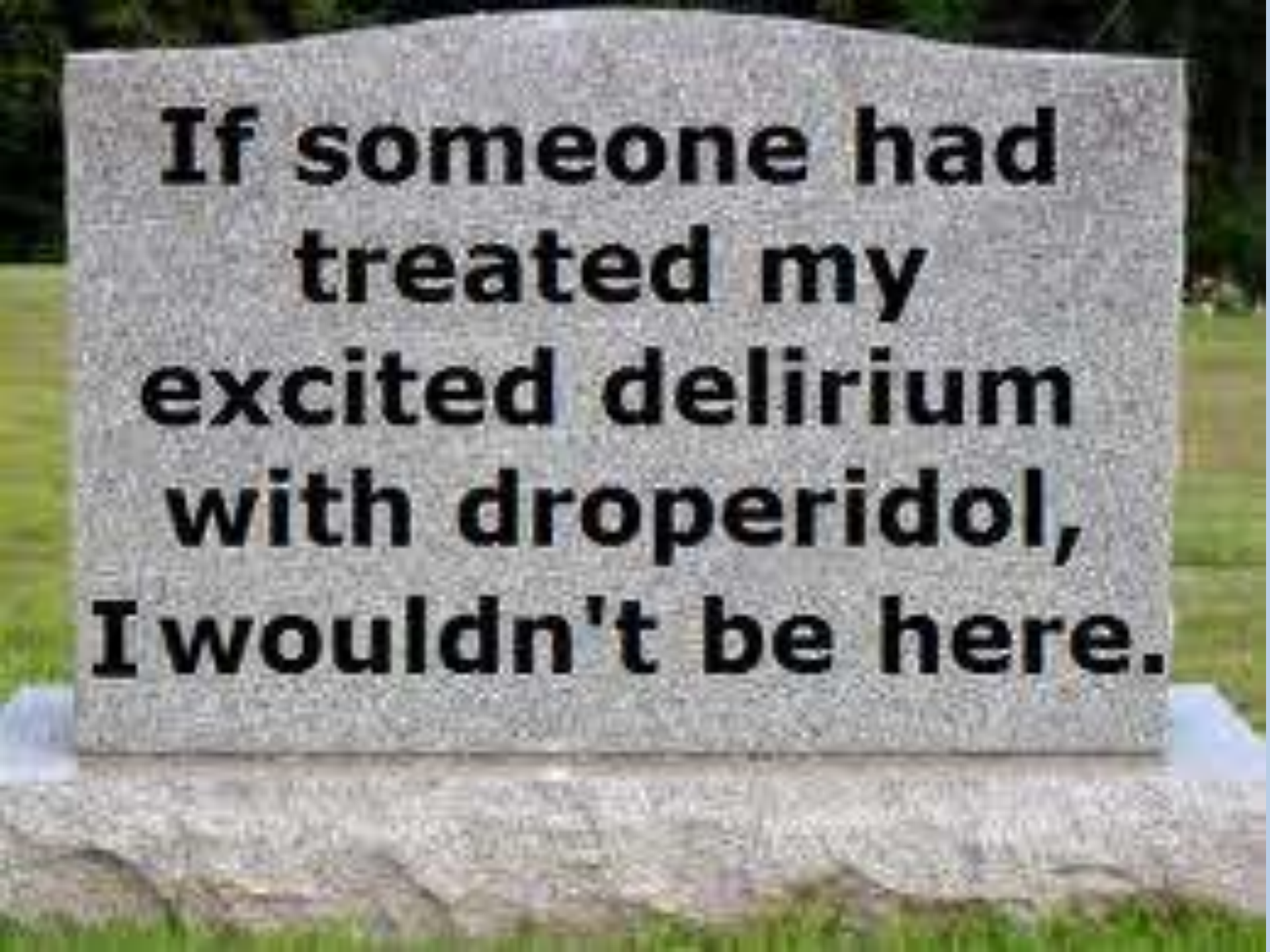
Excited Delirium

- Associated with PCP, cocaine, meth
- Essentially an extreme sympathomimetic toxidrome

Some think that cardiac irritability from stimulants can predispose to cardiac arrest in Tazing.

