Toxicology Review

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Objectives

- ■Drugs of abuse ■Benzodiazepines
 - ■Barbiturates
 - ■Hallucinogens
 - ■Cocaine
 - \blacksquare Amphetamines
 - ■Narcotics ■Rave drugs
- Lithium
- Heavy metals
- Cyanide/Hydrogen sulfate
- Organophosphates
- Local anesthetics
- Mushrooms
- Plants
- Isoniazid
- Hypoglycemics
- Inhalation toxins
- Biologic hazards

1



Benzodiazepines

- ■Stimulation of the benzodiazepine receptor
- ■Increases the sensitivity of the GABA receptor complex ■Leads to inhibitory effects
- Lipid soluble

■Lipiu soluble



3

Clinical Features

- **■**CNS
 - ■Drowsiness
 - ■Dizziness ■Slurred speech
 - ■Confusion
- ■Ataxia
- ■Paradoxical reactions
- ■Respiratory depression

Treatment

- ■Activated charcoal
- ■Elimination enhancement
- ■Not effective

■Respiratory support

5

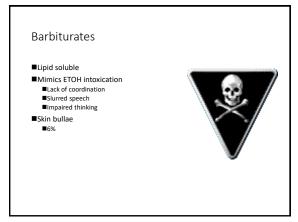
Flumazenil Selective antagonist O.2mg IV q minute (total of 3mg) Seizure Activity Co-ingestions Physically dependent on Benzodiazepines History of seizures

Barbiturates

8

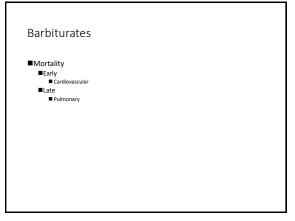
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■Pharmacology
■Enhances the action of GABA receptors
■Inhibits noradrenergic excitation at neuronal junctions

9



Treatment

Airway
Activated charcoal
Multi-dose
Fluid support
Alkalinization of urine
Mincreases the excretion rate (5 to 10 fold)
Hemodialysis
G to 9 times more effective than alkalinization

11 12



Hallucinogens

■PCP

- ■Dissociative anesthetic with brainstem preservation
- ■Nystagmus, agitation, ataxia
- ■Muscle rigidity, seizure, coma, rhabdo, hyperpyrexia
- ■Affects serotonergic and dopaminergic pathways ■Paranoia, anxiety, psychosis
- Marijuana
- ■Mushrooms
 - ■Psilocybin
- ■LSD-like
 ■Mescaline
- Similar to amphetamines



13

14



Cocaine

■Onset

- ■30 sec to 2 minutes
- ■Peak Effect
- ■30 minutes
 ■Duration
- ■1 to 3 hours



15

16

Cocaine (Pathophysiology)

- ■Local Anesthetic
- ■Inhibits conduction of nerve impulses by sodium channel blockade
- ■CNS Stimulant
 - ■Blocks presynaptic reuptake of norepinephrine, dopamine, and serotonin
- ■Cardiac
 - ■Sodium channel blockade
 - ■QRS widening
 - ■QT prolongation

Clinical Features

- **■**Cardiac
 - \blacksquare Arrhythmias
 - Myocarditis
 - $\blacksquare Cardiomy opathy$
 - Aortic dissection
 Coronary artery dissection
 - ■Accelerated atherosclerosis

17 18

Clinical Features

- CNS
 - Seizures
 - Intracranial infarction and hemorrhages
- Renal
 - Rhabdomyolysis

Clinical Features

- **■**Pulmonary
 - ■Hemorrhage
 - ■Edema
 - ■Pneumomediastinum and pneumothorax
- ■GI
 - ■Body stuffers
 - ■Body packers
- ■Obstetrics
 - ■Uteroplacental blood flow decreased

19 20

Treatment

- Sedation
 - Benzodiazepines
- Fluid resuscitation
- Cooling
- Whole bowel lavage
- Wide complex tachyarrhythmia
 - Sodium bicarb
- Beta-blockers (contraindicated)
 - Unopposed alpha-adrenergic receptor stimulation



21 22

Amphetamines

- \blacksquare Competitively inhibit the reuptake of neurotransmitters
- ■Inhibit monoamine oxidase
 - ■Inhibit the breakdown of catecholamines

