MUNI
PHARM

Chemical Warfare Agents
Radiotoxicology

lecture from Toxicology

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Chemical Warfare History

- poisons used as weapons in warfare
- large scale use of toxic chemicals as weapons occurred during the World War I (1914 -1918)
  - German chlorine gas attack in Flanders on April 1915
  - yperite used in 1917 by German army near Ypres in France

Chemical Warfare History

- World War II (1938 -1945)
  - Zyklon B
  - from 1941 used in gas chambers

Chemical Warfare History

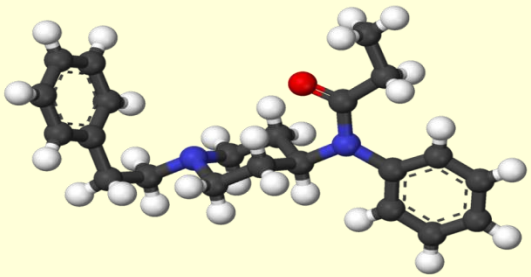
- Vietnam War (1961 -1971)
  - widespread use of chemical defoliants and herbicides
  - distributed in drums marked with color-coded bands (Agent Pink, Agent Green, Agent Purple, Agent Blue, Agent White, Agent Orange)

Tokyo Sarin Attack

- March 20 1995, Tokyo underground
- religious sect Aum Shinrikyo with the leader Shoko Asahara
- 12 people died

Moscow Theater Hostage Crisis

- 23 October 2002 Dubrovka Theater in Moscow
- Chechens Islamists took 850 hostages and after a two-and-a-half day siege they pumped maybe fentanyl into the ventilation
- 129 of hostages were killed



Chemical Warfare

NERVE AGENTS

BLISTER AGENTS (VESICANTS)

CHOKING AGENTS (LUNG IRRITANTS)

INCAPACITATING AGENTS (HALLUCINOGENS)

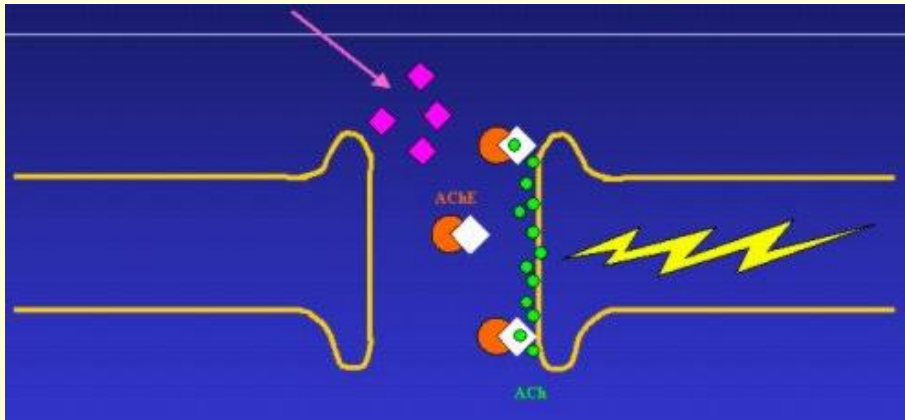
BLOOD AGENTS

TEAR GAS (EYE IRRITANTS)

BIOLOGICAL WARFARE AGENTS

Nerve Agents Organophosphates

- sarin, soman, tabun
- highly lipophilic compounds taken up by ingestion, inhalation and through the skin
- inhibition of acetylcholinesterase (AChE)
- peripheral muscarinic stimulation of exocrine glands and smooth muscles
- respiratory paralysis with bronchorrhea and bronchospasm
- epileptiform stimulation with seizures
- treatment: atropine, diazepam, oximes



Alkylating Blister Agents (Vesicants)

- sulfur and nitrogen mustards (compounds with chloroethyl groups)
- slowly evaporating liquids with a strong odor (garlic, fish)
- highly reactive, lipophilic compounds taken up by ingestion, inhalation and through the skin
- symptom-free interval of several hours, the maximum after 3–4 days
- skin: itching, redness, blistering, necrosis
- systemic toxicity due to alkylation of DNA (potential cancer causing agent)
- treatment: skin cooling, sterile dressings

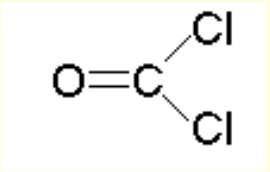
Arsenic-Containing Vesicants

LEWISITE

- lipophilic substance taken up by ingestion, inhalation and through the skin
- wide range of symptoms
- eyes – irritation, blepharospasm, erosion
- airways – irritation, cough, toxic pulmonary edema
- GIT – nausea, vomiting, diarrhea
- skin – irritation, burning, redness, swelling, blistering, necrosis

