Science and Technology

Chemical Weapons Short

By

Mark Bishop

Personal Protection (Military)

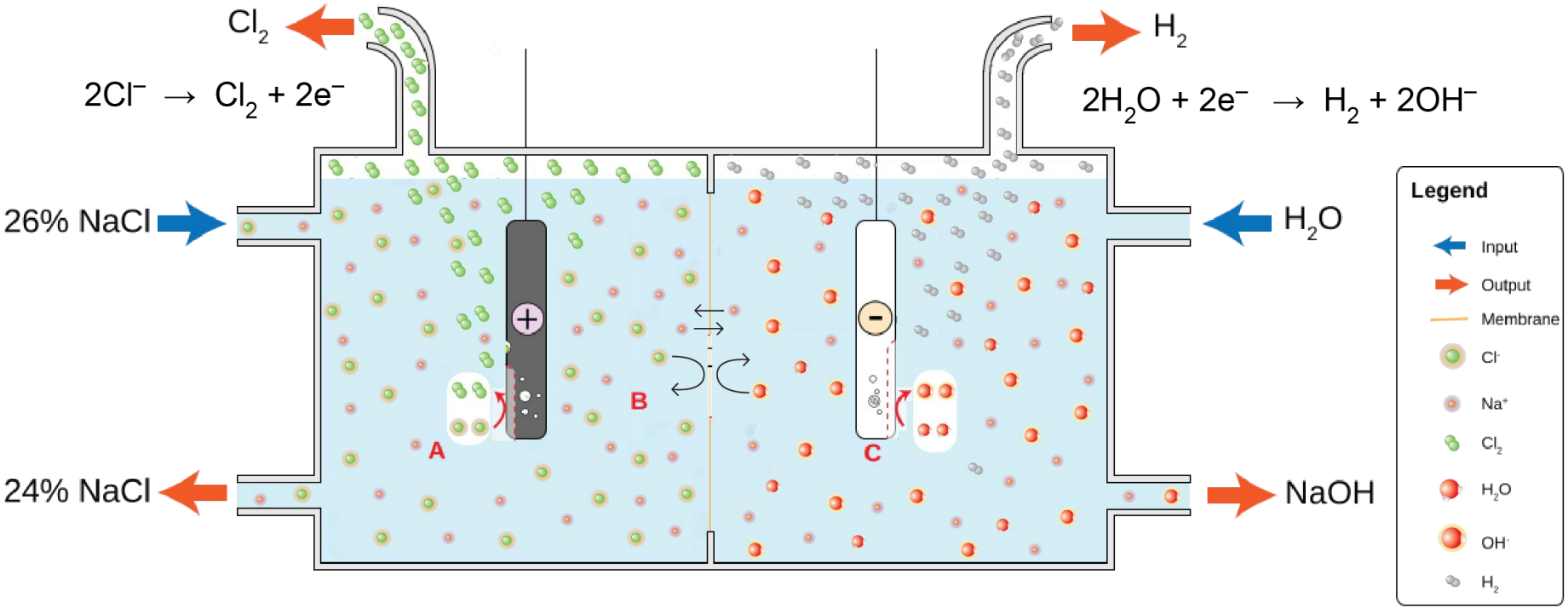
Ways to Obtain Chlorine, Cl_2

- Produce it
- Capture it from production plant
- Divert it during transportation
- From water treatment plant

Production of Chlorine

- Compared to other chemical weapons, chlorine is relatively easy to make by electrolysis of sodium chloride in water.

$$2NaCl(aq) + 2H_2O(l) \rightarrow Cl_2(g) + H_2(g) + 2NaOH(aq)$$



Transportation of Chlorine

- By rail in tank cars

- By highway in cargo tanks and cylinders
- By barge

Chlorine in Water Treatment Plant

- Commonly in one-ton containers

Ways to Disperse Chlorine, Cl_2, as a CW

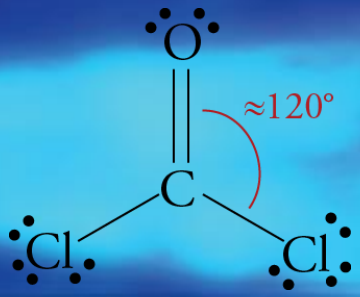
- Stationary device, e.g. pressurized gas tanks
- Car or truck bombs
- Drop containers from planes or helicopters that will burst on impact (barrel bombs)
- Roadside bombs
- Projectiles

A 120-millimeter mortar shell struck fortifications at a Kurdish military position near the Mosul Dam in June, arms experts said, sickening several Kurdish fighters who were nearby.

Credit
Conflict Armament Research and Sahan Research

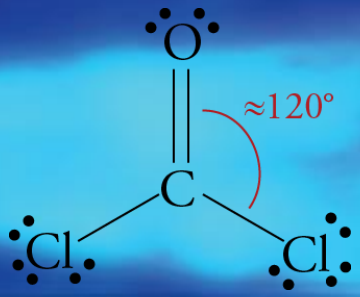
http://www.nytimes.com/2015/07/18/world/middleeast/islamic-state-isis-chemical-weapons-iraq-syria.html

Phosgene, $COCl_2$



- Gas above 46.94°F, so it is easy to disperse.
- Less irritating than Cl_2, so soldiers were slower to put on their gas masks
- Odorless when pure: smells like new-mown hay when not.
- 18 times more toxic than Cl_2
- It causes suffocation by reacting with proteins and disrupting the transfer of oxygen to the body.
- Relatively slow acting (Symptoms begin in 30 minutes to 72 hours, depending on the degree of exposure.)
- No antidotes…treat symptoms…provide oxygen, if necessary

Phosgene, $COCl_2$



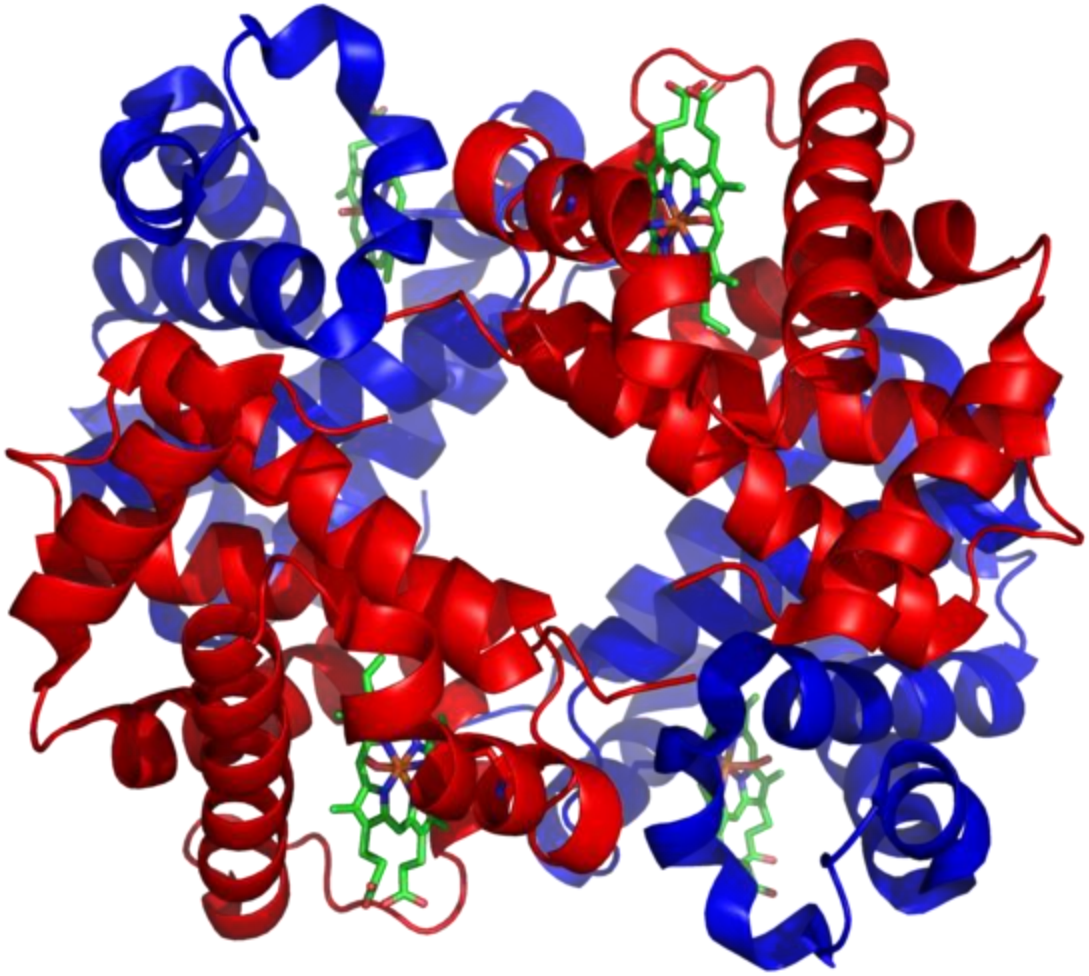
- More difficult to make than chlorine. Produced by passing purified carbon monoxide and chlorine gas through a bed of porous activated carbon, which serves as catalyst. The reactor must be cooled to prevent phosgene from decomposing.

  $$CO + Cl_2 \rightarrow COCl_2$$

- Shipped in cylinders as a liquefied compressed gas.
- Breaks down in water into hydrochloric acid and carbon dioxide.

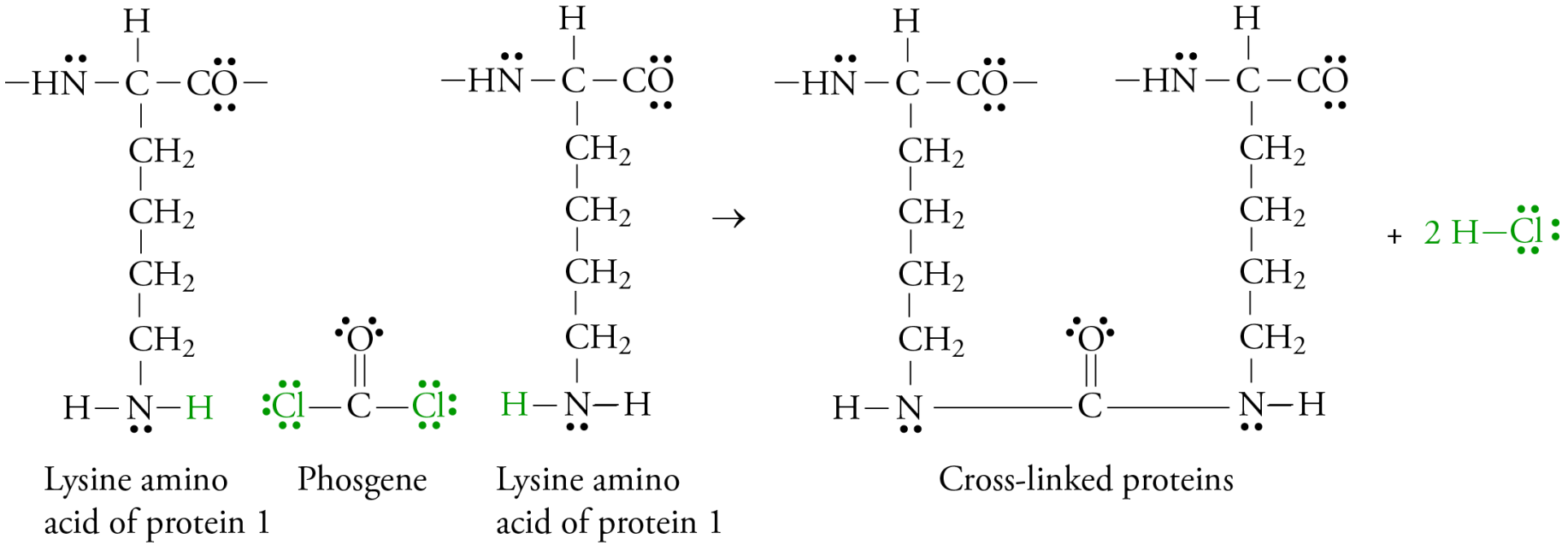
Hemoglobin

- The protein hemoglobin carries oxygen in the blood.



