2024 ACMT Board Review Course Interactive Cram Session #2 June 28, 2024





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Interactive Cram Session

Today's goal is to be **interactive**, **engaging**, and **educational**:

Introductions 5-min "Key Takeaways" Q&A with Speakers Pop Quiz

Today's session is being recorded and will be accessible on-demand.



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DISCLAIMER

According to ABEM policy, the planning committee and faculty for this course are not allowed to have intimate knowledge of the exam or write exam questions. The content of this course is based on the expertise of ACMT members, who are specialists in Medical Toxicology.

We do not have direct knowledge of the exam content. ABEM test question writers are prohibited from participating in any board review or preparatory course. The study materials, including the Quiz Bank and pop quiz questions, are based on years of collective experience from the Board Review Course committee, but we do not guarantee that these questions fully represent the exam content.



CRAM SESSION TOPICS | FRI. JUNE 28, 2024

- The Toxic House
- **Poisonous Plants**
- Warfare/Terrorism
- Chemotherapeutics
- Pesticides





POP QUIZ

10 Qs randomly selected from Quiz Bank

Give it your best guess and then we'll discuss the answers!





Question 1

A medical student presented to the emergency department after being found by fellow students vomiting blood. Shortly after presentation, he rapidly deteriorated. Initial blood gas demonstrated a severe metabolic acidosis. A post mortem methanol concentration was 30 mg/dL. What did the student likely ingest?

- A. Iodine
- B. Potassium permanganate
- C. Phenol
- D. Formalin
- E. Hydrogen peroxide

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Question 1 - Answer

A medical student presented to the emergency department after being found by fellow students vomiting blood. Shortly after presentation, he rapidly deteriorated. Initial blood gas demonstrated a severe metabolic acidosis. A post mortem methanol concentration was 30 mg/dL. What did the student likely ingest?

A. lodine

B. Potassium permanganateC. PhenolD. Formalin

E. Hydrogen peroxide

EXPLANATION: While lodine, phenol, hydrogen peroxide and permangante are all caustic agents, only formalin contains methanol. Acute formalin ingestion will result in a rapid and striking metabolic acidosis. Although methanol is a component of formalin, it is the conversion of formaldehyde to formic acid that is likely the cause of the acidosis. Treatment is supportive with sodium bicarbonate and hemodialysis to correct acidemia.

Question 2

A 4-year-old male was brought to hospital for dark urine. He appears to have scleral icterus on exam, without any other abnormal exam findings. His UA dip is positive for RBCs and bilirubinuria. Blood work revealed a Hgb of 8.3 g/dL and an elevated total bilirubin. Which of the following household items are responsible for the patient suspected diagnosis?

- A. Naphthalene
- B. Camphor
- C. Household bleach
- D. Ammonia
- E. 1,4-dichlorobenzene (paradichlorobenzene)





Question 2 - Answer

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A. Naphthalene

- B. Camphor
- C. Household bleach
- D. Ammonia
- E. 1,4-dichlorobenzene (paradichlorobenzene)

EXPLANATION: The patient has hemolytic anemia. Naphthalene causes hemolysis. Patients with G6PD are particularly susceptible.

Camphor toxicity is associated with CNS depression and seizures and GI symptoms, it has not been associated with hemolytic anemia. Household bleach contains low concentration (generally 3% - 8%) of sodium hypochlorite (base/alkaline). When ingested it causes a caustic GI injury. Generally, young children do not ingest a large enough amount to cause a significant injury with household product concentrations. Higher concentration products are associated with pool or sanitation cleaning products. This patient does not have any sign of GI caustic injury and household bleach is not associated with hemolytic anemia. Ammonia is also an alkaline household cleaning product that will cause GI injury. Ammonia is not associated with hemolytic anemia. 1,4-dichlorobenzene (paradichlorobenzene) is less severe than naphthalene, hemolytic anemia has been reported with paradichlorobenzene but is far less common. Paradichlorobenzene is used as a moth repellent and in urinal cakes. It can be a product of abuse and chronic use can cause a leukoencephalopathy.





A couple is foraging and find a plant they believe to be a wild carrot. They eat the root and shortly thereafter develop vomiting followed by seizures. They are later found dead. Which of the following plants is most likely responsible?