Choking Agents (Lung Irritants)

- poisons that damage the lungs such as phosgene ($COCl_2$), chlorine gas (Cl_2), chloropicrin
- major role as choking agents in WWI
- lead to choking and toxic lung edema



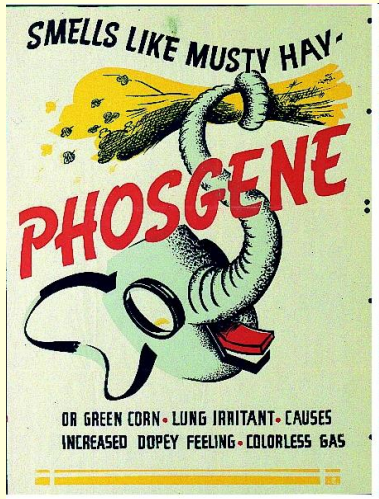
Choking Agents (Lung Irritants)

PHOSGENE

- smell range from decaying fruit to fresh-cut grass or mouldy hay

- irritation of eyes, nose and throat, chest tightness occur rapidly followed by shortness of breath and coughing

- the dose greater than 30 ppm a minute leads to severe lung damage and fatal lung edema



- at high concentrations, individuals lose their sense of smell and their ability to assess the danger

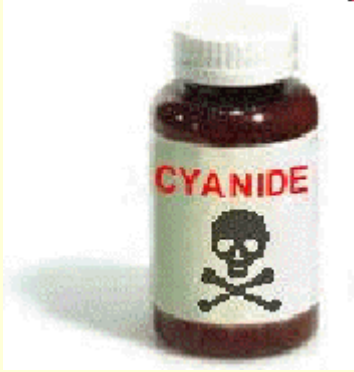
Psychically Incapacitating Agents

- 3-quinuclidinyl benzilate (BZ), hallucinogens (atropine, scopolamine, LSD, hyoscyamine)

- lead to the production of temporary mental effects that will render individuals incapable of concerted effort

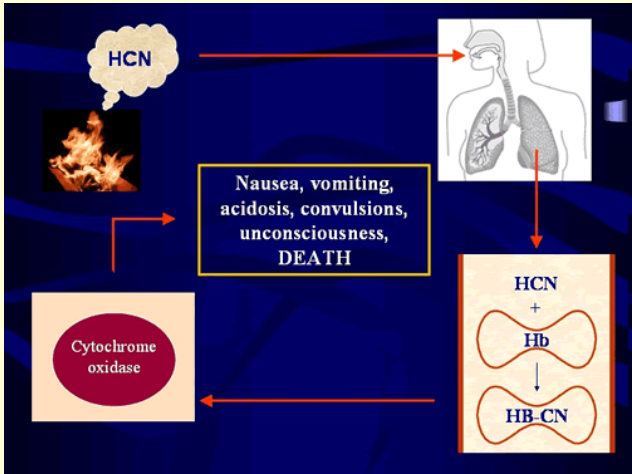
- disturbances in the level of consciousness
- poor judgment and insight
- stupor, confusion, confabulation
- hallucinations, ilusions

Blood Agents



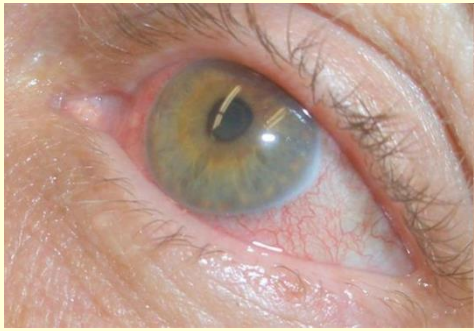
Hydrogen cyanide (HCN)

- high toxicity by inhalation or ingestion
- high vapor pressure at room temperature
- immediate effect – stops cellular respiration by inhibiting an enzyme cytochrome c oxidase in mitochondria
- concentration of 3500 ppm (about 3200 mg/m3) will kill a human in about 1 minute
- chemical weapon in WWI
- used as Zyklon B in gas chambers during WWII



Eye Irritants (Tear Gases)

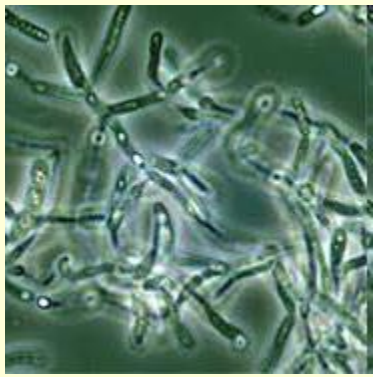
- chloroacetophenone, chlorobenzylidene malononitrile