Treatment

- Cardiac monitoring
- Benzodiazepines
- Avoid beta-blockers



23 24



Narcotics • Overdose · Pinpoint pupils Midrange/dilated if CNS hypoxia • Hypoventilation Pulmonary edema

25 26

• Heroin

- - Quinine
 - Lactose

 - Baking soda
 - Codeine

■ Heroin

■ Methadone

■ Morphine

Narcotics

- 20 to 200:1 ratio of adulteration
- Sucrose Talc
- Mannitol
- Meperidine ■ Hydromorphone
- Oxycodone

Narcotics

27

- Withdrawal
 - Piloerection • Lacrimation
 - Yawning
 - Rhinorrhea
- Sweating
- Myalgia
- Abdominal cramping and vomiting
- Irritable and confused

Narcotic Withdrawal

■Heroin

28

Narcotics

Acute Intoxication

• Slowed respirations

· Nausea and vomiting

Drowsiness

• Euphoria

Miosis

Pruritus

- ■12-14 hours after last dose
- ■Methadone
 - ■24-36 hours after last dose
- ■Not life threatening
- ■Methadone ■Clonidine
 - ■Inhibiting adrenergic activity at alpha-2 adrenergic receptors

29 30

Treatment

- ■Naloxone
 - ■Antagonizes opiate receptor sites in the CNS
 - ■Serum half-life is one hour (duration 2-3 hours)
 - ■2.0mg in adults
 - ■0.01mg/kg in children
 - ■May be given:
 - ■Subcutaneously
 - \blacksquare Intratracheally
 - ■Intramuscular ■Intravenously



31 32

GHB

- ■Gamma-hydroxybutyric acid
- ■Similar in structure to GABA
- ■Maximal plasma concentration
- ■20-30 minutes
- ■Half-life 27 minutes

CNS Effects

- ■Binds to GABA-B receptors in the brain
- ■Inhibits noradrenaline release in the hypothalamus
- ■Mediates release of an opiate-like substance in the brain

33

GHB

- ■Oral Dose
- ■10mg/kg Am
- ■20-30mg/kg Drowsiness and sleep

- Towsiness

 50-70mg/kg
 Deep coma
 Usually lasts 3-6 hours
 Accompanied by myoclonic jerks and agitatic

Treatment

34

- ■Airway support
- ■Cardiac monitoring
- ■Reversal of GHB
 - \blacksquare Physostigmine ■ Reverse sedation in clinical trials
 ■ Risks
 ■ Bradycardia
 ■ Asystole
 ■ Seizures

35 36

MDMA (Ecstasy)

- ■Amphetamine derivative
- ■Catecholamine release from presynaptic vesicles
 - ■Sympathomimetic effects
- ■Massive release of serotonin

Treatment

- ■Supportive care
- ■Cooling
- ■Seizures

■Benzodiazepines

37

38

Ketamine

- Structurally similar to PCP
 - Dissociative anesthetic with brainstem preservation
 Nystagmus, agitation, ataxia
- Muscle rigidity, seizure, coma, rhabdo, hyperpyrexia
- Used as a dissociative anesthetic
- "Special K"



39

40

Pathophysiology

- ■Competes with other similar-molecular-weight ions resulting in displacement
 - ■Sodium
 - ■Potassium
 - Magnesium
 - ■Calcium
- ■Decreases in intracellular cAMP
- ■Interferes with the release and reuptake of norepinphrine

Clinical Effects

- GI symptoms
- Cardiovascular
- Prolonged QT Bradycardia
- Renal
- polyuria
- CNS
- Tremor

 Memory loss

 Weakness

 Ataxia
- Serum levels do not predict CNS levels

Treatment

- · Activated charcoal is ineffective
- Whole-bowel irrigation
- Aggressive hydration
- Hemodialysis
 - Levels > 3.5 mEq/L (>4.0 in an acute ingestion)
 - · Coma, seizures, CV collapse, renal failure
 - Little or no change in levels after 6 hours of hydration
 - Levels > 1.0 after 36 hours of treatment