Excited Delirium

- General anesthetics still work
- Paralytics will still lead to full muscular atony


If someone had
treated my
excited delirium
with droperidol,
I wouldn't be here.

Case 2

HPI: 35-year old female with history of bipolar disease brought in by husband with AMS. She is unable to provide a history, but husband states she has been ill recently with a URI. He states all pill bottles are accounted for and the patient has no history of suicide attempts.

PMH: Bipolar disease, borderline PD, chronic low back pain, sciatica, PTSD

SH: Smokes ½ PPD, occasional EtOH, no illicits

Case 2 – Physical Exam

VS: HR 120, BP 150/90, Temp 38.5, RR 30

Gen: Flushed-appearing, confused

Pupils: **Dilated, sluggish**

Chest: clear bilaterally

CV: Tachy, no murmur

Abd: slightly distended, **no bowel sounds**

Neuro: Increased muscle tone globally

Case 2 – ED Course

- EKG: frequent ectopy
- CTH – normal
- Foley placed –
  - 900mL out
- Husband brings med list
  - Zyprexa
  - Amitryptiline (new for sciatica)
  - Multivitamin
  - Vicodin
  - Flexeril
  - Hydroxyzine
  - OTC Benadryl for URI & sleep

What Did this Patient Take?

- Methamphetamine
- Multivitamin
- Diphenhydramine (Benadryl)
- Pesticide

Anticholinergic Syndrome

Cholinergic Syndrome

Sympathomimetic Syndrome

Opioid / Ethanol /
Sedative Toxidrome

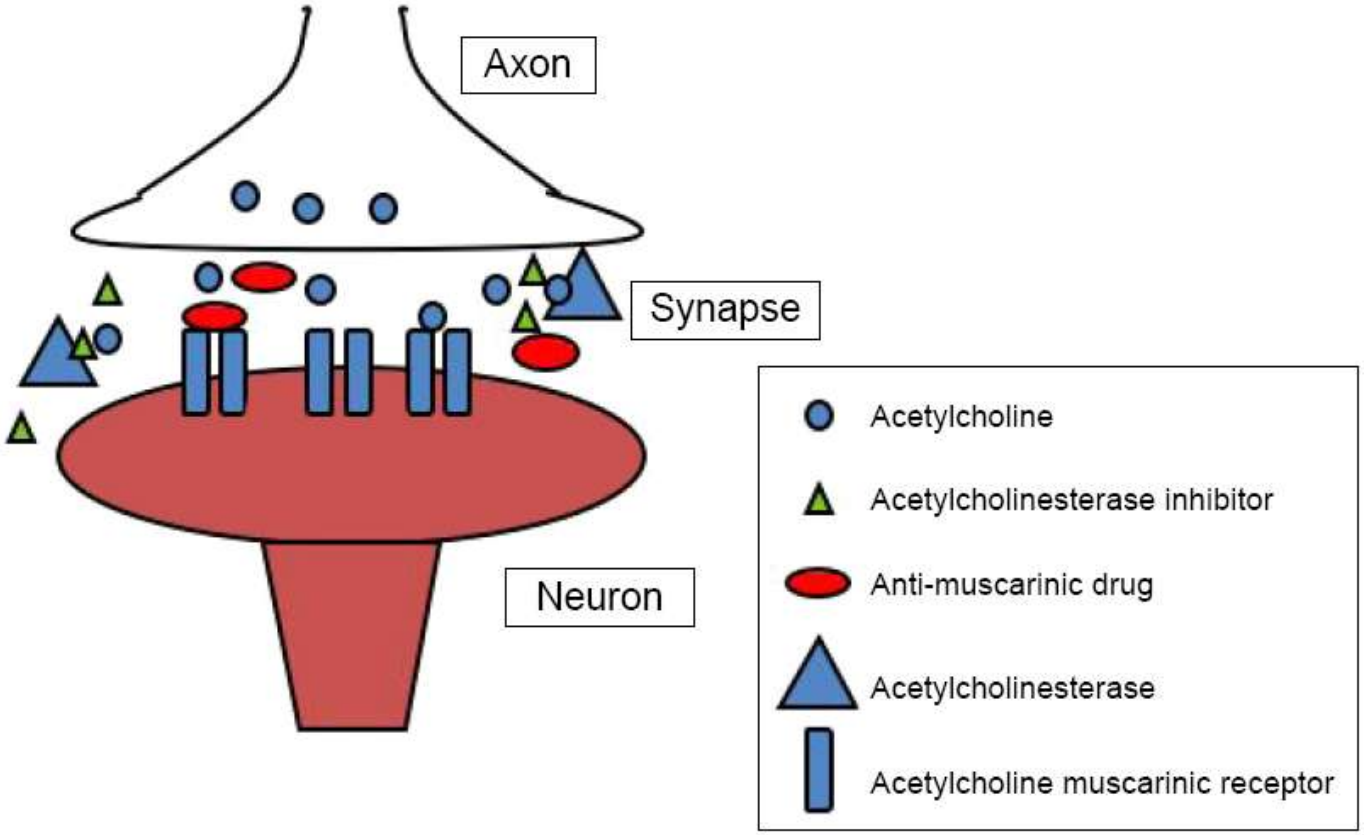


Figure 1 Pharmacodynamic drug–drug interaction in a cholinergic synapse: acetylcholinesterase inhibitor (AChEI) and anti-muscarinic drug.
Notes: The concomitant administration of AChEIs (green triangles) and anticholinergic drugs may result in a pharmacodynamic interaction in the synapse where the beneficial increment of acetyl-choline (blue circle), related to AChE (blue triangles) inhibition, is at least partially reversed by anti-muscarinic drugs (red ellipse) at receptor levels (blue bars).

Anticholinergics block the muscarinic receptors to prevent interaction with acetylcholine

Anticholinergic Toxidrome

Signs and Symptoms

Delirium

Tachycardia

Dry, flushed skin

Mydriasis

Myoclonus

Hyperthermia

Urinary retention

Decreased bowel sounds

Seizures

Dysrhythmias

Anticholinergic Toxidrome

Mad as a Hatter

Hot as a Hare

Blind as a Bat

Dry as a Bone

Red as a Beet

Bloated as a Bladder

Tachy as a Squirrel

Case 2 – Hospital Course

Patient admitted to ICU for supportive care

Repeat doses of ativan

After 5 days, improved

Determined to be a combination of diphenhydramine with other anticholinergics

Anticholinergic Drugs

- Antihistamines: hydroxyzine, benadryl, meclizine
- Neuroleptics: thorazine, seroquel, zyprexa
- Tricyclic antidepressants: amitriptyline, doxepin
- Antiparkinsonian drugs: benztropine
- Ophthalmic drugs: atropine
- Antispasmodics: oxybutynin, cyclomine
- Plants: Jimson Weed, Deadly Nightshade