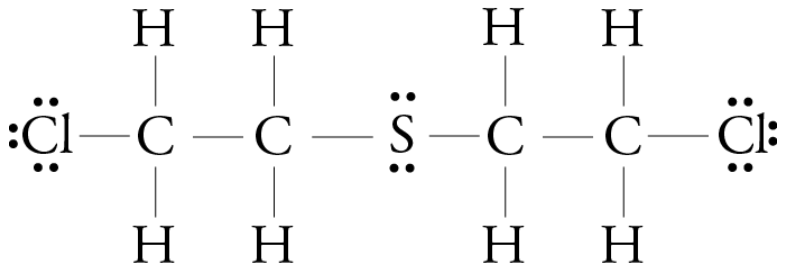
Phosgene Reactions with Protein

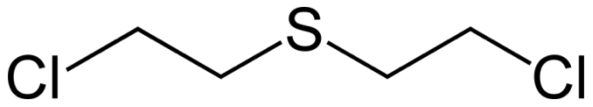
- Phosgene reacts with amino acids in proteins by acylation, adding an acyl group (a group with a CO double bond).
- It reacts with the amines of the proteins, linking protein together.
- The altered proteins no longer function in their normal way.

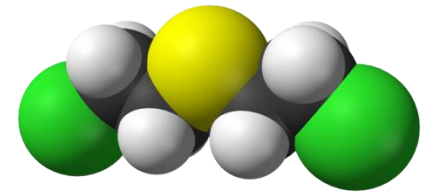


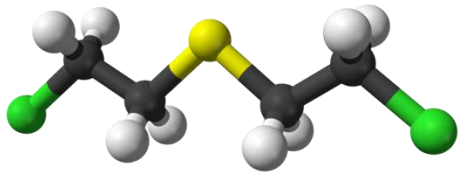
Sulfur Mustard, H or HD

- Called “mustard” because of its horseradish- or garlic-like smell when impure.
- It is fat-soluble, so it dissolves in the oils in the skin, causing severe chemical burns and blisters.



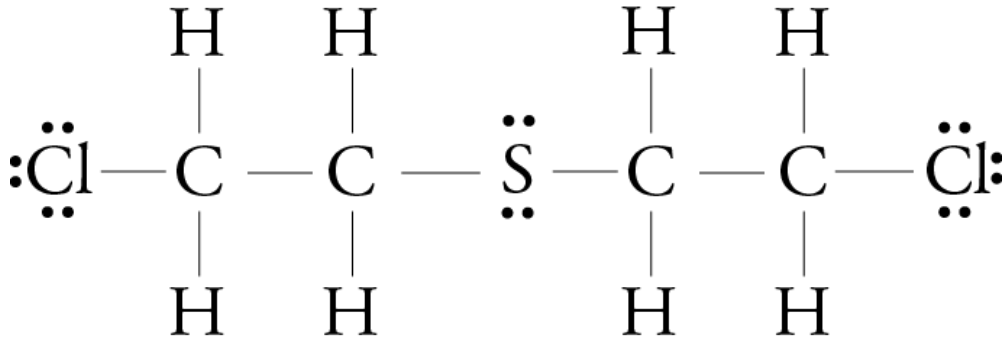






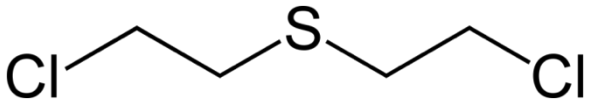
Ways to Describe Organic Compounds

- Lewis structures



- Condensed Formulas, $ClCH_2CH_2SCH_2CH_2Cl$

- Line Drawings



Sulfur Mustard

- Viscous liquid
- Colorless when pure, yellow or brown when impure
- Disseminated as an aerosol
- Can contaminate water and food
- Damages cells within minutes of contact.
- Pain and other health effects are delayed until hours after exposure.
- Can cause temporary or permanent blindness
- There is no antidote.

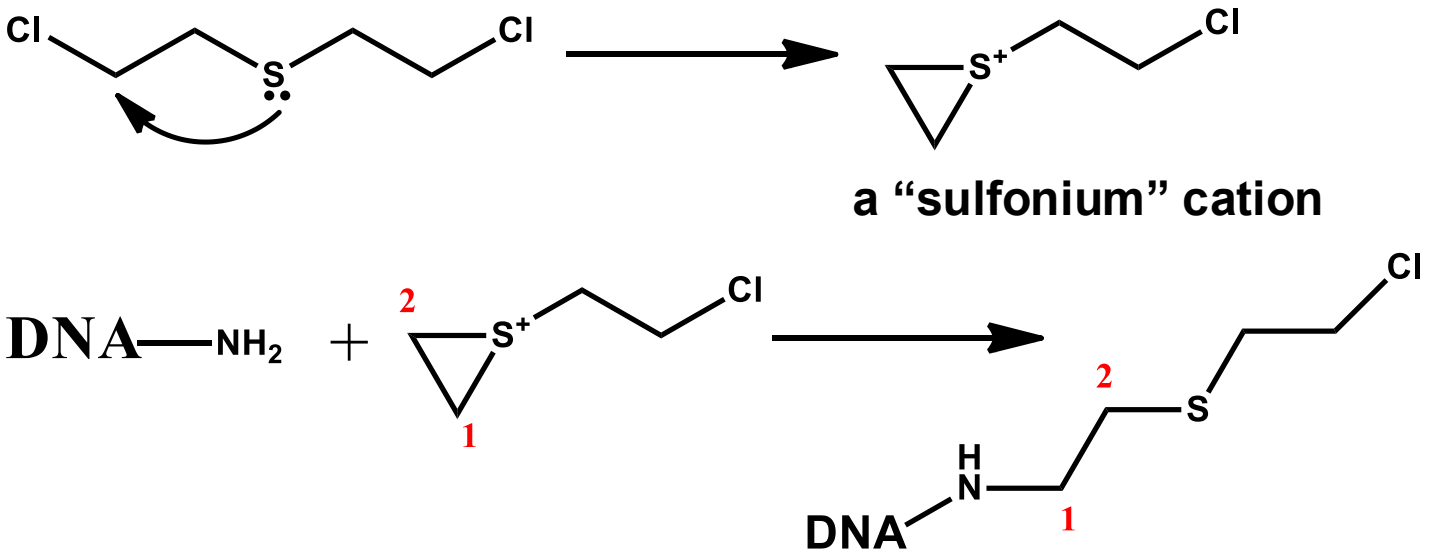
Sulfur Mustard (cont.)

- “H” usually refers to an impure form of sulfur mustard with 20-30% impurities…has short shelf-life. It is relatively easy to make.
- “HD” refers to a more pure form (96% pure) that can be stored longer.
- It can remain on the ground for weeks, making the area dangerous long after its dispersal.

155 mm artillery shells that contained "HD" (distilled sulfur mustard agent) at Pueblo chemical weapons storage facility until it was recently destroyed

Effect of Sulfur Mustard on DNA

Sulfur mustard forms a sulfonium ion, which attaches to a number of different biomolecules, including proteins and the nucleotides of DNA, disrupting cell division and function. This can lead to cellular death or cancer.



Sulfur Mustard Physiological Effects and Symptoms

- Damages the cells within the bone marrow that are necessary for making blood cells. This affects the body's immune system.
- Affects a part of the nervous system responsible for everyday bodily function,
- Leads to excessive saliva, tears, and urine; gastrointestinal (GI) cramping and diarrhea; vomiting (emesis); and constricted or pinpoint pupils (miosis).

Sulfur Mustard Dissemination

- Sulfur mustard has a fairly high boiling point (217 °C), so although it can be dispersed as a gas, it is more likely to be dispersed as an aerosol.
- Can be dispersed by munitions.
- Liquid can contaminate water or food.

Sulfur Mustard Treatment

- Can limit the formation of blisters by applying soap and water, dilute household bleach, or a solution called DS2 (2% sodium hydroxide, NaOH, 70% diethylamine, $CH_3CH_2NHCH_2CH_3$, and 28% ethylene glycol monomethyl ether, $CH_3OCH_2CH_2OH$)
- Early rinsing of the exposed area with Betadine (providone-iodine) dissolved in glycofurol will reduce symptoms.

Sulfur Mustard Treatment

- After initial treatment, patients with blisters are treated in the same way that any burn victim would be treated.
- Because the symptoms do not appear for hours, it is less likely that the treatments would be done in time to avoid problems.
- Fatal in about 2% of exposures in WW1, so mostly used as an incapacitating agent.

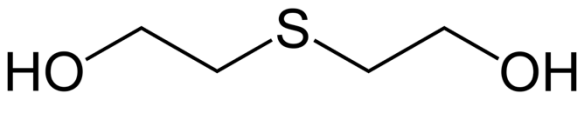
Factors Affecting the Ability to Make CW

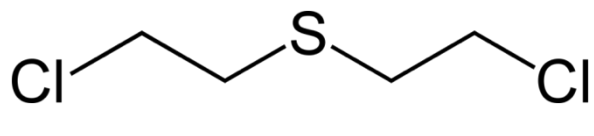
- Scientific and industrial expertise
- Availability of precursors
- Availability of equipment
- Money available
- Desired quantity
- Desired purity
  - For a variety of reasons, products of chemical reactions are rarely pure, so after the initial reactions, steps are taken to purify the product.
- Concern for safety of workers
- Concern for the environment

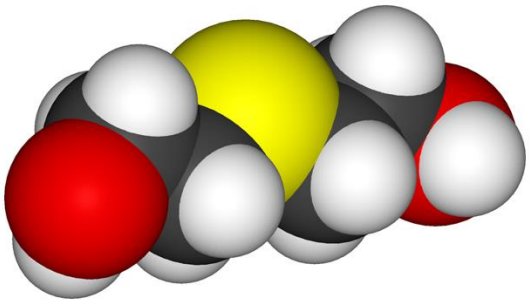
Production of Sulfur Mustard

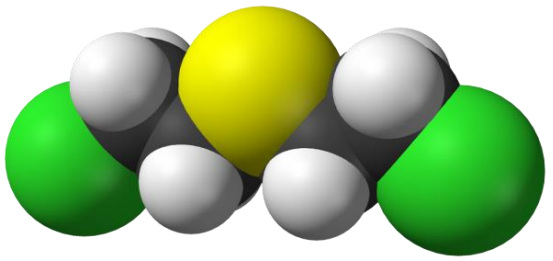
- There are many ways to make sulfur mustard.
- The simplest way is combining thiodiglycol and concentrated hydrochloric acid.

$$(HOCH_2CH_2)_2S + 2HCl \rightarrow (Cl\text{-}CH_2CH_2)_2S + 2H_2O$$





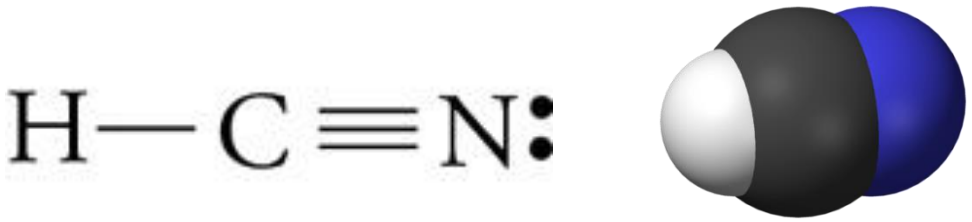




Production of Sulfur Mustard

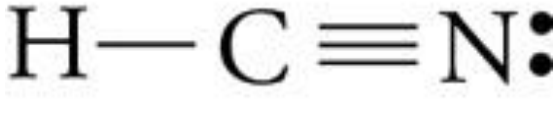
- Thiodiglycol (CWC Schedule 2 Part B)
  - Used to make many things, including epoxy resins, pen inks, plastics, pesticides, dyes, and photographic developing solutions.
  - Produced in several countries, including Germany and the UK.
  - Many firms purchase it.
- If thiodiglycol can be obtained, making sulfur mustard is not difficult.
- It does not require sophisticated equipment.
- Distillation leads to improved purity, which allows longer storage.