- A. Abrus precatorius
- B. Cicuta maculata
- C. Dieffenbachia spp
- D. Lophophora williamsi
- E. Phytolacca Americana





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B. Cicuta maculata /

- C. Dieffenbachia spp
- D. Lophophora williamsi
- E. Phytolacca Americana

EXPLANATION: The plant ingested was Cicuta maculata, or water hemlock. The root contains cicutoxin, which may produce seizures and death. It has been mistaken for an edible wild carrot. Abrus precatorius is a toxalbumin-containing plant, which would produce gastroenteritis following ingestion of the toxin, abrin. Severe poisonings may result in multi-organ system failure and death after several days. Dieffenbachia is a common houseplant with calcium oxalate present in the leaves. Ingestion of the leaves may produce mucous membrane irritation but not seizures. Lophophora williamsi is peyote, a cactus known for producing hallucinations. Phytolacca americana is pokeweed, which may produce severe gastroenteritis when ingested, but seizures are not expected.

Question 4

The seeds of the plant shown in this image contain which of the following?

- A. Atropine
- B. Cathinone
- C. Coniine
- D. Lysergic acid
- E. Thujone







Question 4 - Answer

The seeds of the plant shown in this image contain which of the following?

A. Atropine

B. Cathinone

C. Coniine

D. Lysergic acid

E. Thujone



EXPLANATION: The seeds of Morning Glory flowers contain Lysergic acid.



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Weaponized sulfur mustard (HD) has which of the following specific physical properties?

- A. Colorless solid or yellow-brown liquid, irritating
- B. Colorless to white to pale yellow, freshly mown hay odor
- C. Colorless to white to pale yellow, freshly mown hay odor
- D. Yellow-brown, garlic or onion odor
- E. Yellow-green gas, strong bleach odor



Question 5 - Answer

Weaponized sulfur mustard (HD) has which of the following specific physical properties?

- A. Colorless solid or yellow-brown liquid, irritating
- B. Colorless to white to pale yellow, freshly mown hay odor
- C. Colorless to white to pale yellow, freshly mown hay odor

D. Yellow-brown, garlic or onion odor

E. Yellow-green gas, strong bleach odor

EXPLANATION: Pure sulfur mustards are colorless, viscous liquids at room temperature. When used in impure form, such as warfare agents, they are usually yellow-brown in color and have an odor resembling mustard plants, garlic, or horseradish, hence the name.

Question 6

A 25-year-old soldier sustains a blast injury. He has extensive burns and, upon removal of dressings, his wounds begin to smoke. The team immediately begins irrigation and debridement of the wounds. The most likely agent responsible is:

- A. Barium styphnate
- B. Lithium
- C. Red phosphorus
- D. Trinitrotoluene
- E. White phosphorus

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Question 6 - Answer

A 25-year-old soldier sustains a blast injury. He has extensive burns and, upon removal of dressings, his wounds begin to smoke. The team immediately begins irrigation and debridement of the wounds. The most likely agent responsible is:



- A. Barium styphnate
- B. Lithium
- C. Red phosphorus
- D. Trinitrotoluene
- E. White phosphorus /

EXPLANATION: White phosphorus is an agent found in ammunition and easily penetrates tissue due to its high lipophilicity. This agent can spontaneously combust when exposed to ambient oxygen. Wounds may fluoresce under UV lighting. Burns should be covered with a damp dressing.



Which of the following agents would be contraindicated in a patient with severe pulmonary fibrosis?

- A. Bleomycin
- B. Cisplatin
- C. Doxorubicin
- D. Chlorambucil
- E. Methotrexate





Question 7 - Answer

Which of the following agents would be contraindicated in a patient with severe pulmonary fibrosis?

A. Bleomycin

- B. Cisplatin
- C. Doxorubicin
- D. Chlorambucil
- E. Methotrexate

EXPLANATION: Bleomycin has been associated with bronchiolitis obliterans with organizing pneumonia (BOOP) and pulmonary fibrosis. Doxorubicin is associated with cardiomyopathy, and pericarditis. Chlorambucil is a purported nervous system toxin causing encephalopathy and seizures. Methotrexate inhibits folate synthesis and is not associated with pulmonary fibrosis but is associated with hypersensitivity pneumonitis and hilar adenopathy.





Which of the following antineoplastic agents is associated with hemolyticuremic syndrome?

- A. Arsenic trioxide
- B. Busulfan
- C. Cytarabine
- D. Mitomycin
- E. Vinca alkaloids





Question 8 - Answer

Which of the following antineoplastic agents is associated with hemolyticuremic syndrome?