Serotonin Syndrome

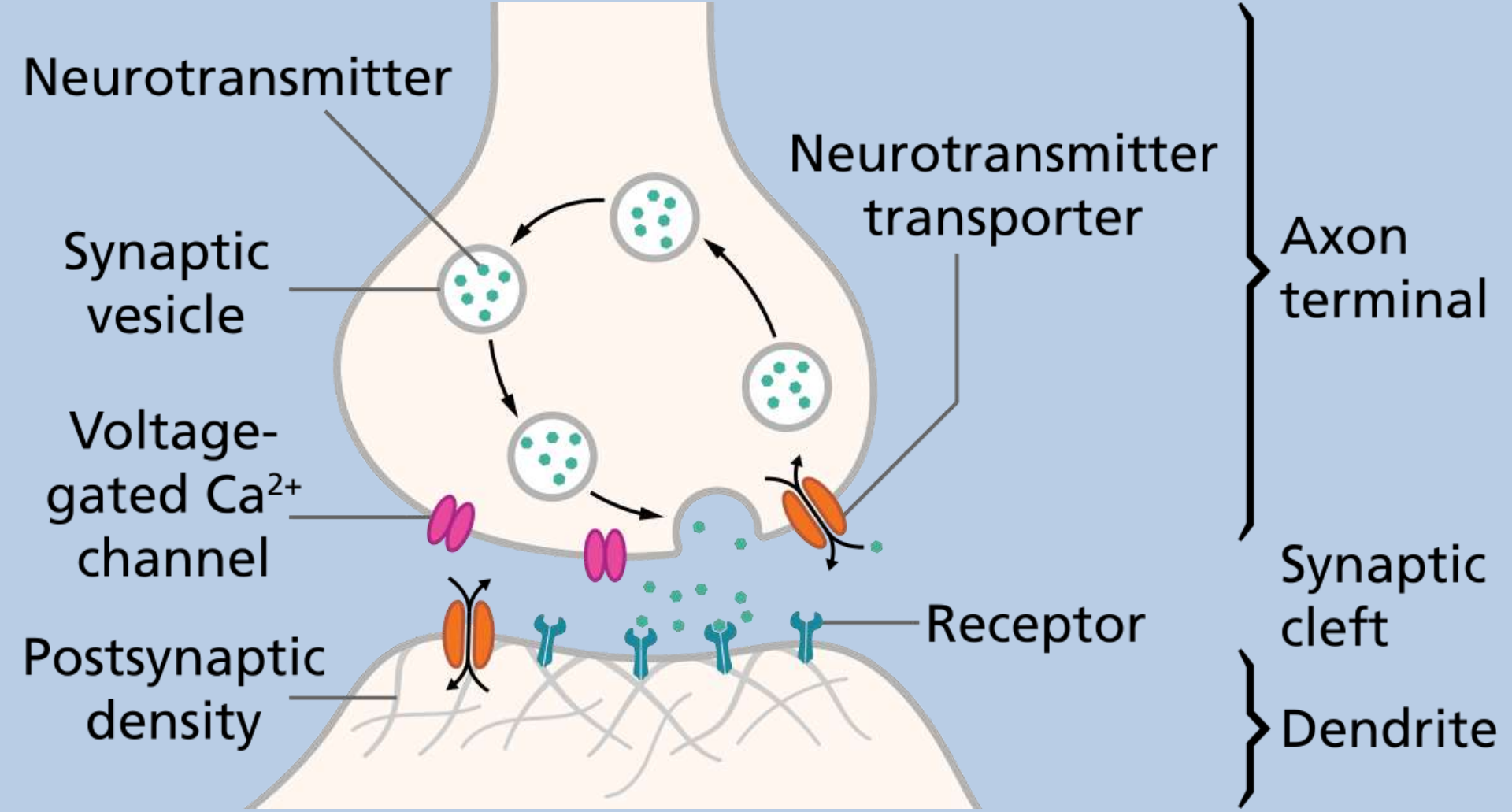
- Spontaneous **clonus**
- Inducible **clonus** PLUS agitation or **diaphoresis**
- Ocular **clonus** PLUS agitation or diaphoresis
- Tremor PLUS **hyperreflexia**
- Hypertonia PLUS temperature above 38ºC PLUS ocular **clonus** or inducible **clonus**

Appears similar to anticholinergic or stimulant overdose.

The Slippery Slope of Medications

Polypharmacy

Serotonin Syndrome



Schematic of Neuronal Synapse

Serotonin Syndrome

@PANDORASPILMAN #EMB

What Drugs Cause It?