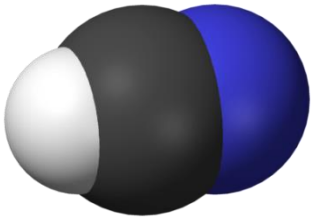
Hydrogen Cyanide, HCN



- Volatile liquid – boiling point 26 °C (79 °F)
- The gas is colorless.
- Fatal at concentrations as low as 300 mg/m^3 in air.
- According to OPCW, there are no confirmed uses as CW, but may have been used by U.S., France, and Italy in WWI and by Iraq against Iran and the Kurds.
- Unlike chlorine and phosgene, it's less dense than air, so it disperses too quickly to be effective outside.

Hydrogen Cyanide, HCN





- Affects almost every cell in the body by disrupting cellular respiration
- Effects can happen in seconds and death within minutes, depending on the level of exposure
- Bitter almond odor, which some people cannot smell, which makes it somewhat undetectable when dispersed as a gas.
- Can be used to poison water and food
- Absorbed quickly through the skin

Hydrogen Cyanide, HCN

- Most HCN is made from the following reaction at 1200 °C over a platinum catalyst.

$$2CH_4 + 2NH_3 + 3O_2 \rightarrow 2HCN + 6H_2O$$

- Used commercially for fumigation, electroplating, mining, chemical synthesis, and the production of synthetic fibers, plastics, dyes, and pesticides, so it is on Schedule 3, Part A of the CWC.
- HCN can be converted into sodium cyanide, NaCN, or potassium cyanide, KCN, and transported in water solution.

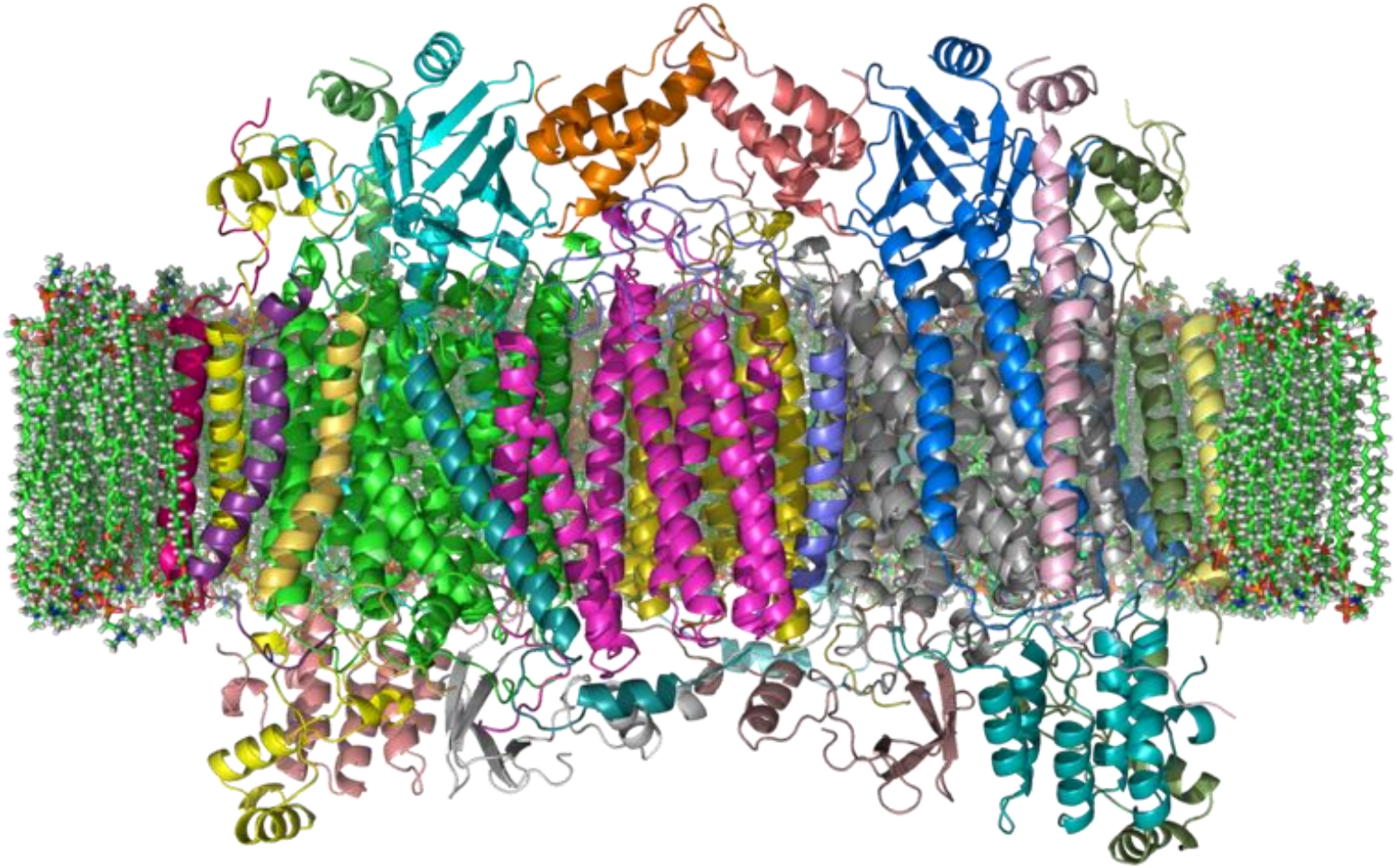
Cellular Respiration

- Many chemical reactions in our bodies form less stable products and therefore require energy.
- This energy comes from coupling the endergonic reactions (that require energy) with exergonic reactions (that release energy).
- The most important exergonic reaction involves the conversion of ATP into ADP and a phosphate group.
- ATP is produced in the mitochondria, which are organelles (subcellular structures that have one or more specific jobs in our cells).

Cellular Respiration

- The primary reaction that provides mitochondria with the energy to build ATP is the combination of oxygen with pyruvate ions that come from the breakdown of glucose. The products are carbon dioxide, water, and the energy that makes the formation of ATP possible. This is called cellular respiration.
- HCN disrupts cellular respiration by inhibiting an enzyme (cytochrome oxidase) in mitochondria that delivers electrons to oxygen, which is a necessary step in cellular respiration. HCN binds to iron in cytochrome oxidase.

Cytochrome c Oxidase in cell membrane



Cellular Respiration

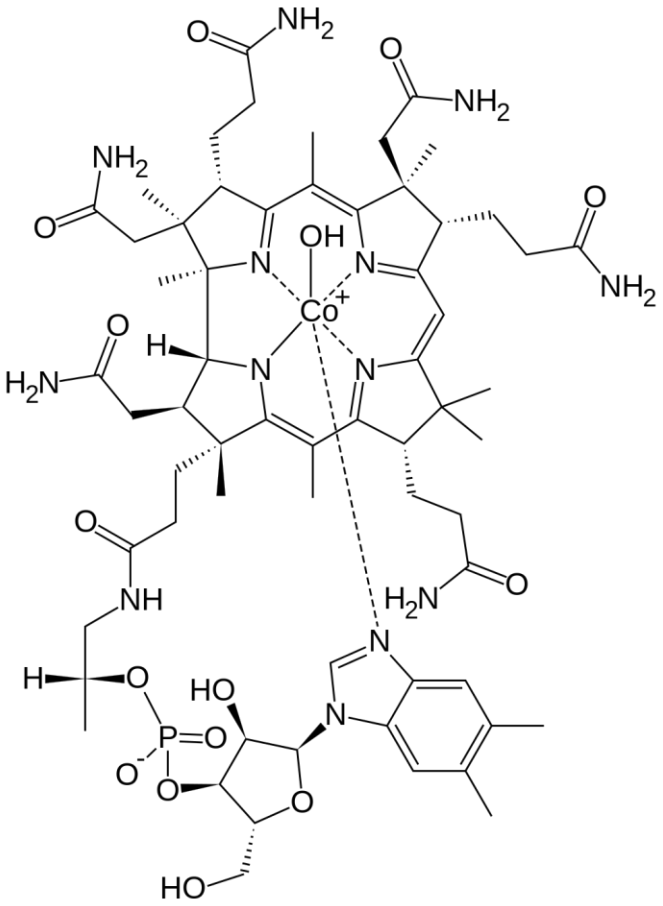
- Acts very quickly to cause dizziness, vomiting, loss of consciousness, and death
- Because the central nervous system (brain), the cardiovascular system (heart and blood vessels), and the pulmonary system (lungs) are particularly sensitive to low oxygen, they are affected most.

One HCN Antidote

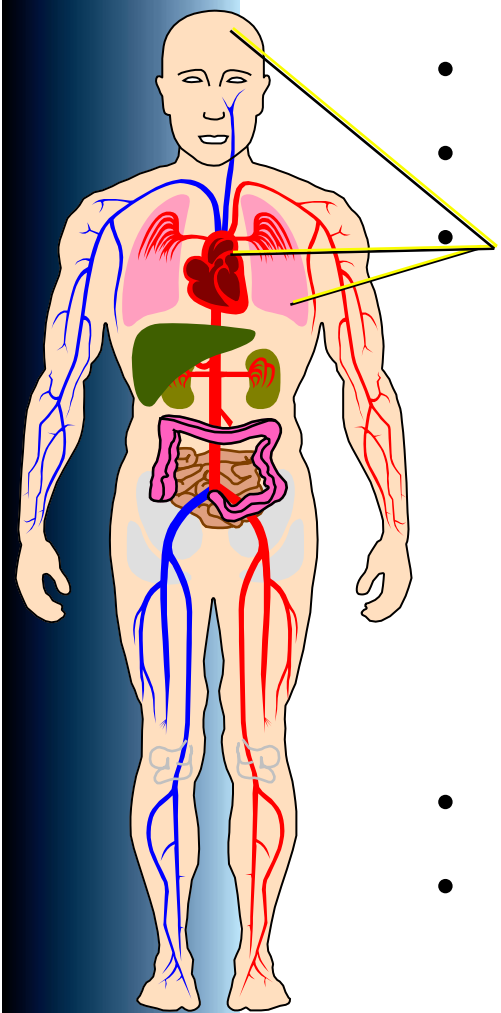
- Best administered by health professional
- First - a small inhaled dose of amyl nitrite
  - Nitrites oxidize some of hemoglobin's iron from the Fe^{2+} state to the Fe^{3+} state, converting the hemoglobin into methemoglobin.
  - Cyanide preferentially bonds to methemoglobin rather than the cytochrome oxidase, converting methemoglobin into cyanmethemoglobin.
- Second - intravenous sodium nitrite
- Third - intravenous sodium thiosulfate
  - Converts the cyanmethemoglobin to thiocyanate, sulfite, and hemoglobin. The thiocyanate is then excreted in the urine.