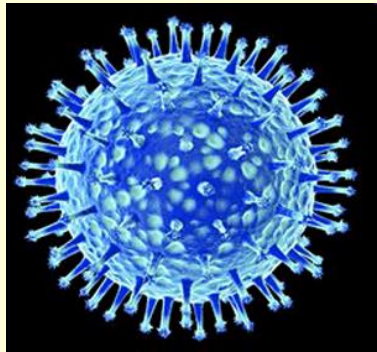
- used for self-defense and riot control
- primarily taken up by inhalation
- mechanism of action has not been established
- intense stimulation of the mucosae (eyes, nasopharynx)
- high concentrations cause headache, nausea and toxic pulmonary edema

Biological Warfare Agents

- specific application devices (bomb, letter bomb, poisoning of water supply) that release biological agents
  - living organisms (bacteria, viruses, fungi) or their toxins
- usually release of odorless and invisible aerosol

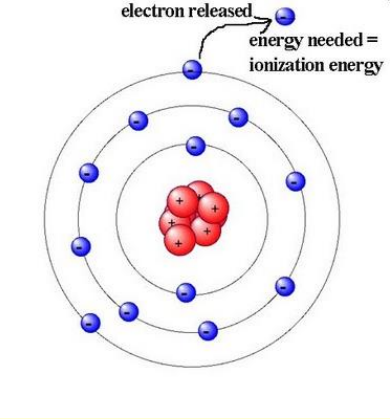


- fear of bioterrorism
- genetic manipulation of pathogens with increased virulence, resistance and stability



Biological Warfare Agents

- smallpox (variola virus)
- anthrax (*Bacillus anthracis*)
- plague (*Yersinia pestis*)
- tularemia (*Francisella tularensis*)
- brucellosis (*Brucella species*)
- encephalitis (viruses)
- hemorrhage (viruses)
- Botulinum toxin (*Clostridium botulinum*)
- Staphylococcus aureus toxin



Radiation

Ionizing radiation

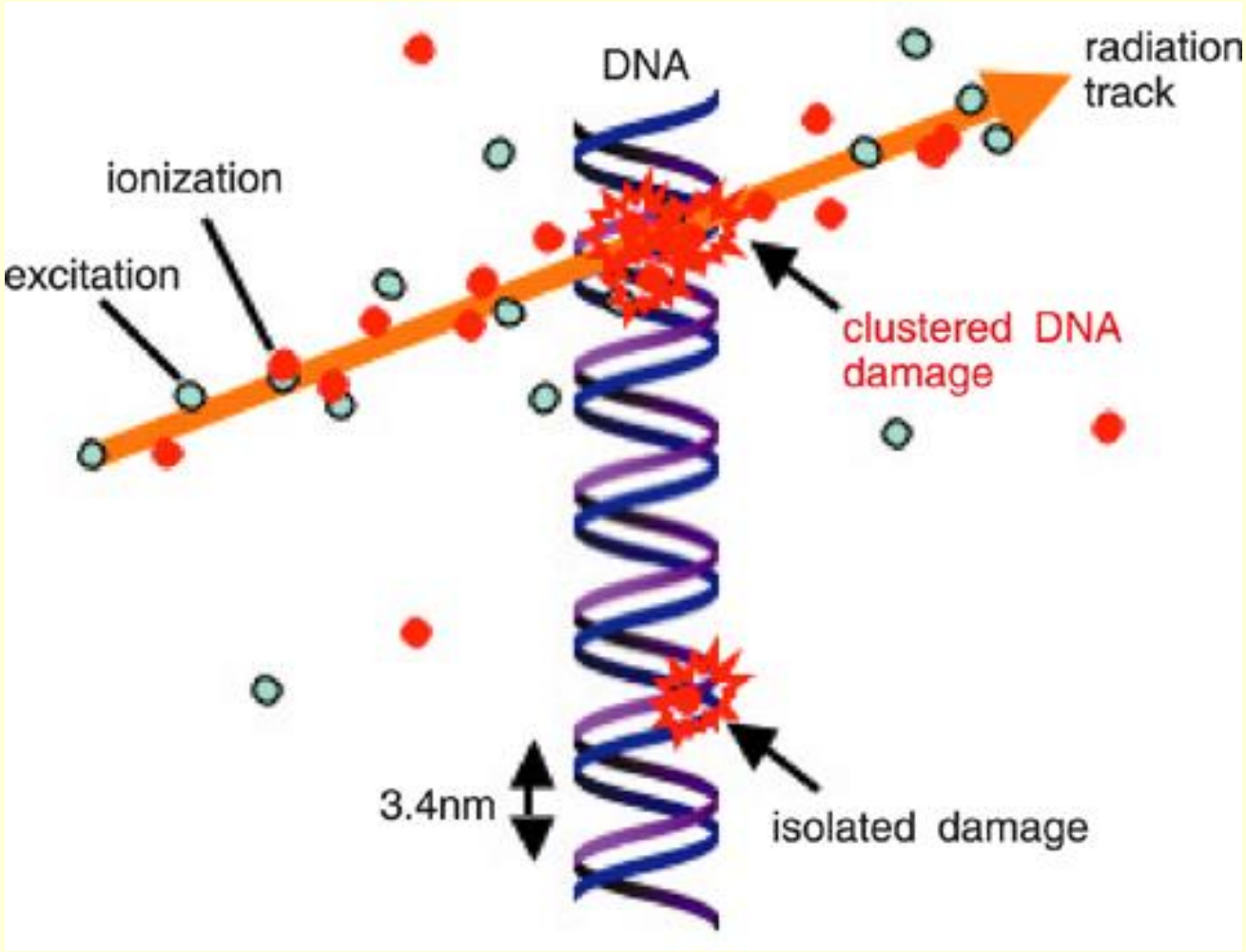
- high-energy electromagnetic radiation (X-rays, γ-rays) and particulate radiation (α-rays, β-rays, protons, neutrons, heavy ions)