TCAs · Triptans · SSRIs · MAOIs · 5HT3 antagonists · Amphetamines · Cocaine · SNRIs · Linezolid · MDMA · St. John's Wort · Tramadol

* more likely to occur if exposure to 2 or more drugs *

Features

ALTERED MENTAL STATUS

AUTONOMIC INSTABILITY

NEUROMUSCULAR HYPERACTIVITY

Management

Convulsions

- 1st line = lorazepam 4mg IV
- may require repeat dose of benzodiazepines
- 2nd line = barbiturates
  - ↳ phenobarbitol sodium 10mg/kg. Max rate 100mg/min. Max dose 1g

Agitation and Delerium

- 1st line = diazepam (PO/IV) 0.1-0.3mg/kg
  - ↳ repeat dose IV can be given after 10-15 mins if patient remains agitated
- 2nd line = Haloperidol 5-10mg PO or 2-10mg IV
  - * CONTRAINDICATED IN PARKINSONS DISEASE *
- severe cases - consider chlorpromazine 12.5-25mg IV

Hyperthermia

- temperature monitoring if >39°C via rectal probe
- cooling methods → Ice baths
  - → Internal/invasive
  - → Ice packs
  - → mist + fan
- may need intubation and paralysis

DANTROLENE 1mg/kg IV to max 10mg/kg → If muscular hyperactivity

Rhabdomyolysis

- when CK 5 times upper limit of normal
- commence IV fluids
- consider urine alkalinization
  - ↳ 225ml of 8.4% sodium bicarbonate over 1hr
- consider haemofiltration

Case 3

HPI: 35-year old Spanish-speaking only patient brought in by friends with AMS. He is unable to provide a history. Friends state he just started acting funny. They do not believe he was recently partying.

PMH: None

PSH: Appendectomy

SH: Moves between Mexico, OR and WA; migrant farm worker.

Case 3 – Physical Exam

PE: T 35.2 P 48 BP 100/40 RR 30

Gen: altered, confused, calm, intermittently vomiting

HEENT: Pupils 2mm bilaterally, tears running from eyes, hypersalivation

Chest: fine rales bilaterally, tachypneic

CV: bradycardic, no murmur

Abd: Soft, nontender, fecal incontinence

Neuro: Sleepy-appearing, moves all extremities

Skin: Diaphoretic

What Did this Patient Take?

- Heroin withdrawal
- Mushroom ingestion
- Organophosphate ingestion
- Accidental organophosphate exposure

