Toxicology Review

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1

Objectives

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

2

Benzodiazepines

3

Benzodiazepines

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

4

Clinical Features

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

5

Treatment

- Activated charcoal
- Elimination enhancement
  - Not effective
- Respiratory support

6

Flumazenil

- Selective antagonist
- 0.2mg IV q minute (total of 3mg)
- Seizure Activity
  - Co-ingestions
  - Physically dependent on Benzodiazepines
  - History of seizures

7

Barbiturates

8

Barbiturates

- Lipid soluble
- Mimics ETOH intoxication
  - Lack of coordination
  - Slurred speech
  - Impaired thinking
- Skin bullae
  - 6%

9

Barbiturates

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

10

Barbiturates

- Mortality
  - Early
    - Cardiovascular
  - Late
    - Pulmonary

11

Treatment

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

12

Hallucinogens

13

Hallucinogens

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

14

Cocaine

15

Cocaine

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

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

17

Clinical Features

- Cardiac
  - Arrhythmias
  - Myocarditis
  - Cardiomyopathy
  - Aortic dissection
  - Coronary artery dissection
  - Accelerated atherosclerosis

18

Clinical Features

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

19

Clinical Features

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

20

Treatment

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

21

Amphetamines

22

Amphetamines

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

23

Treatment

- Cardiac monitoring
- Benzodiazepines
- Avoid beta-blockers

24

Narcotics

25

Narcotics

- **Overdose**
  - Pinpoint pupils
    - Midrange/dilated if CNS hypoxia
  - Hypoventilation
  - Pulmonary edema

26

Narcotics

- Heroin
  - 20 to 200:1 ratio of adulteration
    - Quinine
    - Lactose
    - Sucrose
    - Talc
    - Mannitol
    - Baking soda

- Heroin
- Methadone
- Morphine
- Codeine
- Meperidine
- Hydromorphone
- Oxycodone

27

Narcotics

- Acute Intoxication
  - Drowsiness
  - Euphoria
  - Miosis
  - Slowed respirations
  - Nausea and vomiting
  - Pruritus

28

Narcotics

- Withdrawal
  - Piloerection
  - Lacrimation
  - Yawning
  - Rhinorrhea

- Sweating
- Myalgia
- Abdominal cramping and vomiting
- Irritable and confused

29

Narcotic Withdrawal

- Heroin
  - 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

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
    - Intratracheally
    - Intramuscular
    - Intravenously

31

Rave Drugs

32

GHB

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

33

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

34

GHB

- Oral Dose
  - 10mg/kg
    - Amnesia and hypotonia
  - 20-30mg/kg
    - Drowsiness and sleep
  - 50-70mg/kg
    - Deep coma
      - Usually lasts 3-6 hours
      - Accompanied by myoclonic jerks and agitation

35

Treatment

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

36

MDMA (Ecstasy)

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

37

Treatment

- Supportive care
- Cooling
- Seizures
  - Benzodiazepines

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

41

Clinical Effects

- GI symptoms
- Cardiovascular
  - Prolonged QT
  - Bradycardia
- Renal
  - polyuria
- CNS
  - Tremor
  - Memory loss
  - Weakness
  - Ataxia
  - Seizures

- **Serum levels do not predict CNS levels**

42

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

Heavy Metals

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)**

45

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
    - BAL
    - EDTA
    - DMSA

46

Arsenic

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

47

Iron

- Toxic dose 30-40 mg (elemental)/kg
  - 0-6 hours — Gastro, dehydration
  - 6-48 hours — quiescent phase
  - 12-48 hours — acidosis, coma, hepatic
  - 2-6 weeks — recovery, scaring
- Serum Fe level (TIBC not reliable)
- Charcoal doesn't bind
- X-ray
- Treatment = whole-bowel irrigation and chelating agent (deferoxamine)

48

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 Hydrogen Sulfate

50

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 of methHb to compete for cyanide

51

Hydrogen Sulfate

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

52

Organophosphates

53

Organophosphates

- Pesticides/insecticides
- Rapidly absorbed
- **Garlic odor**
- Muscarinic/cholinergic (SLUDGE): pinpoint pupils, salivation, lacrimation, defecation
  - Irreversibly binds acetylcholinesterase
- Treatment: atropine (high dose- until secretions dry) and 2-PAM (pralidoxime)

54

Local Anesthetics

55

Local Anesthetics

- Amides
  - Lidocaine
  - Bupivacaine
  - Much less allergenic
    - methylparaben
- Esters
  - Tetracaine
  - Procaine

- Side effects: CNS (seizures), CV
- Maximum lidocaine dosing
  - Plain 4mg/kg
  - with epi 7mg/kg

56

Mushrooms

57

GI Symptoms

- Onset < 2 hours
  - *Chlorophyllum*
  - *Amanita*
  - *Cantharellus*

- Treatment
  - Hydration
  - Antiemetics

- Onset 6-24 hours
  - *Gyromitra*
  - *Amanita*
    - Activated charcoal
    - High dose pcn

- Follow LFT's

58

Muscarinic

- Onset < 30 minutes
- Species
  - *Inocybe*
  - *Clitocybe*

- Symptoms
  - SLUDGE
- Treatment
  - Atropine

59

CNS Excitement

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

60

Hallucinations

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

61

Disulfiram

- Onset 2-72 hours after mushroom
  - < 30 minutes after ETOH
- Species
  - *Coprinus*
- Symptoms
  - Headache, flushing, tachyca
  - DIB
- Treatment
  - Supportive

62

Plants

63

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

64

Common Plant Exposures

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

65

Toxicodendron Species

- Poison Ivy
- Poison Oak
- Sumac

66

Holiday Plants

- Holly
  - GI symptoms
- Poinsettia
  - Local irritation
- Mistletoe
  - GI symptoms
- Easter Lily
  - Non-toxic

67

Isoniazid

68

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

Hypoglycemics

70

Oral Hypoglycemic Agents

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

- **Admit for observation**

71

Insulin Toxicity

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

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

72

Inhalation Toxins

73

Nerve Agents

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

74

Nerve Agents

- High risk of secondary contamination
- Treatment
  - Oxygen
  - Atropine
  - 2-PAM
- Military Mark 1 auto injector kit
  - 2mg atropine
  - 600g 2-PAM

75

Biologic Hazards

76

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

77

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

78

Ricin

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

79

Random Pearls

80

Random Pearls

- Drug causes of non-cardiogenic pulmonary edema
  - Opiates
  - Phenobarb
  - Salicylates
- 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

81

Random Pearls

- 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

82

Random Pearls

- Cyanide
  - 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

83

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

84

85