- radiation capable of producing ions when interacting with matter – x-rays, alpha, beta, gamma, cosmic rays

Nonionizing radiation

- short-wave radiation (ultraviolet, laser), radiowaves, microwaves, electric and magnetic fields

Biological Effects of Ionizing Radiation



Alpha Particles

- two neutrons and two protons
- charge of +2
- emitted from nucleus of radioactive atoms
- transfer energy in very short distances (10 cm in air)
- shielded by paper or layer of skin
- primary hazard from internal exposure
- alpha emitters can accumulate in tissue (bone, kidney, liver, lung, spleen) causing local damage

Beta Particles

- small electrically charged particles similar to electrons
- charge of -1
- ejected from nuclei of radioactive atoms
- emitted with various kinetic energies
- shielded by wood, body penetration 0.2 to 1.3 cm depending on energy
- can cause skin burns or be an internal hazard of ingested

Gamma Rays

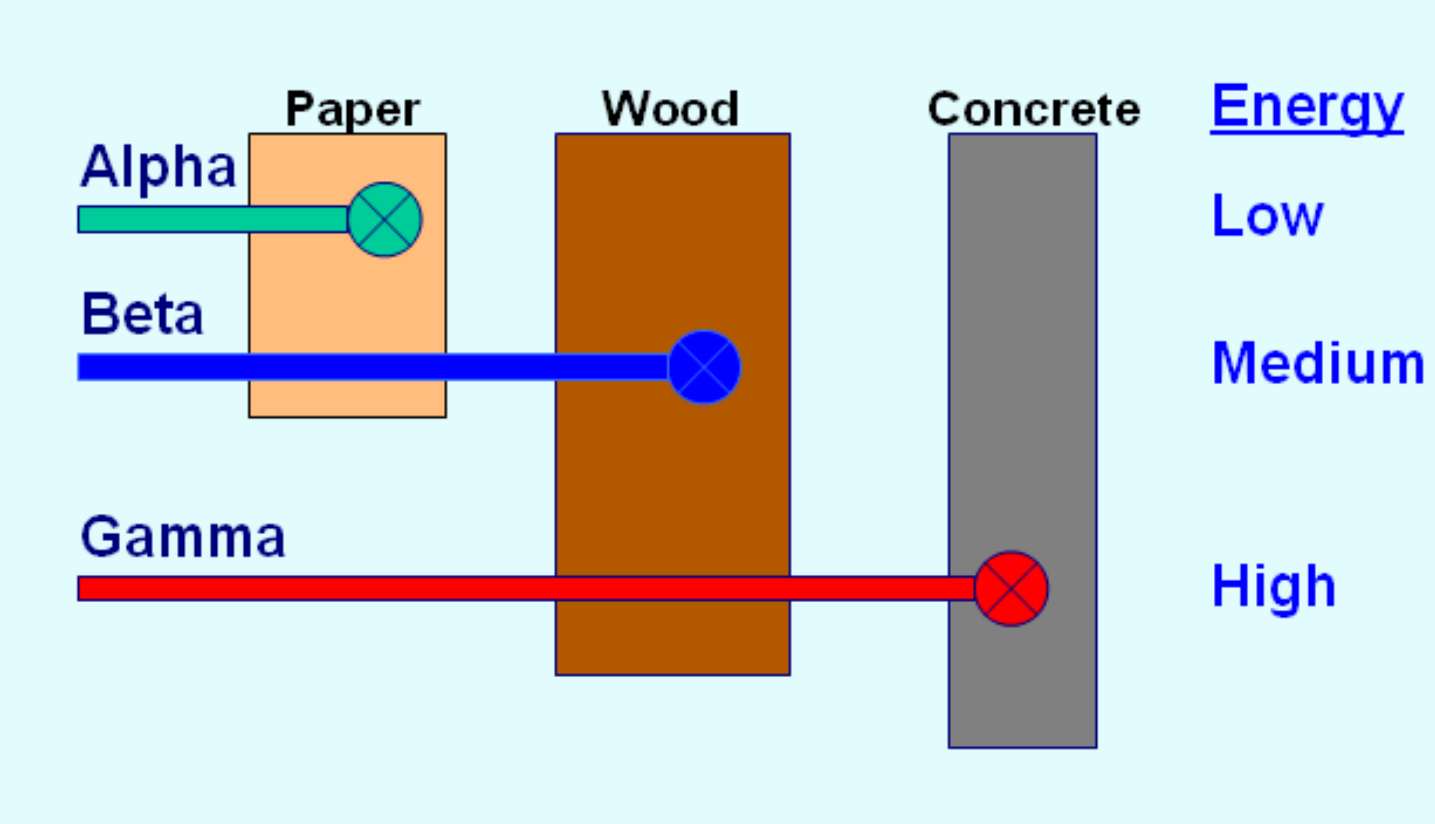
- electromagnetic photons or radiation (identical to X-rays except for source)
- emitted from the nucleus of radioactive atoms – spontaneous emission
- emitted with kinetic energy related to radioactive source
- highly penetrating – extensive shielding required
- serious external radiation hazard

X-rays

- overlap with gamma-rays
- electromagnetic photons or radiation
- produced from orbiting electrons or free electrons – usually machine produced
- produced when electrons strike a target material inside and an x-ray tube
- emitted with various energies & wavelengths
- highly penetrating – extensive shielding required
- external radiation hazard
- discovered in 1895 by Roentgen

Radiation

- abilities to penetrate matter differ considerably



Radiation

Half life

- rate of decay of the radioisotope
