Clinical Toxicidromes

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Case 1

• A 25 year old male presents to the EMS with an altered mental status and agitation
• He is tachycardic and has a mild elevation in blood pressure
• He has horizontal nystagmus and dry axillae on examination
Case 1

- His speech is mumbled and he seems to be picking at things in the air
- Shortly after your assessment he has a tonic clonic seizure that remits spontaneously
- An empty bottle of Tylenol PM is found in his pocket
Case 2

- A 34 year old female presents to the EMS with bradypnea, miosis and an altered mental status
- The administration of naloxone results in a prompt reversal of her symptoms
- She becomes agitated and does not want to be transported to the hospital
Case 3

- A 45 year old male farm worker presents to EMS with profuse salivation, diarrhea, respiratory distress, AMS and tachycardia
- The odor of garlic is emanating from him
- He is sedated and intubated
- A pink frothy sputum fills up the ET tube
Case 4

- A 22 year old female, with a PMH significant for anxiety and depression, presents to the EMS obtunded
- She is minimally responsive to noxious stimuli
- Her vital signs are within normal limits with the exception on a low blood pressure
Objectives

- Describe the most common toxidromes
- Highlight signs/symptoms that establish each toxidrome
- Discuss management and antidotes if available
Introduction

• Toxidrome
  – describe signs/symptoms that consistently result from particular toxins
  – Groups drugs together according to these signs/symptoms
  – Vital signs and end organ manifestations
The “Usual” Suspects

- Sympathomimetic toxidrome
- Anticholinergic toxidrome
- Cholinergic toxidrome
- Opioid toxidrome
- Sedative Hypnotic toxidrome
Sympathomimetic Toxidrome/Withdrawal
Introduction

• Mimics “Fight or Flight” response
• Alcohol/drug withdrawal → same effects as sympathomimetic drugs
• Drugs:
  – Caffeine, cocaine, amphetamines, methamphetamines, Ritalin, LSD, Theophylline, MDMA
Characteristics

- Tachycardia, dysrhythmias
- Hypertension
- Diaphoresis
- Piloerection (Goosebumps)
- Delusions, paranoia
- Seizures
- Hyperthermia
- Mydriasis (Dilated Pupils)
Caffeine

- Toxic dose is >10g (10,000mg)
- Coffee: Tall Starbucks 260mg
- Red Bull: 80mg/can
- Jolt: 72mg/can
- Coca-Cola: 46mg/can
- ‘Wakeups’ (Caffeine pill): 100mg/pill
- Toxic doses can cause seizure, arrhythmias, respiratory failure, death
Cocaine

- Powder
- Crack
- Short and long term cardiac effects
- Increased risk of heart attack x24 in the first hour post use
Treatment

- Prehospital treatment
  - Safe, rapid transport with O2 administration and cardiac monitoring
  - Caution: vomiting, seizures, violence
  - +/- benzos/sedation
Anticholinergic and Cholinergic Toxidromes
Introduction

- Anticholinergic poisoning (AP) commonly occurs but is frequently unrecognized
Anticholinergic Poisoning

• Central
  – CNS stimulation followed by depression
  – Mild cognitive impairment
    – seizures and coma
  – Fragmented mumbled speech
  – Hallucinations
  – Picking at clothes, in the air or bed sheets
  – Tremor, ataxia and clonic movements may occur

• Peripheral
  – Decreased salivation, sweating and bronchial secretion
  – Bladder and intestinal motility may be affected
  – Variable effect on pupil size
  – Tachycardia
  – Flushed appearance
Anticholinergic Poisoning

- The degree of central and peripheral anticholinergic effects vary depending on the drug or toxin involved.

- There is a marked individual variation in response to the anticholinergic agents.
Anticholinergic Poisoning

- Children: particularly sensitive to anticholinergic agents
  - increased risk for AP
  - Receptor sensitivity
- Children with Down syndrome commonly have a genetically determined hypersensitivity to anticholinergic agents
Anticholinergic Poisoning

- A mnemonic for recalling some of the signs and symptoms of anticholinergic poisoning:
  - Mad as a hatter
  - Blind as a bat
  - Dry as a bone
  - Red as a beet
  - Hot as a pistol
Blind As A Bat

• Blind as a bat
  – Pupils will be very dilated!!
  – Near vision will be blurry
Dry As A Bone

- Blockade of cholinergic tone to salivary glands
- Decreased salivation, dry mouth, intense thirst and difficulty swallowing
Red As A Beet