HCN Antidote

- Hydroxocobalamin (vitamin B_{12a}) is available in Cyanokit antidote kits.
- Given in up to two 5 g intervenous treatments.
- Cyanide is converted in cyanocobalamine, which is safely eliminated by the kidneys.



Nerve Agents



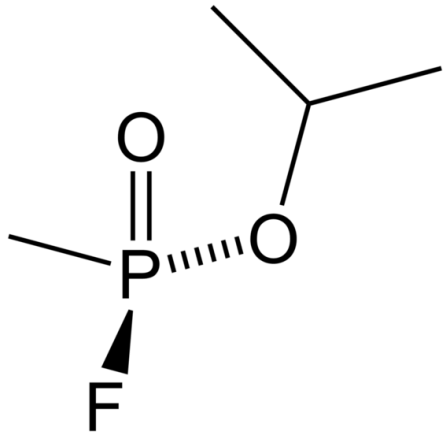
- Tabun, **sarin**, soman, cyclosarin, **VX**, **Novichok**
- Modes of action: contact, inhalation
- Physiological effects
  - Disrupt the mechanism by which nerves transfer messages to organs
  - Causes seizures and loss of body control
  - Exhausts muscles, including heart and diaphragm
  - Lethal dose can cause death from respiratory failure in five minutes
- Form when disseminated: liquid, vapor, aerosol
- Required defensive gear: protective mask & clothing

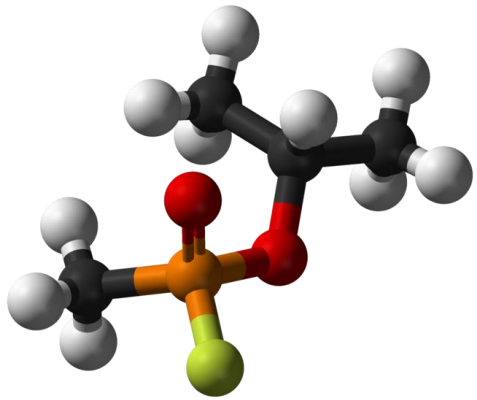
Nerve Agents

- Cause contraction of pupils, profuse salivation, convulsions, involuntary urination and defecation, and eventual death by asphyxiation as control is lost over respiratory muscles.
- U.S. and the Soviet Union developed and stockpiled large quantities of nerve agents in a chemical arms race that mirrored the nuclear arms race.

Sarin (GB)

- Developed by the Germans in 1939
- Adopted as the standard nerve agent for the U.S. in 1948.
- Odorless and colorless liquid
- Relatively stable when stockpiled
- Relatively volatile
- Can cause death in minutes
- Breaks down fairly rapidly in the environment
- Has antidotes
- Hard to make





http://chemapps.stolaf.edu/jmol/jmol.php?model=FP%28%3DO%29%28OC%28C%29C%29C

Sarin (GB)

- Can be absorbed into the body by inhalation, ingestion, skin contact, and eye contact.
- Odorless and tasteless so it an be used to poison water and food.

Sarin (GB)

- If sarin does not have a high purity, it degrades fairly rapidly.
- Its shelf-life can be extended with stabilizers.
- A very large amount of sarin has been made, but very little of it has been used.
  - March 1988 - Iraq used against Kurd city of Halabja
  - April 1988 – Iraq against Iran.
  - 3/20/1995 - Used in the Tokyo Subway attack by Aum Shinrikyo
  - 8/21/2013 – Ghouta, Syria
  - 4/4/2017 – Khan Shaykhun, Syria
  - 4/7/2018 – Douma, Syria

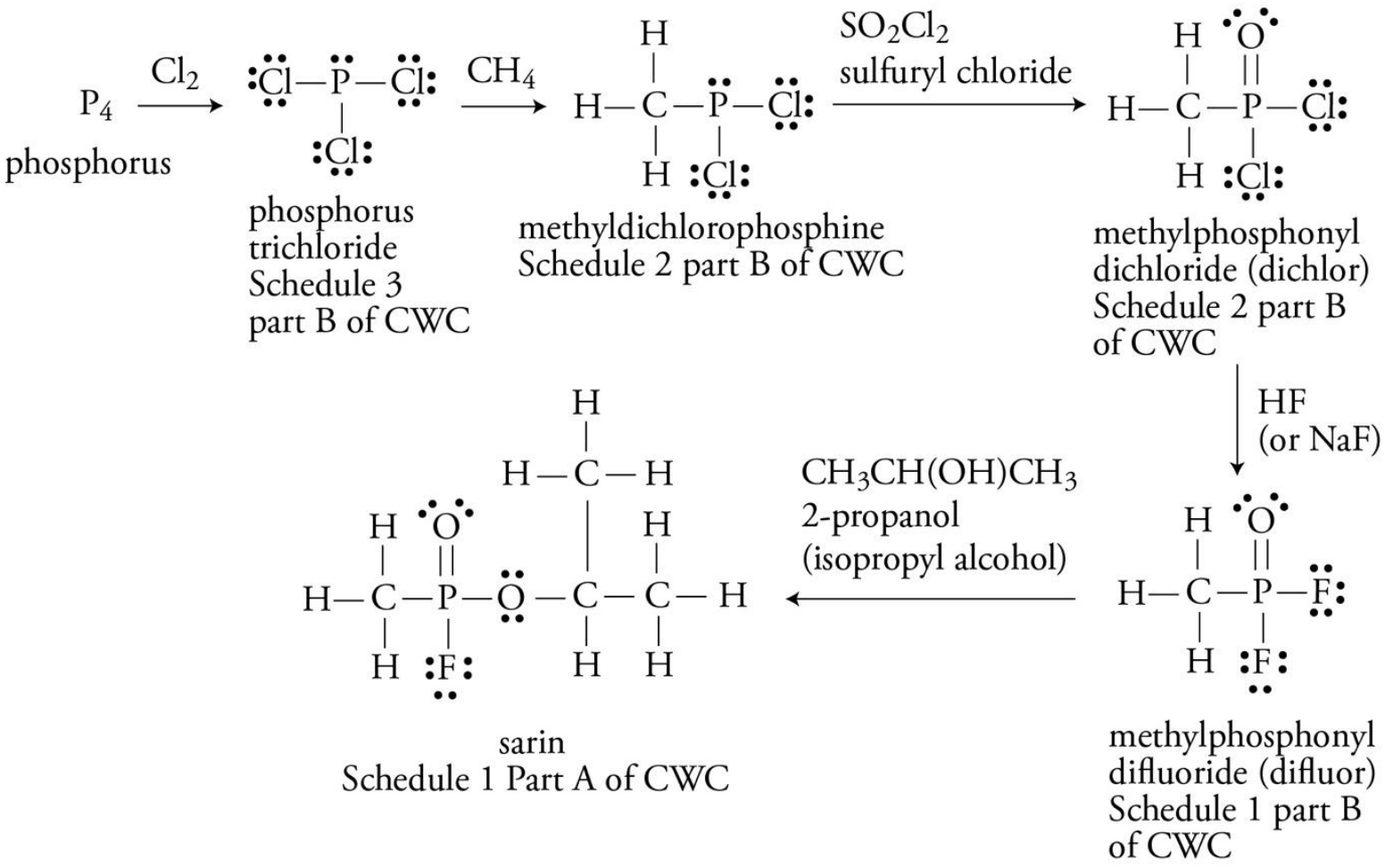
Factors Affecting the Ability to Make Chemical Weapons

- Availability of chemical and chemical engineering knowledge.
- Availability of precursors
- Availability of chemical equipment
- Knowledge of production techniques

Because all of these are increasing, there are about 100 countries that have the capability to make simple chemical weapons, such as chlorine, phosgene, hydrogen cyanide, and sulfur mustard.

Because the synthesis of nerve agents requires high temperatures and highly corrosive chemicals, a smaller number of countries could make nerve agents.

Rough Steps in Production of Sarin



Production of Sarin

- Most easily prepared from methylphosphonyl difluoride and isopropyl alcohol.

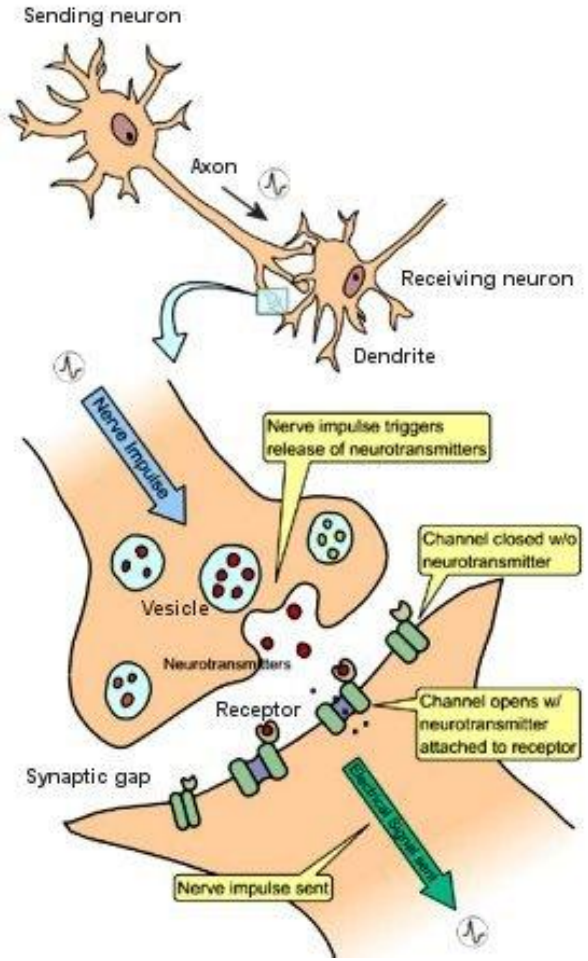
  $CH_3P(O)F_2 + (CH_3)_2CHOH \rightarrow [(CH_3)_2CHO]CH_3P(O)F + HF$

- Three technical hurdles when making from simpler substances.
  - Involves corrosive hot hydrochloric acid, HCl, and hydrogen fluoride, HF, so need corrosion resistant equipment, e.g. vessels and pipes of an alloy that is 40% nickel…Monel and Hastalloy.
  - Alkylation reaction in which a methyl, $-CH_3$, group is added to the phosphorus atom is technically difficult.
  - Distillation necessary to produce high-purity necessary for long storage.
- Requires expensive chemical facilities

Neurotransmitters

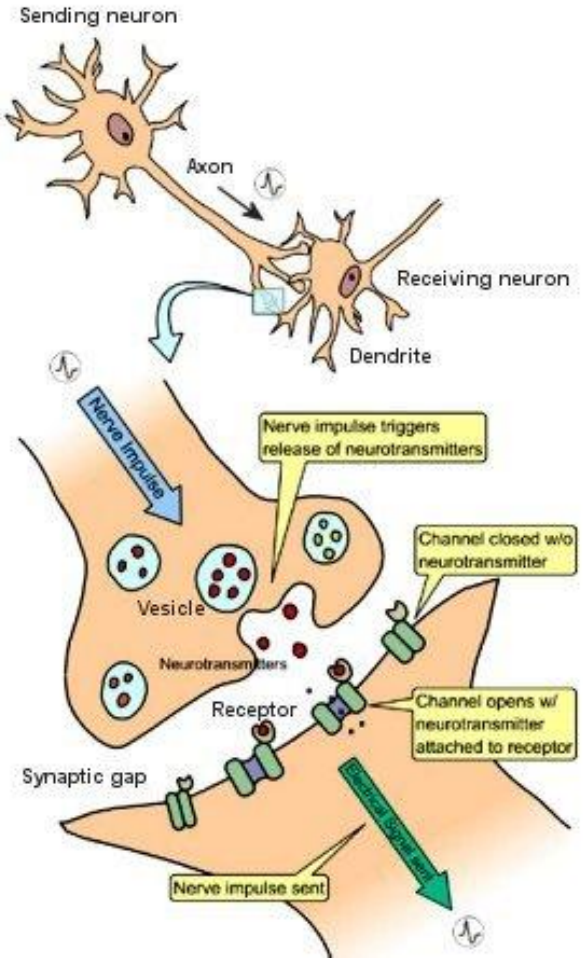
- Neurotransmitters cause nerve cells to fire.