43 44

Lead

- CNS
 - Damage to the microvascular system
 - Disruption of the blood-brain barrier
 - Cerebral edema
 Seizures
- Kidney
- Affects the proximal tubule
- Toxic hepatitis
- Clinical features
 - Encephalopathy, seizures, parathesias, abdominal pain, peripheral neuropathy ("classic"=wrist drop)

Lead

- · Combination of abdominal or neurologic dysfunction with hemolytic anemia=lead toxicity
- Anemia and basophilic stippling
- PbB level > 10 microgram/dL
- X-ray
- Treatment
- Whole bowel irrigation
 Chelation therapy EDTA DMSA

45 46

Arsenic

- ■Severe gastroenteritis, muscle twitches, delirium, hepatic/renal
- ■Diagnosis: 24 hour urine
- ■Treatment: chelation (BAL)

Iron

- ■Toxic dose 30-40 mg (elemental)/kg
 - ■0-6 hours

Gastro, dehydration

- ■6-48 hours
- quiescent phase
- ■12-48 hours
- acidosis, coma, hepatic recovery, scaring
- ■2-6 weeks
- ■Serum Fe level (TIBC not reliable)
- ■Charcoal doesn't bind
- ■Treatment = whole-bowel irrigation and chelating agent (deferoxamine)

Mercury

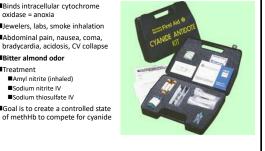
- ■Interferes with enzyme activity
- ■CNS, GI, renal toxicity
- ■Metallic mercury: benign if ingested but very dangerous is inhaled or injected
- ■Diagnosis: 24 hour urine
- ■Treatment: lavage and chelation (BAL)



49

Cyanide

- ■Binds intracellular cytochrome oxidase = anoxia
- ■Jewelers, labs, smoke inhalation
- ■Abdominal pain, nausea, coma, bradycardia, acidosis, CV collapse
- ■Bitter almond odor
- ■Treatment
 - ■Amyl nitrite (inhaled)
- ■Sodium nitrite IV ■Sodium thiosulfate IV
- ■Goal is to create a controlled state



Hydrogen Sulfate

■Inhalation

50

- ■Local irritant effects
- ■Arrest of cellular respiration = aerobic metabolism (similar to cyanide)
- ■Rotten egg odor
- ■GI, CNS, CV collapse
- ■Treatment: amyl nitrite, sodium nitrite, therapy

? Hyperbaric oxygen

51



Organophosphates

- Pesticides/insecticides
- · Rapidly absorbed
- Garlic odor

52

- Muscarinic/cholinergic (SLUDGE): pinpoint pupils, salivation, lacrimation, defecation · Irreversibly binds acetylcholinesterase
- Treatment: atropine (high dose- until secretions dry) and 2-PAM (pralidoxime)



53 54



Local Anesthetics

- Lidocaine
- Bupivacaine
- Much less allergenic methylparaben

56

- Tetracaine
- Procaine
- Side effects: CNS (seizures), CV
- Maximum lidocaine dosing

 - Plain 4mg/kg
 with epi 7mg/kg



55



GI Symptoms

- Onset < 2 hours
 - ${\color{red} \bullet} \ {\it Chlorophyllum}$
 - Amanita
 - Cantharellus
- Treatment
 - Hydration Antiemetics
- Onset 6-24 hours
 - Gyromitra
 - Amanita
 - Activated charcoal
 - High dose pcn
- Follow LFT's

57

Muscarinic

- Onset < 30 minutes
- Species
- Inocybe
- Clitocybe
- Symptoms • SLUDGE
- Treatment
- Atropine



CNS Excitement

■Species

58

- **■**Amanita
- **■**Symptoms
 - ■Intoxication
 - ■Ataxia
 - ■Anticholinergic effects
- ■Treatment
 - ■Supportive sedation (benzo's or phenobarb)



59 60

Hallucinations

- Onset < 30 minutes
- Species
 - Psilocybe
 - Gymnopilus
- Treatment
 - Supportive sedation



Disulfiram

- Onset 2-72 hours after mush room
 - < 30 minutes after ETOH
- Species
 - Coprinus
- Symptoms
- Headache, flushing, tachyc
- Treatment
- Supportive