Anticholinergic Syndrome

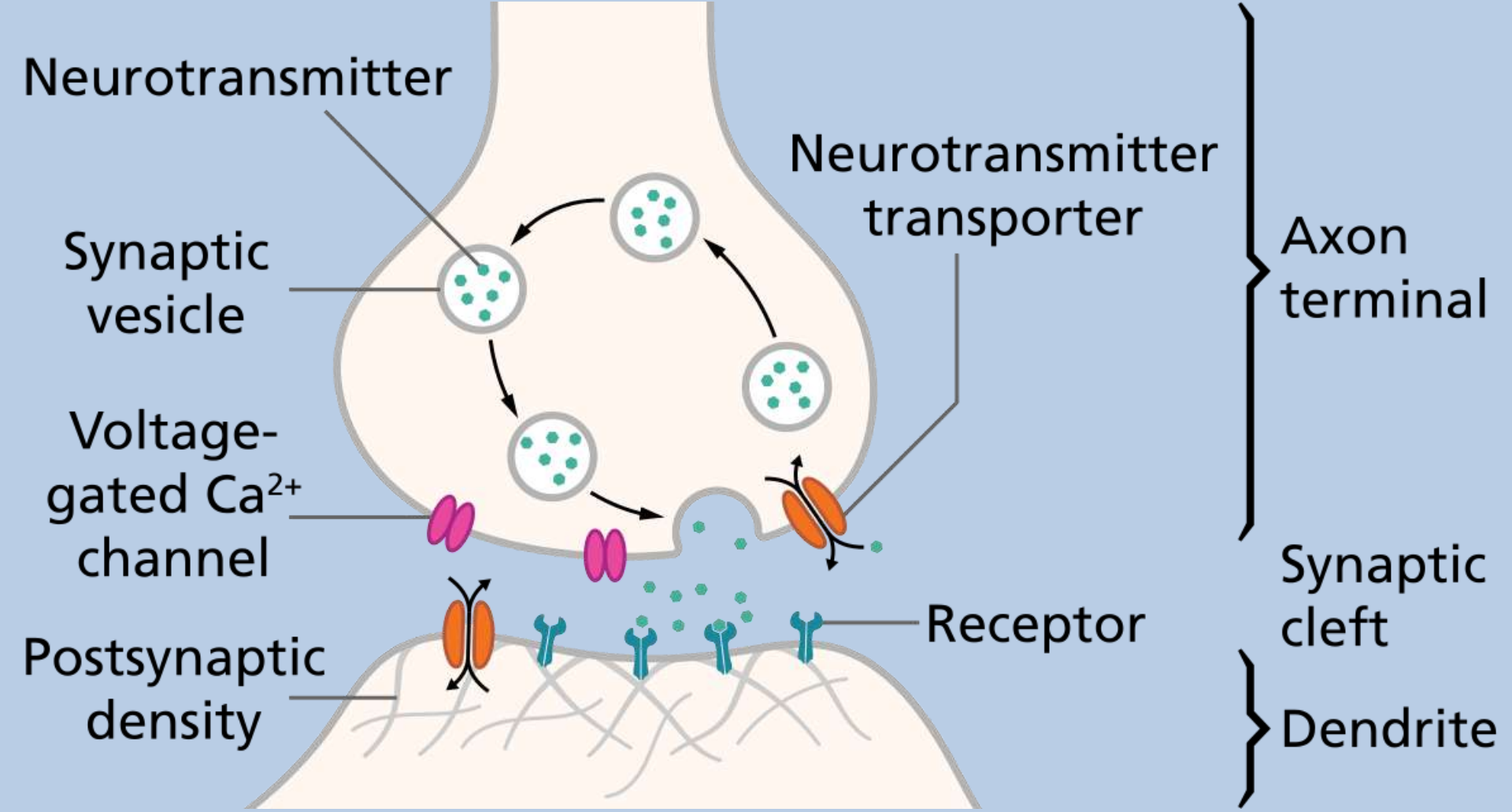
Cholinergic Syndrome

Sympathomimetic Syndrome

Opioid / Ethanol /
Sedative Toxidrome

Organophosphates

- In the U.S. more than 18,000 products are licensed for use
- Each year, more than 2 billion pounds of pesticides on crops, homes, schools, parks, and forests
- Number one cause of suicide in the developing world
- China – 170,000 deaths per year, mostly deliberate