A. Arsenic trioxide

- B. Busulfan
- C. Cytarabine

D. Mitomycin <

E. Vinca alkaloids

EXPLANATION: Mitomycin is well-described to be associated with hemolytic-uremic syndrome. Arsenic trioxide causes QTc prolongation and torsades de pointes. Busalfan (sometimes spelled "busalphan") causes pulmonary fibrosis, hyperpigmentation, and hyperuricemia. The pyrimidine analog cytarabine is associated with acute respiratory distress syndrome and cerebellar ataxia. Vinca alkaloids cause peripheral neuropathy and SIADH.





What is the mechanism of action of norbormide?

- A. Causes diabetes mellitus
- B. Causes hemolysis
- C. Causes pulmonary edema
- D. Causes severe vasoconstriction
- E. Causes status epilepticus





Question 9 - Answer

What is the mechanism of action of norbormide?

- A. Causes diabetes mellitus
- B. Causes hemolysis
- C. Causes pulmonary edema
- D. Causes severe vasoconstriction /
- E. Causes status epilepticus

EXPLANATION: Norbormide is a rodenticide, specifically targeting of rats, that causes severe vasoconstriction.

There are multiple pecidices associated with diabetes, a rodenticide that leads to beta cell destruction and hyperglycemia is PNU. A rodenticide associated with status epilepticus is teramine.





Which of the following agents may be used in the management of paraquat ingestion to reduce pulmonary toxicity?

- A. Leucovorin
- B. Olestra
- C. Oxygen
- D. Prussian blue
- E. Putrescine





Which of the following agents may be used in the management of paraquat ingestion to reduce pulmonary toxicity?

A. Leucovorin

B. Olestra

C. Oxygen

D. Prussian blue
E. Putrescine

EXPLANATION: Putrescine is a structurally similar polyamine to paraguat and can competitively inhibit uptake of paraguat into type II alveolar cells. Treatments such as activated charcoal, NAC, vitamin C and E, and Hemodialysis/Hemoperfusion are common in some areas but benefit are not proven. Immunosuppression with corticosteroids or cyclophosphamide is reasonable to consider when treating patients early after an exposure or those with only a faintly positive dithionite urinary test, however their use has not been fully proven.



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FEEDBACK SURVEY

Before you leave, please fill out the feedback survey.

This survey should appear in your browser when the meeting ends.

Let us know how we can improve the next interactive cram session!





COMING UP! Interactive Cram Session #3 July 12, 2024

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- Hydrocarbons
- Alcohols & Glycols
- Aquatic Toxicity
- Radiation
- Cardiovascular Toxins





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ACMT BRC CRAM SESSION: TOXIC HOUSE

MY GENERAL ADVICE

- It's impossible to know it all
- Focus on minutia in early prep, then syndromes, -isms and buzzwords during "crunch time"

IODINE / IODOPHORES / IODIDES

- Clinical: Caustic & Oxidant (Cytotoxic)
- Systemic (Acute)
 - GI (N/V & Pain)
 - Multi-organ
 - CNS with coma to seizures
 - Metabolic acidosis (Many causes including
 clearance of H+;
 <u>Not</u>
 Lactate)
 - Hemolytic anemia
 - Hyperthyroidism
 - Secretions 🛧 all around
 - Respiratory, Renal, CV Crash

lodine toxicity > > lodide

Can see much 1 blood levels with topical Irrigation of open wounds or mucosal surfaces

> <u>lodism</u> – after chronic ingestion of small amts of iodide salts – rash, Much "itis" - laryngitis, bronchitis, esophagitis, conjunctivitis, drug fever, metallic taste, "mumps"

IODIDE

- Measured as chloride by some analyzers
- LOW ANION GAP + ACIDOSIS → THINK IODIDE
- Treatment: turn the iodide to iodine, starchy stuff, effluent turns indigo

PHENOL

- Rabbit syndrome characteristic twitching of mouth
- Painless Caustic Burns with depigmented skin
- Classic treatment is LMW Polyethylene glycol

HYDROGEN PEROXIDE

Two toxicities: (I) Irritant/Caustic formation



- Ocular exposure Irritation
- Treatment:
 - Dilution/irrigation
 - Consider nasogastric aspiration if recent exposure