From http://universe-review.ca/R10-16-ANS.htm



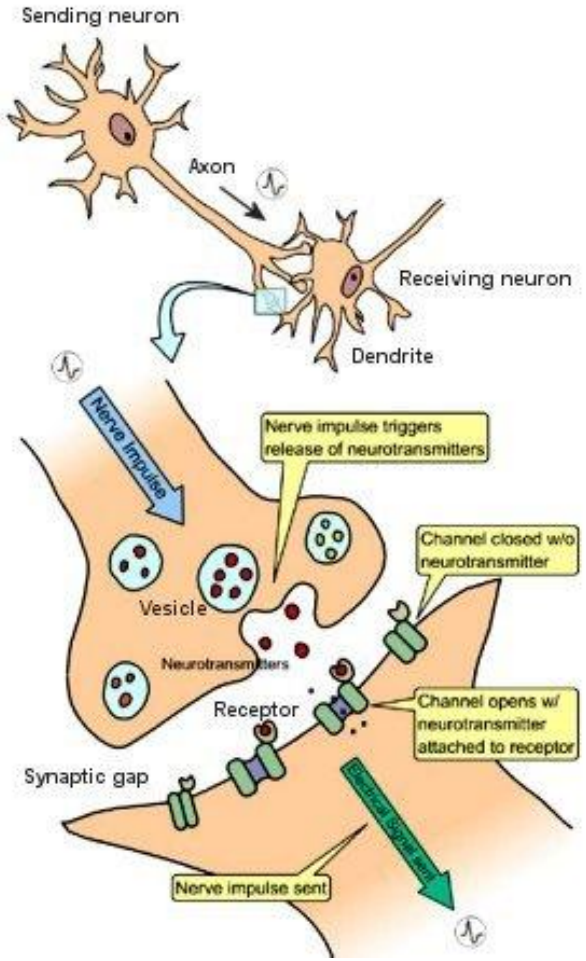
Neuron Transfer

- An electrical impulse travels down neuron 1 and stimulates the release of neurotransmitter molecules into the synaptic gap.
- The neurotransmitter molecules find their receptors and cause changes in the membrane of neuron 2.
- This can cause openings to form in the membrane of neuron 2, allowing specific substances to move through the opening.



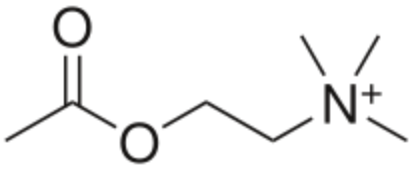
Neuron Transfer

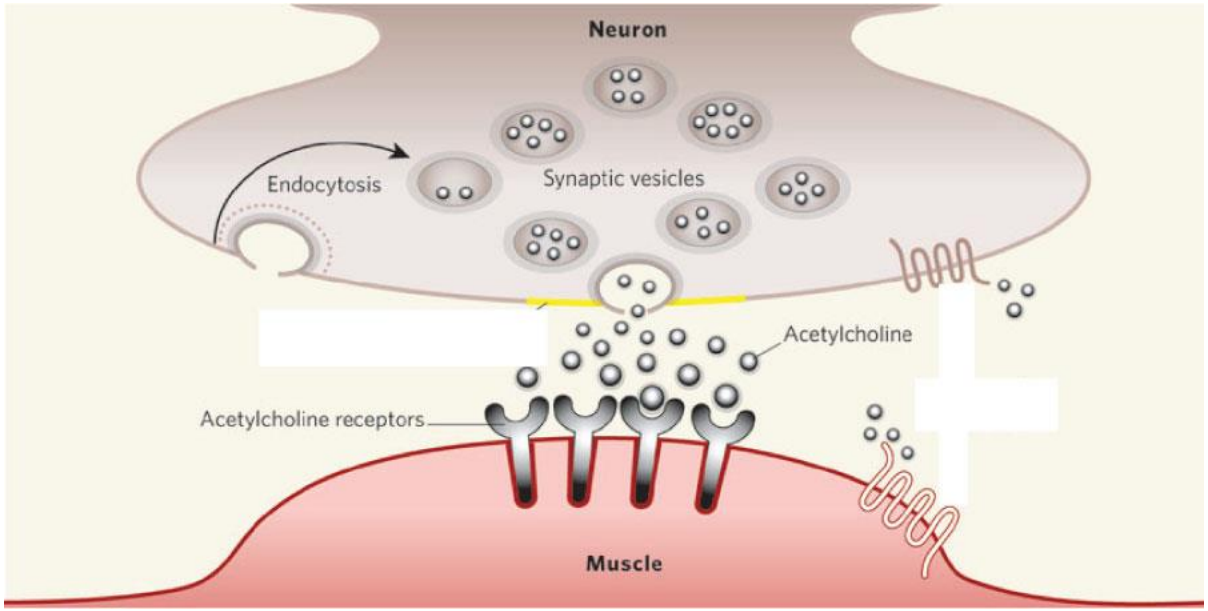
- Acetylcholine triggers flow of positive charge into neuron 2 through Na^+/K^+ gates.
- This causes an excess of plus charge inside neuron 2 and an excess of negative charge outside the neuron.
- When the charge imbalance gets large enough, it causes the firing of an electrical impulse through neuron 2, repeating the process.



Acetylcholine and Muscle Contraction

- Among other things, the neurotransmitter acetylcholine (ACh) released from motor neurons stimulates receptor sites that cause muscle contraction.

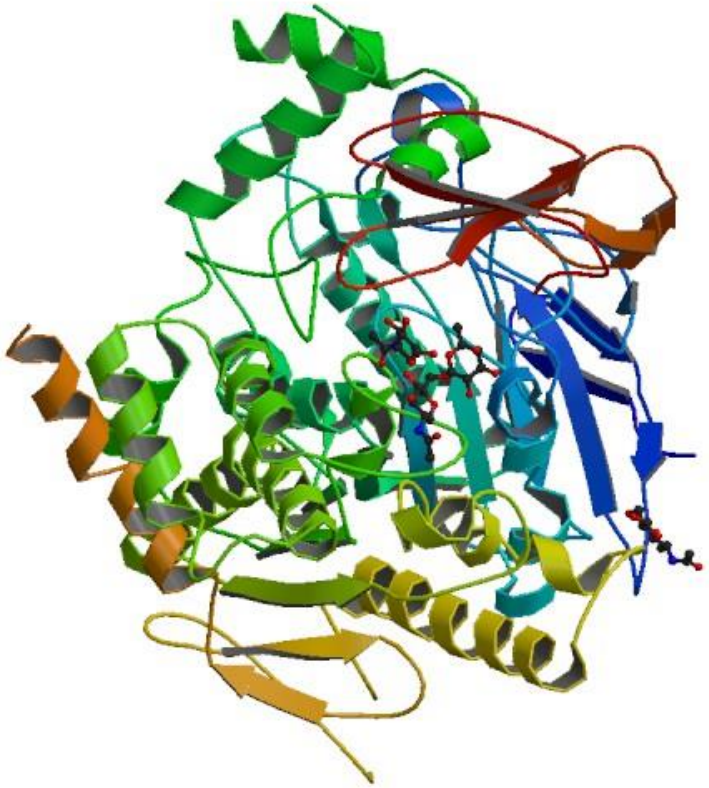




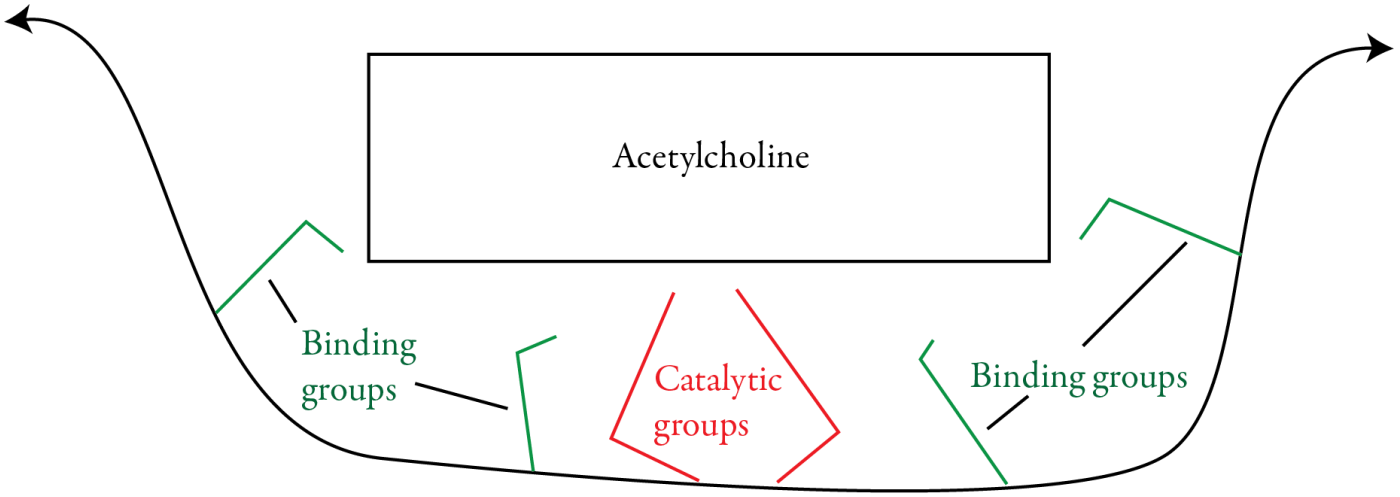
From Nature 436, 473-474 (28 July 2005)

Acetylcholine, Acetylcholinesterase, and Transfer of Nerve Information

- Normally, acetylcholine (ACh) is broken down in the active site of an enzyme, acetylcholinesterase (AChE).
- An enzyme molecule breaks down an acetylcholine molecule in about 80 microseconds, so each enzyme molecule can break down thousands of ACh molecules per second.
- Together, ACh and AChE are like an on-off switch for muscles