Schematic of Neuronal Synapse

Mechanism - Inhibition of Acetycholinesterase

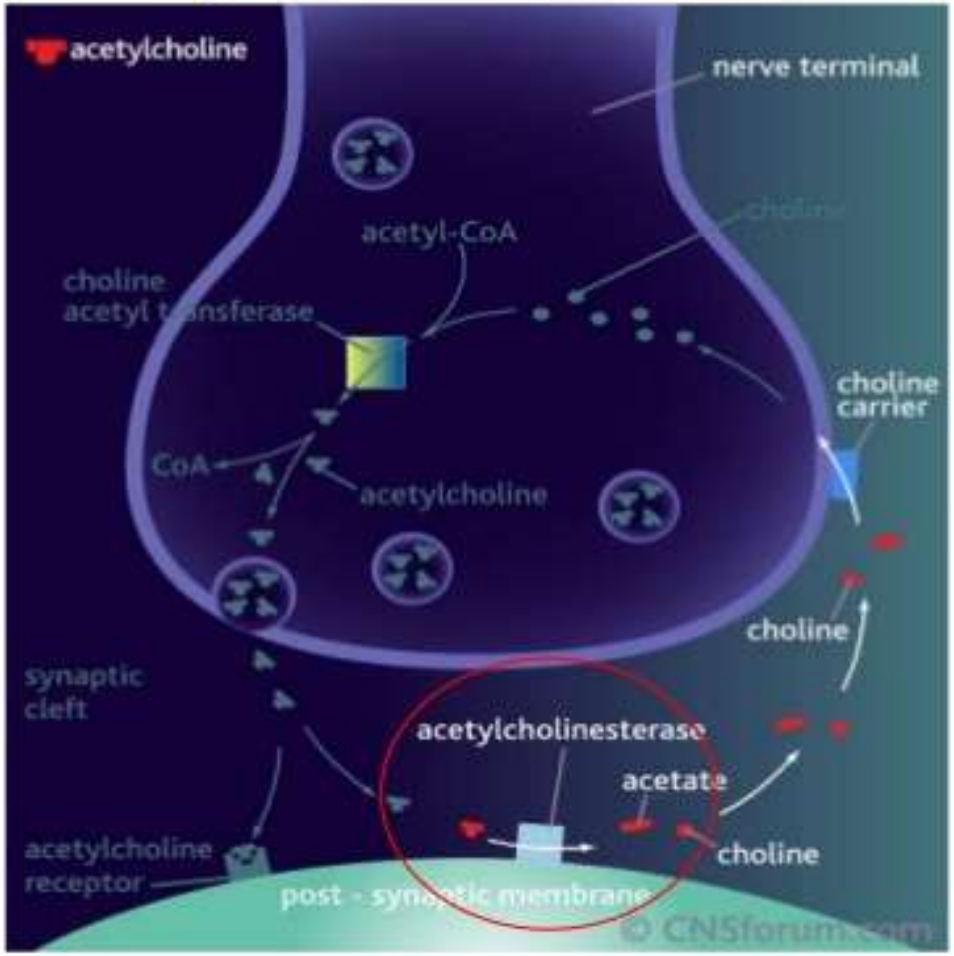
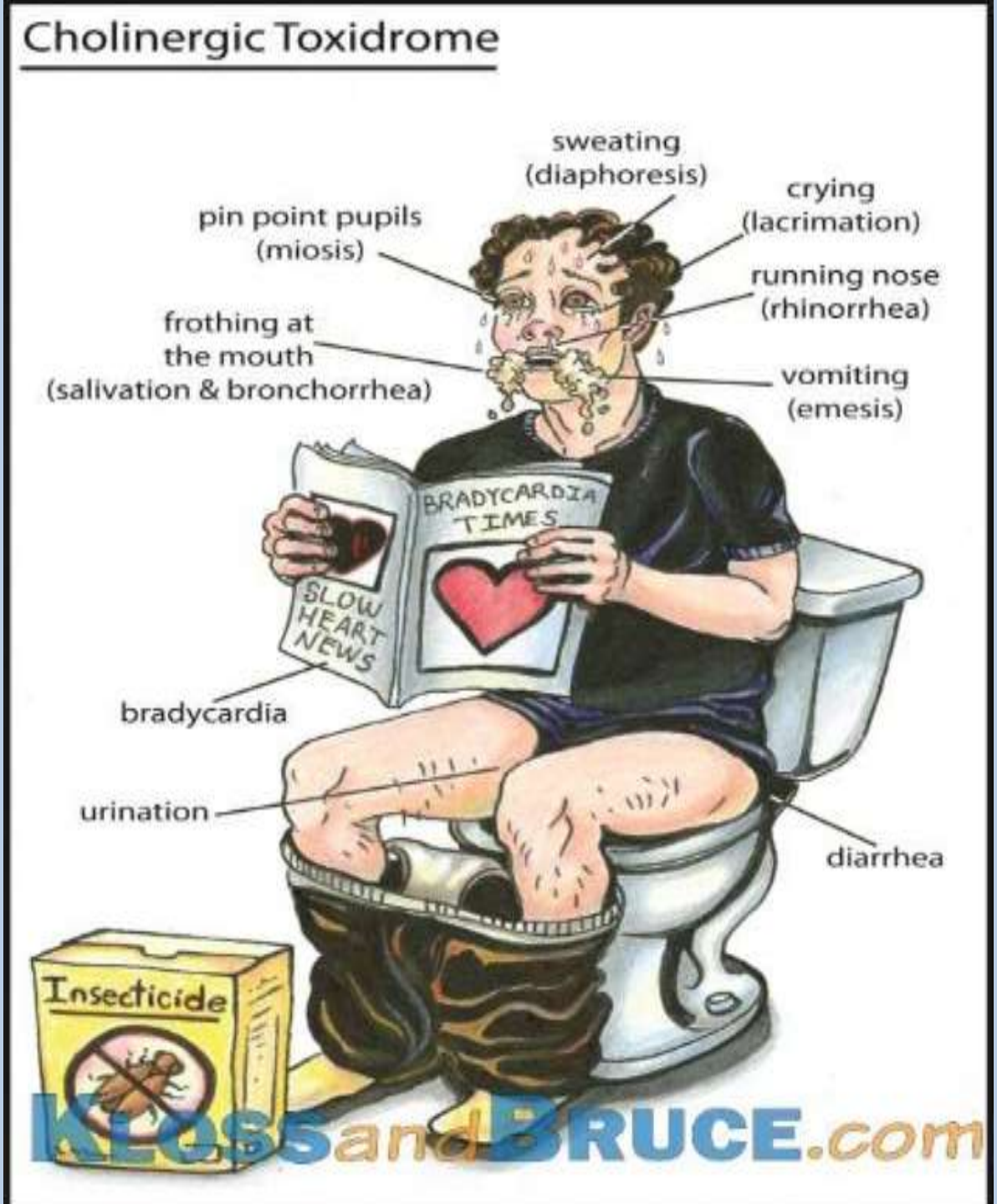