Percent		Injury	Gas from 1 mL	CCs
Household	3-9%	Irritant	10 mL	GI, N/V
Bleaching				
Agents	35%	Caustic	100 mL	
Rocket Fuel	80-90%			
Industrial	> 10%	Caustic	100 mL	GI pain,
				Air embolism

ASSOCIATIONS TO KNOW

- Benzalkonium chloride detergent, in sanitizers/preservative, classic dermal sensitizer
- Potassium permanganate violet colored, breaks down to KOH which is caustic, and MnO2 which causes brown staining, chronic exposure → Manganese toxicity
- Formalin: fomaldehyde + methanol → metabolic acidosis, caustic, but usually no blindness

ANTIDIARRHEALS

- Diphenoxylate
- Diphenoxylic acid is metabolite, more active, delayed effects
- Lomotil = + atropine
- See anticholinergic + opioid effects
- Opioid effects can be delayed, reversed with narcan

- Loperamide:
- Low systemic and poor CNS penetration
- But ABUSED
- Mixed Na, K, Ca channel effects QRS and QTC increase
 - Ventricular dysrhythmias
- Concentration increased by CYP3A4, 2C8 inhibitors
- PGP inhibitors increase CNS

ACID MEDS ANTACIDS

Milk-Alkali Syndrome

- Triad
 - Hypercalcemia
 - Alkalosis
 - Ca⁺⁺ precipitation → ARF)
 - Renal Impairment
- Due to combined ingestion of:
 - Absorbable alkalinizing agent (Sodium Bicarb or Calcium Carbonate)
 - Calcium





LAXATIVES

- Psyllium from plantago ovata can cause allergic reactions
- Mineral oil can decrease absorption of fat soluble vitamins
- Anthraquinones chronic use associated with melanosis coli

PROMOTILICS (PROKINETICS)

Metoclopramide

- 5-HT₃ antagonist, 5HT4 agonist → ↑ Motility
- It 🛧 Lower esophageal tone
- Adverse Events
 - No dose-related deaths
 - EPS: Dystonias, Tardive Dyskinesia!!!
 - NMS!!!
 - Acute OD → Somnolence
 - Hematologic Events
 - MetHemoglobinemia (therapeutic or OD)
 - Neutropenia, Leukopenia, Agranulocytosis

Bethanechol

- Muscarinic agonist →↑ Contractions
- Quaternary amine



IARC I:

- Azo Dyes bladder cancer
- Radon lung cancer emit alpha particles as they decay

Button Batteries – injury due to electrical discharge, prompt removal indicated

B



(A)

PESTICIDES

DEET: Large safety margin, seizures/coma with massive exposures

PYRETHROIDS:

- T syndrome tremor, hypermetabolic state/hyperthermia
- CS syndrome choreathetosis and salivation; seizure
- Type I simple ester without a cyano group at the central linkage
- Type II have a cyano group at the carbon of this ester linkage
- Cyano group enhances neurotoxicity, tend to produce CS syndrome
- Readily hydrolyzed by oral route and toxicity is with large ingestions
- Allergic reactions common

ACMT BRC CRAM SESSION: POISONOUS PLANTS

PEARLS

- When learning what they look like, focus on things that are distinctive or a key element that will determine if it's toxic or not.
- Identifying the toxidrome still helps with plants
- Know where the foragers go wrong
- Many of the slides can function as digital flashcards
- Know the species names

Water Hemlock Vs Poison Hemlock



SODIUM CHANNEL OPENERS

- Grayanotoxins
 - Rhododendron, azaleas, mountain laurels
- Veratrum Alkaloids
 - Zigadenus, veratrum spp
 - Zigadenus bulb like wild onion but no onion odor
- Aconitine alkaloids
 - Monkshood, wolfsbane, aconite
 - Aconite also known for torsades

All sodium channel activators cause: salivation, emesis, paresthesias, weakness, hypotension, bradycardia, arrhythmias



DATURA SPP









leaves offset at stem



Brugmansia spp TROPANE ALKALOIDS



Deadly Nightshade

Henbane

Mandrake

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WORD ASSOCIATIONS

- *Phytolacca americana* proteinaceous mitogens, plasmacytosis, purple fingers
- Areca catechu red stained teeth, muscarinic/nicotinic
- Ipomoea violacea, Argyreia nervosa Ergine = D-Lysergic acid amide hallucinogenic
- Strychnos nux vomica strychnine post-synaptic glycine antagonist, similar to tetanus
- Taxus Taxine B red fleshy aril chemo precursor
- Ackee fruit Blighia sapida hypoglycin A Jamaican vomiting sickness
- Licorice root Glycirrhiza sp glycirrhizic acid inhibits 11-β hydroxysteroid dehydrogenase; unable to convert cortisol to cortisone