- Describes a marked flushing on the face and chest. This is not an effect of cholinergic blockade
Hot As A Pistol

- Hot as a pistol
  - Refers to an elevated body temperature, which may be especially pronounced in young children
  - This is a result of blockade of sweat glands
Anticholinergic Agents

- Anticholinergics
  - Atropine, scopolamine, glycopyrrolate, benztropine, trihexyphenidyl
- Antihistamines
  - Chlorpheniramine, Cyproheptadine, Doxylamine, Hydroxyzine, Dimenhydrinate, Diphenhydramine, Meclizine Promethazine
Anticholinergic Agents

- Antipsychotics
  - Chlorpromazine, Clozapine, Mesoridazine, Olanzapine, Quetiapine, Thioridazine
- Antispasmodics
  - Clidinium, Dicyclomine, Hyoscyamine Oxybutynin, Propantheline
Anticholinergic Agents

- Cyclic antidepressants
  - Amitriptyline, Amoxapine, Clomipramine, Desipramine, Doxepin
  - Imipramine, Nortriptyline, Protriptyline
- Mydriatics
  - Cyclopentolate Homatropine, Tropicamide
Anticholinergic Agents

- Miscellaneous
  - Carbamazepine
  - Cyclobenzaprine
  - Orphenadrine
  - Glutethimide
  - 1A antiarrhythmics
Anticholinergic Plants

- *Atropa belladonna* (deadly nightshade)
- *Cestrum nocturnum* (night blooming jessamine)
- *Datura suaveolens* (angel’s trumpet)
- *Datura stramonium* (jimson weed)
- *Hyoscyamus niger* (black henbane)
- *Lantana camara* (red sage)
- *Solanum carolinensis* (wild tomato)
- *Solanum dulcamara* (bittersweet)
- *Solanum pseudocapsicum* (Jerusalem cherry)
- *Solanum tuberosum* (potato)
- *Arctium lappa* (burdock root)
Not so quiet Chamomile

- In March 1994 the New York City Health Department investigated 7 cases of AC poisoning
- Tea was prepared from leaves labeled as Paraguay tea
- Manifestations occurred within two hours of tea consumption

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<table>
<thead>
<tr>
<th>Adrenergic Syndrome</th>
<th>Anticholinergic Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mydriasis</td>
<td>Mydriasis</td>
</tr>
<tr>
<td>Tachycardia/HTN</td>
<td>Tachycardia/HTN</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>Hyperthermia</td>
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<tr>
<td>Disorientation</td>
<td>Disorientation</td>
</tr>
<tr>
<td>Agitation</td>
<td>Hallucinations</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>Decreased bowel sounds</td>
</tr>
<tr>
<td>Bowel sounds present</td>
<td>(unreliable)</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>Dry skin/mucous membranes</td>
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</tbody>
</table>
Physostigmine

• Physostigmine:
  – inhibits cholinesterase activity
    → increased acetylcholine at cholinergic nerve endings
• Phystiogmine:
  – reverses central/ peripheral effects of AC poisoning
Physostigmine

- Physostigmine
  - severe agitation and refractory seizures, or tachycardia causing hemodynamic compromise
- Avoid use in patients with bradycardia, asthma or conduction delays
Cholinergic Agents

- First potent organic phosphorous compound was synthesized in 1854
- In 1932 the toxic nature of these compounds was described
- The potent nature of these compounds was recognized
  - chemical warfare agents
Cholinergic Agents

- Organic Phosphorous Compounds
- Carbamates
- Arecholine, Pilocarpine, Urecholine (Betanechol), Carbachol, Choline, Metacholine, Mushrooms (Boletus sp., Clitocybe sp., Inocybe sp.)
“Classic” Toxidrome

- Unresponsive
- Pinpoint pupils
- Fasciculation's
- Diaphoresis
- Emesis
- Diarrhea
- Salivation
- Lacrimation
- Urinary incontinence
Pharmacology

• Poisoning from these agents →
  – increase of acetylcholine at cholinergic receptors
Cholinergic Toxidrome

- Can result from either direct or indirect stimulation of cholinergic receptors
  - “SLUDGE”
  - “DUMBELLS”
  - “Damn this sucks I cant stop shitting”
In 1995 in Tokyo, a Sarin release (Shoko Asahara) caused 12 deaths and 5,500 injuries.
Signs and Symptoms in 111 Moderately and Severely Injured Patients on Admission