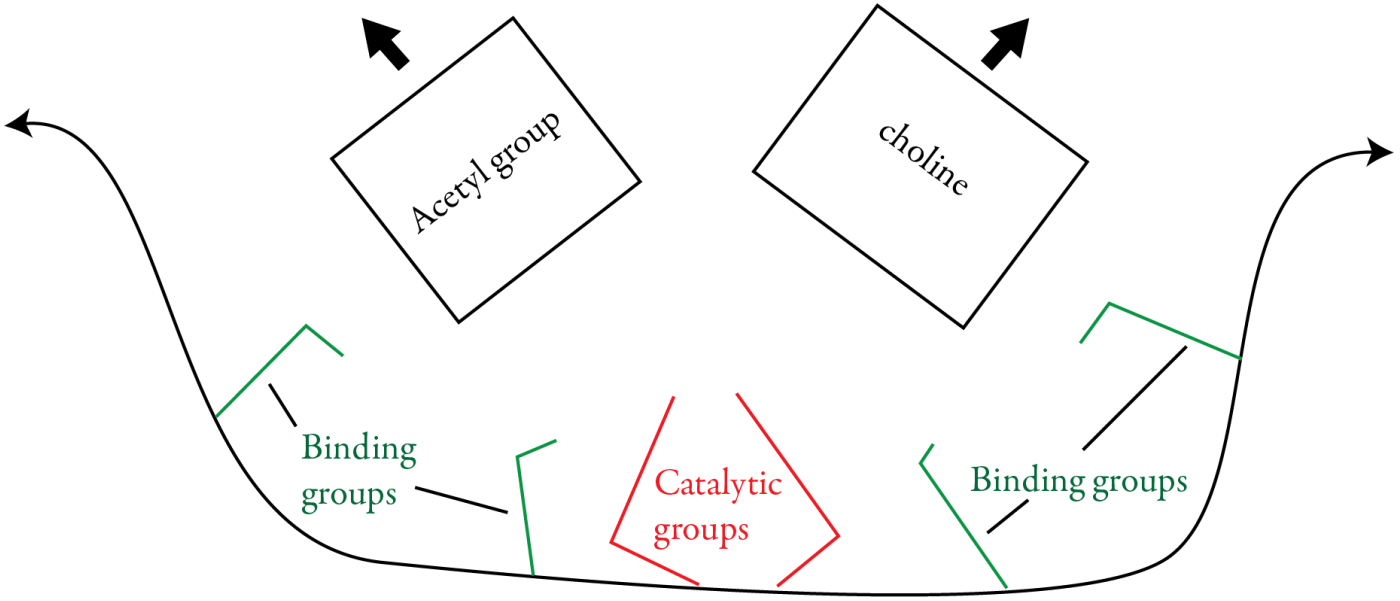


Acetylcholinesterase



Active site of acetylcholinesterase

To



Active site of acetylcholinesterase

Sarin and Acetylcholine-Acetylcholinesterase

- Sarin forms a covalent bond to a serine side chain in the active site of acetylcholinesterase, deactivating it.
- If acetylcholinesterase is deactivated, the acetylcholine levels remain high, and the switch gets stuck in the “on” position.

https://preparatorychemistry.com/nerve_agent_sarin_Canvas.html

Effects of Nerve Agents

- For skeletal muscles: uncontrolled spasms, followed by paralysis
- For involuntary muscles: pupil contraction, excessive salivation, intestinal cramps, vomiting, and constriction of bronchial tubes
- For central nervous system: overstimulates the brain, causing seizures
- Causes glands to be overactive, secreting excess nasal mucus, saliva, and sweat
- Causes death by asphyxiation through constriction of bronchial tubes, suppression of the respiratory center of the brain, and paralysis of the breathing muscles

Low-level Exposure to Nerve Agents

- Low doses lead to inability to think clearly, insomnia, trouble concentrating, and mood swings.
- Continuing exposure to low doses leads to a gradual increase in symptoms.
- It can take up to months for the acetylcholinesterase levels to return to normal.

Treatment for Nerve Agent Exposure

- Be sure that you have complete protective gear.
- Remove as much of the nerve agent as possible before moving person to a non-contaminated area.
- Rinse with soap and water or diluted household bleach.
- Remove contaminated clothing and rinse skin again.

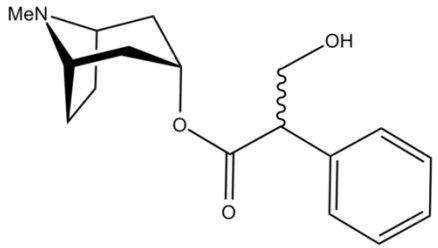
Treatment for Nerve Agent Exposure

- An individual who is known to be exposed to a nerve agent or who exhibits definite signs or symptoms of nerve-agent exposure should have **an immediate injection of the antidotes atropine (first) and pralidoxime (2-PAM) (second), and a sedative/antiepileptic drug, such as diazepam (Valium).**
- Atropine and 2-PAM can be administered with a pressurized syringe with a spring-loaded, recessed needle, such as the United States military Mark I NAAK, which is a dual-chamber autoinjector that contains atropine sulfate and pralidoxime chloride.

Treatment for Nerve Agent Exposure

- The diazepam can be administered from a CANA (Convulsive Antidote, Nerve Agent) autoinjector after the atropine and 2-PAM.

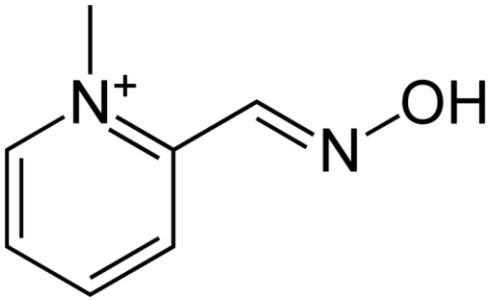
Nerve Agent Antidotes - Atropine

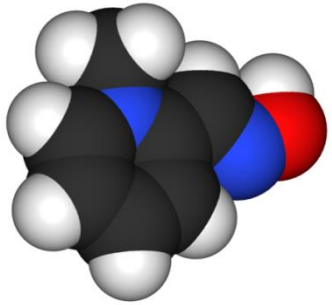


- Standard antidote for organophosphate poisoning
- Competes successfully with one type of acetylcholine receptors. This type of receptor is found in smooth muscles and glands.
- Helps relax muscles
- Stops the most serious symptoms from nerve agent poisoning, *not* the cause
- Must be administered every 5 to 10 minutes until secretions begin to dry up

https://www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750001.html

Nerve Agent Antidotes (2-PAM)



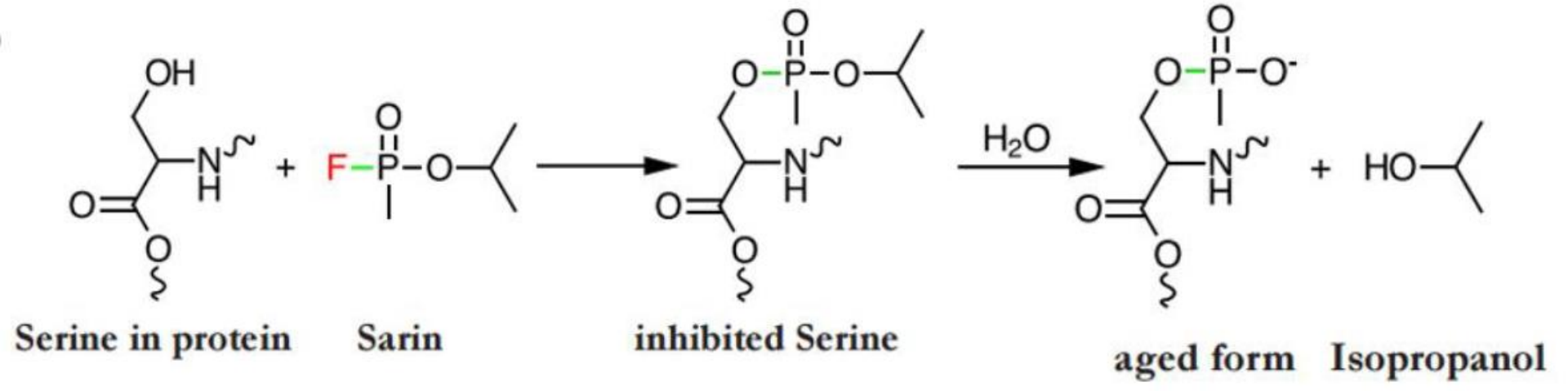


- Pralidoxime (2-pyridine aldoxime methyl chloride,) or 2-PAM
- Removes the nerve agent from the active site of acetylcholinesterase, restoring the enzyme to more normal levels
- Too slow to work well alone
- Works best when administered with atropine, which acts more quickly, giving the slower-acting 2-PAM time to work.
- Does not make it through the blood-brain barrier, so does not alleviate problems within the central nervous system.

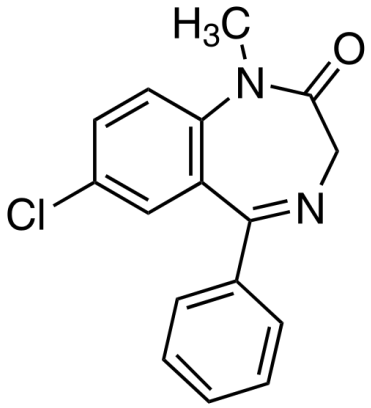
https://www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750001.html

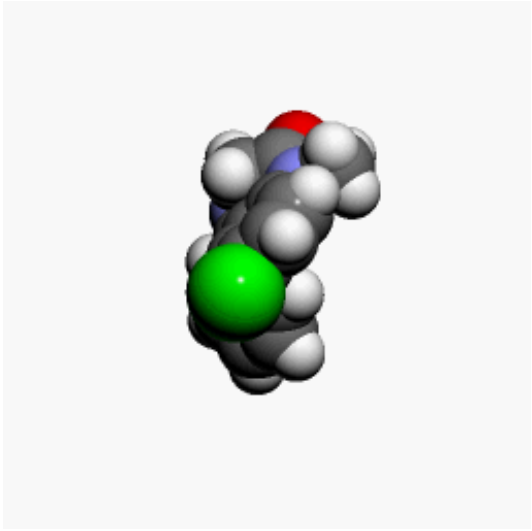
Inhibited and Aged Acetylcholinesterase

- The 2-PAM must be administered as quickly as possible because the loss of the isopropyl group from the sarin yields the *aged* form of the enzyme, and the sarin cannot be removed in this form.



Diazepam (Valium)

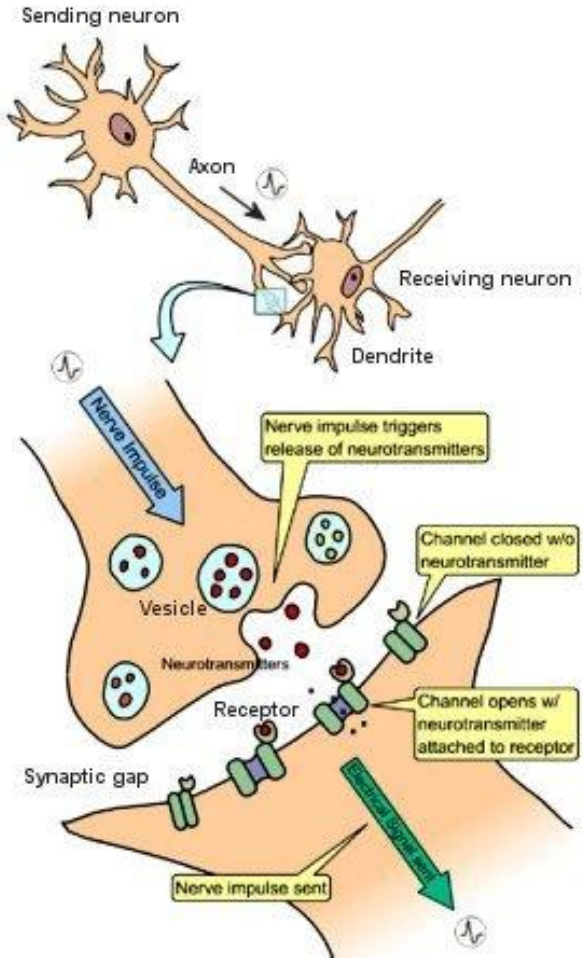




- Because 2-PAM is positive, very little of it gets through the blood-brain barrier.
- Valium (diazepam), which is an anticonvulsant, can be used to lessen the effects on the central nervous system (the brain and spinal cord).