CARDIAC GLYCOSIDES

- Digitalis
- Nerium oleander
- Convallaria Majalis
- Thevetia peruviana
- Helleborus niger

WORD ASSOCIATIONS

- Cassava Manihot escuelenta linamarin cyanogenic glycoside
- During drought: Konzo/Tropical Spastic Paraparesis/Tropical Ataxic Neuropathy UMN disease
- Lathyrus sativa Beta-N-oxalylamino-L-alanine neurolathyrism
- Toxalbumins: bind the 60s ribosomal subunit, inhibit RNA polymerase
 - Ricinis communis castor bean ricin; Abrus precatorius jequirty pea abrin
- Dieffenbachia calcium oxalate crystals raphides, iodoblasts, oral irritation
- Calabar bean Physostigma venenosum physostigine

ACMT BOARD REVIEW COURSE

High-Yield Bullets: Warfare/Terrorism

Shaun D. Carstairs, M.D. FACMT Scripps Healthcare San Diego Rady Children's Hospital

- Anthrax treatment LONG (months)
- When in doubt about $abx \rightarrow doxy$ or ciprofloxacin
- Smallpox
 - Centrifugal rash (vs. centripetal for varicella)
 - Ring vaccination
 - Antiviral tx (e.g., cidofovir)

- Toxin mechanisms
 - Botulinum inhibits SNARE protein, blocks exocytosis
 - Ricin binds 60S ribosome \rightarrow inhibits protein synthesis
 - Staph Enterotoxin B cytokine release

- Nerve agents know volatility, aging extremes
 - Volatility high (sarin); low (VX)
 - Aging fast (soman=minutes); low (VX=days)
- Sulfur mustard alkylator \rightarrow blistering; IARC 1 = resp. CA
- Lewisite know general structure (contains arsenic)
 - Treatment = BAL

- Pulmonary agents
 - Chlorine immediate effects (water soluble)
 - Phosgene delayed effects (not water soluble)
- HAZMAT -- know colors and what they mean
 - Blue = health hazard, Red = fire hazard
 - Yellow = reactivity, White = specific hazard

Questions?

ACMT BOARD REVIEW COURSE

High-Yield Bullets: Chemotherapeutics

Shaun D. Carstairs, M.D. FACMT Scripps Healthcare San Diego Rady Children's Hospital

Chemotherapeutics

- Know what part of cell cycle each agent affects
- Know general structures
 - Platinum compounds, alkylators, abx, antimetabolites
- Know methotrexate mechanism, toxicity/treatment
 - Leucovorin, urinary alkalinization, glucarpidase
- Antidotes incl. treatment of extravasation

Chemotherapeutics

- Know class-specific toxicities
 - Platinoids ototoxicity
 - Mustards hemorrhagic cystitis 2/2 acrolein
 - Bleomycin BOOP, pulmonary fibrosis
 - Anthracyclines cardiotoxicity

- Vinca alkaloids SIADH
- Arsenic trioxide QT prolongation, AV block
- Mitomycin HUS

Questions?

ACMT BOARD REVIEW COURSE

High-Yield Bullets: Pesticides

Shaun D. Carstairs, M.D. FACMT Scripps Healthcare San Diego Rady Children's Hospital

- Know the 3 distinct OP syndromes
 - Acute cholinergic toxicity
 - Intermediate syndrome
 - Delayed neuropathy
- Treatment of cholinesterase inhibitors
 - Decon, antimusc., benzos, oximes (ex. carbamates)

- Organochlorines all excitatory
 - DDT = Na+ channel **opener** (error on slide)
- Pyrethrins Type 1 vs. 2 (2 more toxic, CN group)
- Boric acid "boiled lobster" rash
- Chlorphenoxy herbicides tx w/ urinary alkalinization

- Know paraquat toxicity (pulm. fibrosis 2/2 free radicals)
 - Putrescine analog uptake into alveolar cells
 - Permissive hypoxia
- Dithiocarbamates disulfiram-like reaction
- Methyl bromide nonspecific alkylator \rightarrow general badness
- Sulfuryl fluoride hypocalcemia

Questions?