61

62

64



Highly Poisonous

- Castor bean & Jequirity bean
- Toxalbumin that inhibits protein synthesis
 - · Cytotoxic effects on multiple systems
- Oleander & Foxglove & Lily of the Valley • Digitalis effect
- Poison Hemlock
 - Nicotine effects
 - Severe cases: • rhabdomyolysis
- Water Hemlock GABA antagonist
- Yew
 - cardiotoxin

63

Common Plant Exposures

- ■Fava beans
 - ■G6PD deficiency
 - ■Hemolytic anemia
- ■Jimsonweed & Deadly Nightshade
 - ■Hallucinatory properties
 - ■Anticholinergic crises



Toxicodendron Species

- ■Poison Ivy
- ■Poison Oak
- **■**Sumac



65 66

Holiday Plants

- ■Holly
- $\blacksquare GI$ symptoms
- **■**Poinsettia
- ■Local irritation
- ■Mistletoe
- ■GI symptoms
- ■Easter Lily ■Non-toxic



67

Isoniazid (INH)

- Overdose
 - Seizure
 - Coma
 - Metabolic acidosis
- Consider in pediatric seizures
 - Unintentional OD
- Consider in populations likely to be on INH
- Antidote
 - Pyridoxine (Vit B-6)



69

Oral Hypoglycemic Agents

- Prolonged hypoglycemia
 - Long half life
- Treatment
 - Glucose
 - Glucagon
 - Octreotide
- Can be severe in children
- Admit for observation

Insulin Toxicity

- Pathognomonic of exogenous insulin
 - · Hypoglycemia
 - High insulin levels
 - Suppressed C-peptide levels
- Treatment

68

- Supportive care (IV glucose)
 Depends on type of insulin

71 72

Nerve Agents ■Developed in WWII ■Tabun, Sarin, Soman, GF, ■VX-most potent ■Sarin-most volatile ■Powerful inhibitors of acetylcholinesterase **■**SLUDGE ■Paralysis **■**Death

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Biologic Hazards

- Microorganisms or biological toxins that produce death or disease
- Usually stable, highly infectious, with no effective vaccine
- Undetectable at time of exposure
- · Most likely route of transmission is respiratory

Anthrax

- "wool sorter's disease"
- Inhalation of spores
- Incubation • 1-6 days
- Symptoms
- Fever
 Cough
 Chest pain
- Fatigue
- Sepsis
 Death (within 24 hours)
- Treatment
 - C ipro or doxycycline
 Vaccine



77 78

Ricin

- Cytotoxin
- Inhalation
- Symptoms
- Airway necrosis
- Fever
- Cough
- Sweating
- · Hemorrhagic pulmonary edema
- Treatment

79

supportive

Random Pearls

- · Drug causes of non-cardiogenic pulmonary edema
 - OpiatesPhenobarb
- · Cholinergic poisoning syndrome
- Causes: organophosphates and insecticides
 SLUDGE
- Treatment: Atropine and 2-PAM
- · The presence of hemorrhagic blisters suggests barbiturate toxicity
- · Opiate overdose
 - Respiratory depression, pinpoint pupils, and decreased mental status
 Treatment: naloxone

Random Pearls

80

82

- Over 50% of patients with PCP have nystagmus
- Heavy metal poisoning usually presents as a systemic, bizarre complex in which an occupational history is important.
- · X-ray is useful for iron and lead toxicity
- Disposition of a hypoglycemia induced by an oral hypoglycemic agent is admission
- The most common mistake in treating insecticide toxicity is under-atropinization

81

Random Pearls

- Binds to cytochrome oxidase resulting in cellular asphyxia
- Antidote kit: works by inducing methemoglobinemia
- Pyridoxine is the antidote for INH
- The best treatment for cocaine toxicity is benzodiazepines (Beta-blockers are contraindicated)
- · Charcoal is ineffective for cyanide, iron, lithium, and alcohols

Random Pearls

- Body packer vs. Body stuffer
- Anticholinergic poisoning associated with Jimson Weed
- Cholinesterase is the enzyme inhibited by organophosphates
- Nitroprusside may induce cyanide toxicity
- · Arsine gas presents with the triad: abdominal pain, hematuria, and jaundice