- how long it takes to lose half their strength
- can range from very short to billions of years
- carbon – 5730 years, which makes it valuable for dating

Reducing exposure

- time
  - reduce the spent near the source of radiation
- distance
  - increase the distance from the source of radiation
- shielding
  - place shielding material between you and the source of radiation

Ionizing Radiation Health Effects

- we evolved with a certain level of naturally occurring ionizing radiation from cosmic radiation, radioactive materials in the earth
- we have mechanisms to repair damage

- Exposure – X (J/kg)
  (Related to energy)
- Absorbed Dose – Gray (Gy)
  (amount of energy absorbed)
- Equivalent Dose – Sievert (Sv)
  (makes different sources of radiation equivalent)

Examples of Tissue Sensitivity

Very High	**White blood cells (bone marrow)** **Intestinal epithelium** **Reproductive cells**
High	**Optic lens epithelium** **Esophageal epithelium** **Mucous membranes**
Medium	**Brain – glial cells** **Lung, kidney, liver, thyroid, pancreatic epithelium**
Low	**Mature red blood cells** **Muscle cells** **Mature bone and cartilage**

Radioactive Metals

Radium (Ra)

- isotope ^{226}Ra incorporated into the bones
- disintegrates into the noble gas radon occurring in underground mines
- used in spas for treating rheumatism or gout

- induce damage to bone marrow (hematopoiesis) – leukopenia, osteosarcoma

Radioactive Metals

Uranium (U)

- isotope ^{235}U used as a nuclear fuel
- used as the explosive in the Hiroshima bomb
- damage to kidneys (uranium nephritis) and lungs (toxic pulmonary edema)

Plutonium (Pu)

- isotope ^{239}Pu used in the bomb dropped on Nagasaki
- bound in the blood to transferrin
- stored primarily in the bone marrow and liver