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

- History
- Symptoms & Signs
- Vital signs
- Labs & Imaging
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
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

- Poisonous: The lizard delivers poison through its bite.
- Venomous: The snake delivers venom through its bite, showing the effect on the person's leg.
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

- Neurotransmitter
- Synaptic vesicle
- Voltage-gated Ca\(^{2+}\) channel
- Postsynaptic density
- Neurotransmitter transporter
- Receptor
- Axon terminal
- Synaptic cleft
- Dendrite

Schematic of Neuronal Synapse
# Signs and Symptoms of Sympathomimetics

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
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<tbody>
<tr>
<td>Euphoria</td>
<td>Agitation</td>
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<tr>
<td>InCREASED alertness</td>
<td>Paranoia</td>
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<tr>
<td><strong>Bruxism</strong></td>
<td>Hallucination</td>
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<tr>
<td>AMS</td>
<td><strong>Diaphoresis</strong></td>
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<tr>
<td>Tachycardia</td>
<td>Vomiting</td>
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<tr>
<td>Hypertension</td>
<td>Abd pain</td>
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<tr>
<td>Hyper-reflexia</td>
<td>Palpitations</td>
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<tr>
<td>Tremors</td>
<td>Chest pain</td>
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</tbody>
</table>

- **Mild** symptoms include mild euphoria, increased alertness, bruxism, AMS, tachycardia, hypertension, hyper-reflexia, and tremors.
- **Moderate** symptoms include agitation, paranoia, hallucination, diaphoresis, vomiting, abdominal pain, palpitations, and 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 toxi-drome

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
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

- Neurotransmitter
- Synaptic vesicle
- Voltage-gated Ca\(^{2+}\) channel
- Postsynaptic density
- Neurotransmitter transporter
- Axon terminal
- Synaptic cleft
- Dendrite

Schematic of Neuronal Synapse
SEROTONIN SYNDROME

@PANDORASPILMAN #EMB

**What Drugs Cause It?**
- TCA*
- Triptans
- SSRIs
- MAOIs
- 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
- Agitation
- Confusion
- Delirium
- Hallucinations
- Tachycardia
- Fever
- Flushing
- Hyper/hypotension
- Shivering
- Teeth grinding
- Hyperreflexia
- Myoclonus
- Autonomic instability
- Neuromuscular hyperactivity

**Agitation and Delirium**
- 1st line: lorazepam 1mg IV
- May require repeat dose of benzodiazepines
- 2nd line: barbiturates by phenobarbital sodium
  1mg/kg. Max rate: 30mg/min. Max dose: 1500mg

**Convulsions**
- 1st line: lorazepam 1mg IV
- May require repeat dose of benzodiazepines
- 2nd line: barbiturates by phenobarbital sodium
  1mg/kg. Max rate: 30mg/min. Max dose: 1500mg

**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
  - IV 1mg/kg up to 10mg/kg

**Rhabdomyolysis**
- When CK, 5 times upper limit of normal
- Commence IV fluids
- Consider urine alkalization by 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

Neurotransmitter

Synaptic vesicle

Voltage-gated $\text{Ca}^{2+}$ channel

Postsynaptic density

Neurotransmitter transporter

Axon terminal

Synaptic cleft

Dendrite

Receptor

Schematic of Neuronal Synapse
Mechanism - Inhibition of Acetylcholinesterase
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

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<thead>
<tr>
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<th>Effect</th>
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<tbody>
<tr>
<td>D</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>U</td>
<td>Urination</td>
</tr>
<tr>
<td>M</td>
<td>Miosis</td>
</tr>
<tr>
<td>B</td>
<td>Bronchorrhea/Bradycardia/Bronchospasm</td>
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<td>Emesis</td>
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<tr>
<td>G</td>
<td>Gastrointestinal upset</td>
</tr>
<tr>
<td>E</td>
<td>Emesis</td>
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</table>
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
BAYER
PHARMACEUTICAL
PRODUCTS.

Send for samples
and Literature to

ASPIRIN
The substitute for
the salicylates

APRISTOL
ARISTOL
The analgesic and
constituent

PROTARGOL
Protargol
The antiseptic

CRYPTOS CURB
CRYPTOCUR
The salicylic and
constituent

SULFONAL
Sulfonald
The anti-constituent

QUINALGEN
Quinalgen
The anti-cough

EUROPHEN
Europhen
The anti-drenching

HEROIN
Heroin
The sedative for

LYCETOL
Lycetol
The anti-acid solvent

HEROIN-HYDROCIN
Heroin-hydrocin
The sedative for

SALOPHEN
Salophen
The antirheumatic and

FARBOFABRIKEN OF
ELBERFELD CO.

40 STONE STREET,
NEW YORK.

& THE H. SORENSEN
CO.
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