Neuron Transfer

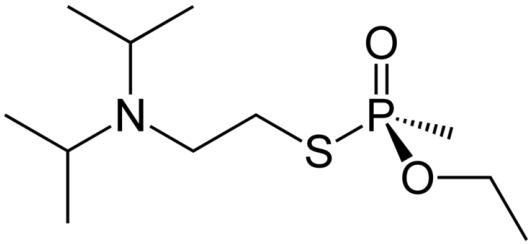
- Acetylcholine triggers flow of positive charge into neuron 2 through Na^+/K^+ gates.
- GABA triggers the flow of negative charge into neuron 2 through Cl^- gates, slowing the buildup of the charge imbalance that causes neuron 2 to fire.
- Valium and other benzodiazapines make it easier for GABA to work.

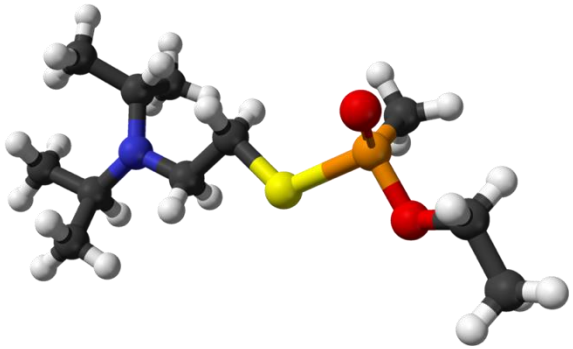


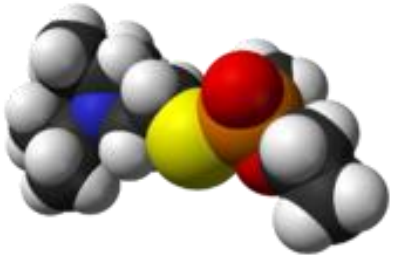
Possible New Antidotes

- Midazolam (Versed) instead of diazepam (Valium)
  - Faster acting
  - Fewer complications
- Different oxime instead of 2-PAM
  - Because 2-PAM is positive, little if any crosses the blood-brain barrier.
  - Developing oximes that are neutral until they pass into the brain where they become positive, which is necessary for their function.

VX



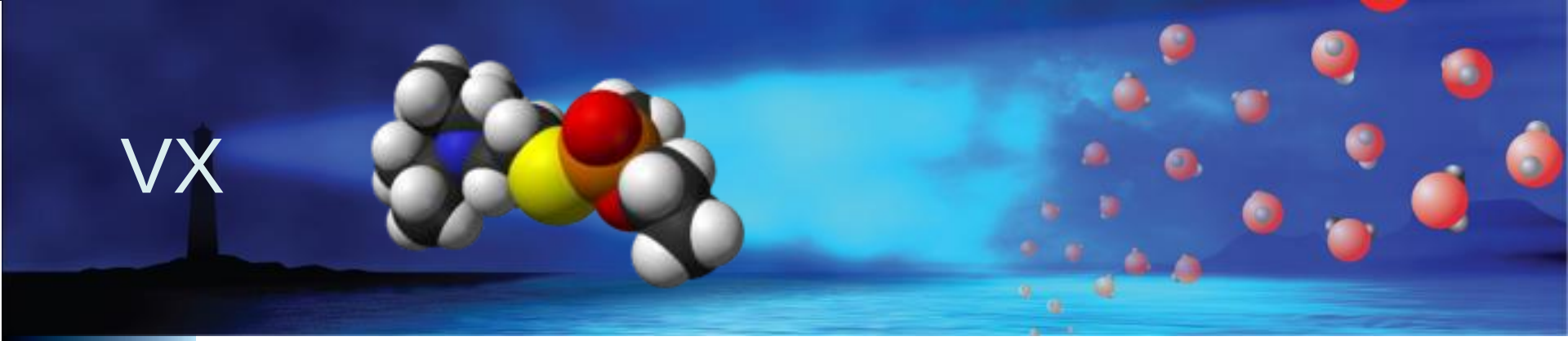




- One of several similar substances that were considered “venomous” and called V-agents.
- First produced in England in 1954
- Odorless, amber-colored, oily liquid with a volatility and viscosity similar to motor oil.

http://chemapps.stolaf.edu/jmol/jmol.php?model=CCOP%28C%29%28%3DO%29SCCN%28C%28C%29C%29C%28C%29C

VX



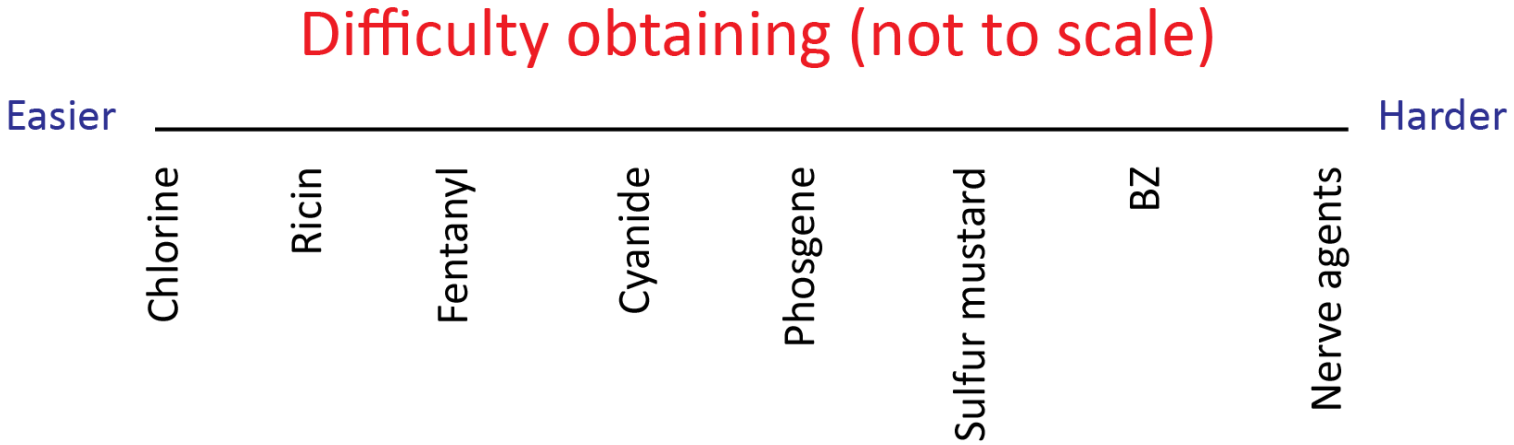
- Three times more toxic that sarin when inhaled and a thousand times more toxic when absorbed by the skin. A small drop on the skin could kill an adult in fifteen minutes.
- Dispersed as an aerosol (boiling point = 298 °C or 568 °F)
- Clings to whatever it hits
- When sprayed on the ground, remains lethal for up to three weeks, so it can be an *area denial weapon*.
- Used to kill Kim Jong-nam, half brother to North Korean leader Kim Jong-un, 13 February 2017 in the Kuala Kumpur International Airport Malaysia.

Sarin or VX?

- Sarin –
  - Deadly so inflicts high casualties
  - Evaporates about as rapidly as water and reacts fairly quickly with water to form less harmful substances, allowing attacking force to seize territory without major risk to its own troops.
  - Compared to VX nerve agent, sarin is also relatively easy to disseminate.
- VX
  - Due to its viscous nature, VX is more difficult to disperse. It requires some sort of aerosolization.
  - As little as one drop of VX on skin can be fatal, unless very swift medical treatment.
  - VX nerve agent would require labor-intensive and time-consuming decontamination procedures.

Difficulty Obtaining

- This is a very rough ranking of the level of difficulty in obtaining different chemical weapons.
- It takes into consideration the difficulty in producing them, stealing from production plant, stealing them in transportation, etc.



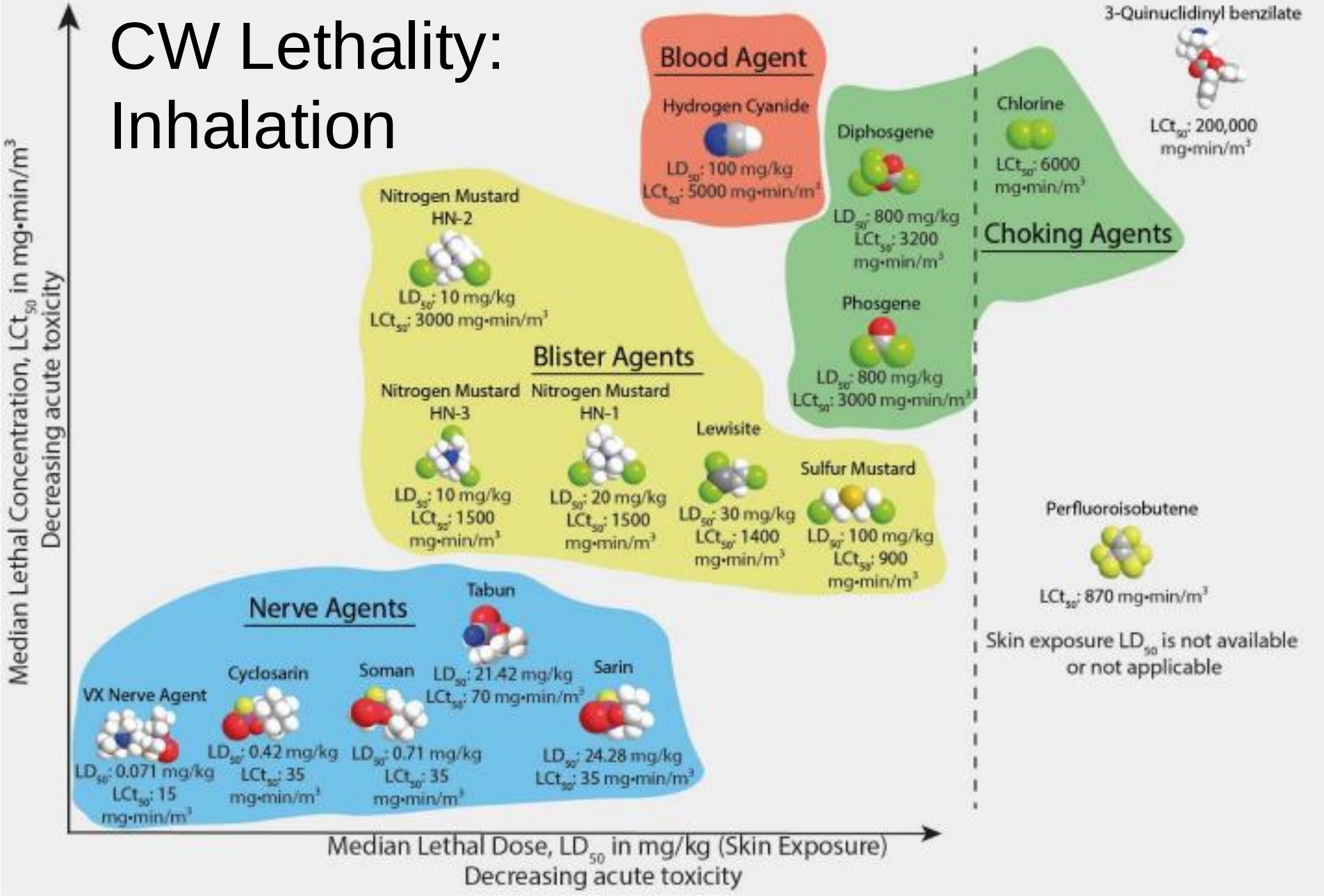
Dosage Units

- LD_{50} = dose of chemical expected to kill 50% of an exposed population…typical units = mg/kg of body weight
- LCt_{50} = concentration of a chemical (in vapor or aerosol phase) expected to kill 50% of a population exposed for a specified period of time…often expressed as the product of chemical's concentration in air (mg/m^3) and the duration of exposure (min)…units = $mg \cdot min/m^3$
- ED_{50} = dose of a chemical expected to cause a defined effect in 50% of an exposed population…typically expressed in units of mg/kg of body weight.