<table>
<thead>
<tr>
<th>Signs or Symptoms</th>
<th>No of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miosis</td>
<td>110 (99)</td>
</tr>
<tr>
<td>Eye pain</td>
<td>50 (45)</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>44 (40)</td>
</tr>
<tr>
<td>Injection</td>
<td>30 (27)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>70 (63)</td>
</tr>
<tr>
<td>Cough</td>
<td>38 (34)</td>
</tr>
<tr>
<td>Wheezing</td>
<td>9 (6)</td>
</tr>
<tr>
<td>Nausea</td>
<td>67 (60)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>41 (37)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Headache</td>
<td>83 (75)</td>
</tr>
<tr>
<td>Weakness</td>
<td>41 (37)</td>
</tr>
<tr>
<td>Fasciculations</td>
<td>26 (23)</td>
</tr>
<tr>
<td>Decreased LOC</td>
<td>19 (17)</td>
</tr>
<tr>
<td>Seizures</td>
<td>3 (2)</td>
</tr>
</tbody>
</table>
Opioid Toxidrome
The Opiate Toxidrome

- Pin point pupils
- Altered mental status
- Decreased bowel sounds
- Respiratory depression
Introduction

• Opioid:
  – compounds related to opium

• Opiates:
  – drugs derived from opium

• Endogenous opioids:
  – naturally occurring ligands for opioid receptors
Opioids

- Morphine
- Codeine
- Tramadol
- Heroin
- Meperidine
- Diphenoxylate
- Hydromorphone
- Fentanyl
- Methadone
- Propoxyphene
- Pentazocine
- DXM
- Oxycodone
- Hydrocodone
μ-Receptor Effects

- Analgesia
- Rewarding behavior
- Mood
- Respiratory depression
- Cardiovascular
- Gastrointestinal
- Neuroendocrine
Opioid Effects

• Analgesia
  – Therapeutic doses:
    • analgesia without loss of consciousness
    • pain is less intense, less discomforting or entirely gone
Opioid Effects

- Miosis
  - most $\mu$ and $\kappa$ receptor agonists cause pupillary constriction
    - Largely unknown mechanism
Opioid Effects

• Respiration
  – Respiratory depression:
    • direct effect on the brainstem respiratory centers
  – Opioids:
    • depress all phases of respiratory activity
Opioid Effects

- Maximal respiratory depressant effects:
  - 5-10 minutes after IV administration
  - 30 minutes after IM administration
  - 90 minutes after SQ administration
Opioid Effects

- Cardiovascular effects
  - Peripheral vasodilatation
  - Reduced peripheral resistance
- These lead to hypotension
  - Histamine release
Opioid Effects

• Gastrointestinal Tract
  – Stomach
  – Small intestine
  – Large Intestine
  – Biliary tract
Naloxone

- Opioid antagonist
- Rapidly metabolized to inactive metabolites
- Duration of action is about 45 minutes
- Recommended dose to start is 0.4mg
Sedative Hypnotics
Sedative Hypnotic Toxidrome

- CNS depression
- Slurred speech
- Ataxia
- Usually relatively normal vital signs
Sedative-Hypnotics

- CNS depressants
- Used clinically as anti-anxiety agents, muscle relaxants, antiepileptics and preanesthetic medications
  - Barbituates
  - Benzodiazepines
Behavioral Effects

- Depress behavior
- Moderate excitement
- Induce calmness
- Benzodiazepines are considered safer than barbituates
GHB Toxicity

- AKA “Liquid Ecstasy” “Liquid X” “Georgia Homeboy” “Great Hormones at Bedtime” “Easy Lay”
- Disinhibition
- Sedation
- Nausea/vomiting
- Myoclonic Movements, Seizures
- Coma
- Respiratory Depression
Rohypnol tablets are white and are single- or cross-scored on one side with "ROCHE" and "1" or "2" encircled on the other.
Flunitrazepam

- Available legally in Mexico and Europe
- Not approved or manufactured in US
- Odorless, tasteless, colorless
- Often used with ETOH
- Flunitrazepam: AKA Mexican Valium, Forget pill, Rophy, Rope, Rib roaches, R-2
Flunitrazepam

• Potent benzodiazepine about 10x diazepam
• Time Course
  – onset - within 30 minutes
  – peaks at 2 hours
  – persists for 8 hours
  – blackouts can last for 24 hours
Summary

• Clinical toxidromes may help in the management of a patient
• Signs and symptoms may be subtle
• there is intra and inter-individual variations in presentations to similar toxins
• Never believe an overdose patient
Questions??