Image accessed from CNSForum.com

Cholinergic Toxidrome



Cholinergic Toxidrome

Mechanism

Overstimulation of cholinergic receptors

Signs and Symptoms

Confusion

CNS Depression

Miosis

Weakness

Salivation

Lacrimation

Pulmonary edema

Urinary/fecal incontinence

GI cramping

Emesis

Diaphoresis

Bradycardia

Seizures

Cholinergic Toxidrome

Mnemonics for muscarinic effects

D	Diarrhea
U	Urination
M	Miosis
B	Bronchorrhea/Bradycardia/Bronchospasm
E	Emesis
L	Lacrimation
S	Salivation

S	Salivation
L	Lacrimation
U	Urination
D	Diarrhea
G	Gastrointestinal upset
E	Emesis

Case 3 – ED Course

- Patient given escalating doses of atropine to control secretions
- Intubated
- Admitted to ICU

Opioid / Ethanol / Sedative Toxidrome

Signs and symptoms

Coma

Respiratory depression

Pupils are small (miosis)

Hypotension

Bradycardia

Hypothermia

Pulmonary edema

Decreased bowel sounds

Hypo-reflexia

Intoxication versus Withdrawal

- Sedatives cause everything to slow down during intoxication
- Most sedatives have significant withdrawal
- Everything speeds up during withdrawal

Sedative Highlights

- Response to naloxone (Narcan) is NOT diagnostic of opiate overdose
- Many opiates have a longer half-life than naloxone or other reversal agents; rebound apnea when it wears off
- Although very rare, you CAN die from acute severe opiate withdrawal

Sedative Highlights

- Seizures from alcohol withdrawal can occasionally require INSANE doses of benzodiazepines.

- Don’t be afraid to intubate, especially very early in acute intoxication.

Sedative Highlights

- Check the blood glucose
- Consider possibility of other alcohols
  - Isopropyl alcohol
  - Ethylene glycol
  - Methanol

Sedative Highlights

- Do NOT give flumazenil for benzodiazepine OD
- Stimulant withdrawal ≈ sedative overdose
- Sedative withdrawal ≈ stimulant overdose

Anticholinergic Syndrome

Cholinergic Syndrome

Sympathomimetic Syndrome

Opioid / Ethanol / Sedative Toxidrome

Last Minute Tips

- Benzos are good for everyone except for sedative overdose
- Supportive care for everyone (IV fluids, intubate prn, sedation)
- Dry vs. diaphoretic? Hyper-reflexia? Pupils big or small? Vomiting/Diarrhea vs no bowel sounds?

Last Minute Tips

- Bradycardia: sedative, cholinergic
- Tachycardia: everything else
- Withdrawals give opposite of toxic syndrome

Last Minute Tips

- Check the blood glucose
- Don’t be afraid to intubate
- Flumazenil is bad