Dosage Units

- ECt_{50} = concentration of chemical (vapor phase) expected to cause a defined effect in 50% of a population exposed for a specified period of time; typically expressed as product of chemical's concentration in air (mg/m^3) and the duration of exposure (min)…typical units = $mg \cdot min/m^3$.
- ICt_{50} = median incapacitation concentration, concentration of chemical (vapor phase) expected to incapacitate 50% of a population exposed for a specified period of time, typically expressed as product of chemical's concentration in air (mg/m^3) and the duration of exposure (min)…typical units = $mg \cdot min/m^3$

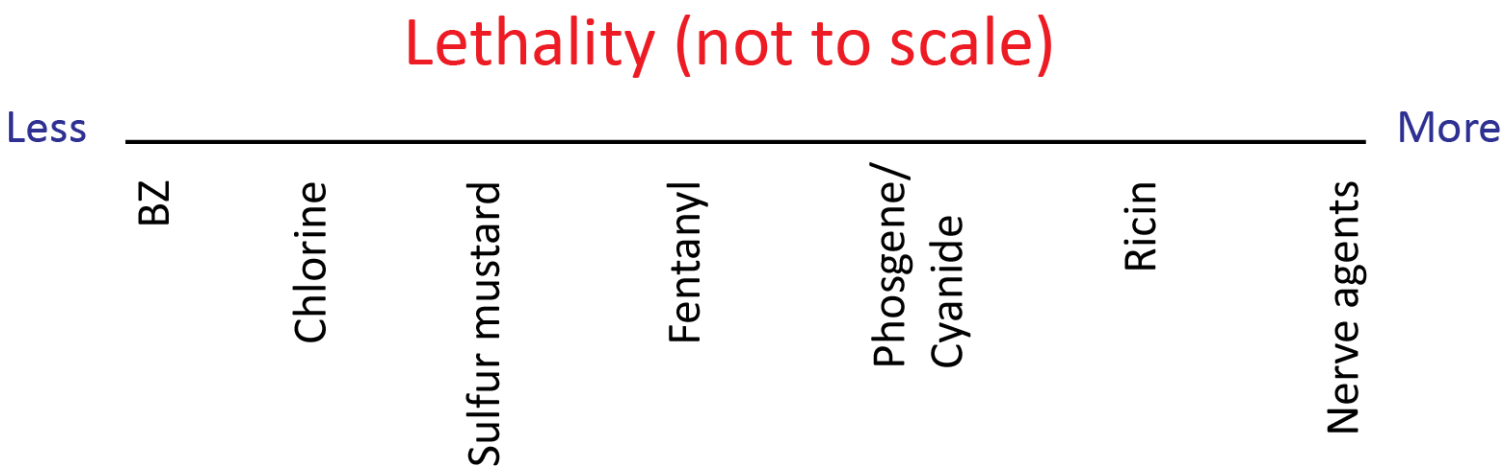
CW Lethality: Inhalation



Source: Organisation for the Prohibition of Chemical Weapons (OPCW)

Lethality

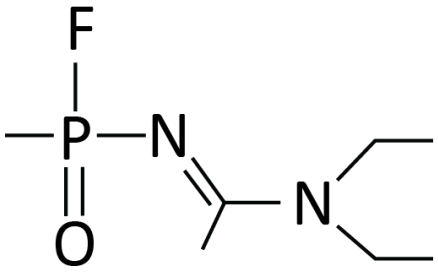
- There are many variables that determine lethality, including mode of dispersal, level of exposure, health of person exposed, etc.
- All the chemical weapons we have talked about can be lethal, but this scale gives a very rough ranking of the likelihood of them being lethal.



Russia's Novichoks

- Novichok (new guy or newcomer) – a category of similar solid and liquid nerve agents developed in the Soviet Union in the 1970s and 1980s
- A lot of uncertainty associated with Novichoks
- One goal was to develop binary agents that could be made from relatively safe substances similar to normal industrial substances, making it easier to conceal the production.

Russia's Novichoks (Mirzayanov)



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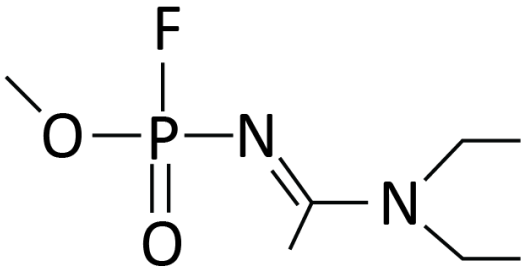

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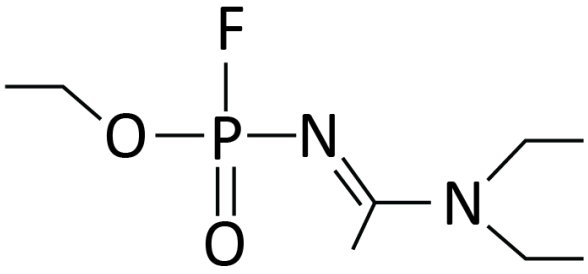

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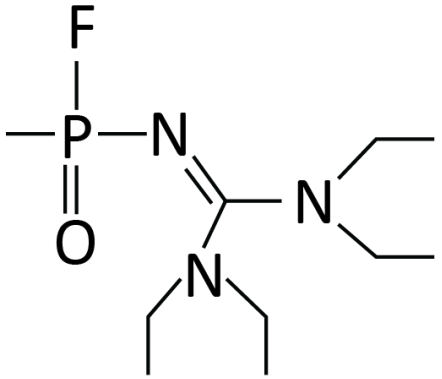

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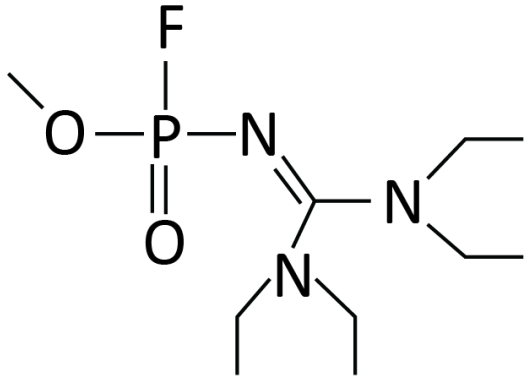

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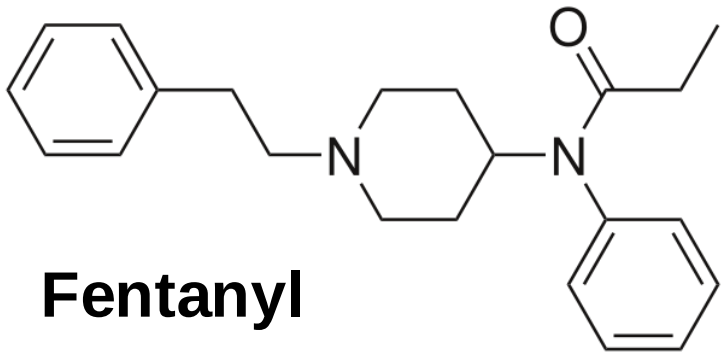
State Secrets: An Insider's Chronicle of the Russian Chemical Weapons Program by Vil Mirzayanov

Fentanyl

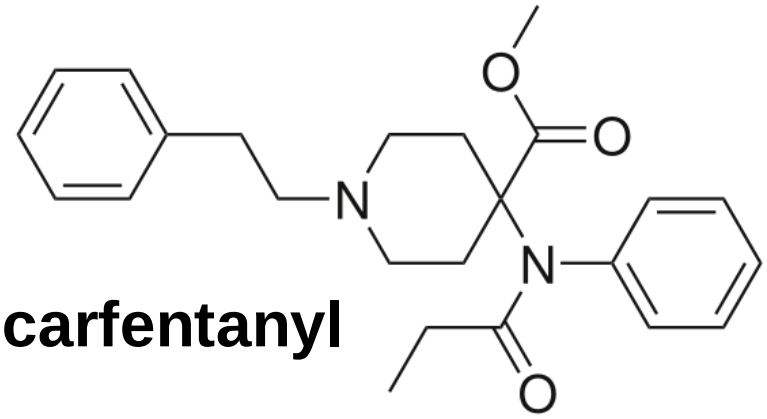
- Odorless, crystalline solid
- Can be absorbed into the body by inhalation, ingestion, or skin contact
- Inhalation results in rapid absorption. Oral exposure will occur within in a few minutes. Skin exposure results in absorption over hours to days.
- Can be released into the air as fine particles or as an aerosol created from a solution (fentanyl dissolved in a solvent)
- Depresses central nervous system and respiratory function
- Can be fatal
- Can be used to contaminate water and food

Fentanyl and Carfentanyl

- Both potent, synthetic narcotics that stimulate opioid receptors.
- Fentanyl is approximately 100 times more potent than morphine and 50 times more potent than heroin.
- Carfentanyl is about 10,000 times more potent than morphine and 5000 times more potent than heroin.



Fentanyl



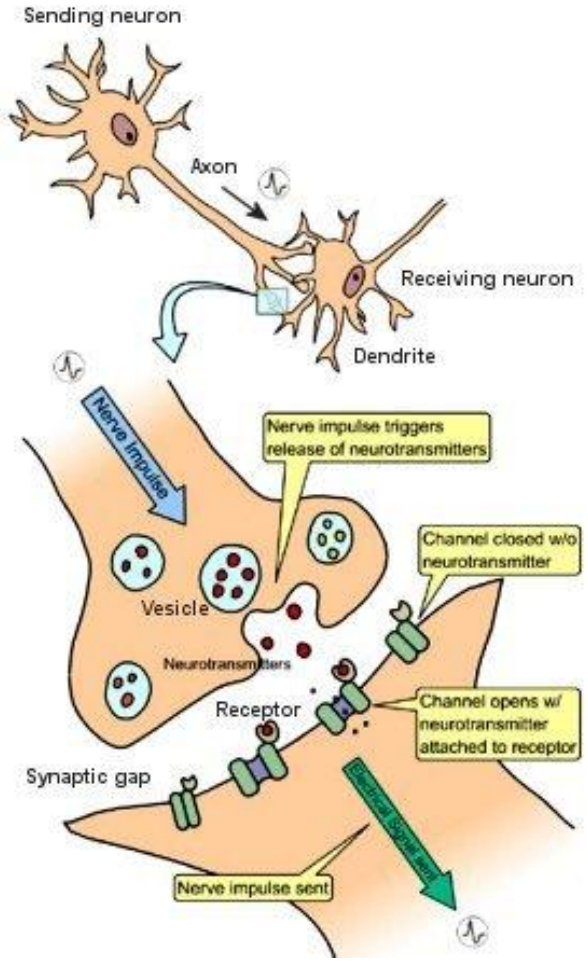
carfentanyl

Opioids

- The synthetic opioids are thought to bind to the same opioid receptors as natural substances, such as endorphins and enkephalins.
- There are opioid receptors throughout the body that can lead to a variety of effects, including pain relief, sedation, respiratory depression, constipation, and a strong sense of euphoria.

Neuron Transfer

- Acetylcholine triggers flow of positive charge into neuron 2 through Na^+/K^+ gates.
- GABA triggers the flow of negative charge into neuron 2 through Cl^- gates, slowing the buildup of the charge imbalance that causes neuron 2 to fire.



Opioids and Pain

- There are natural neurons that inhibit the pain response.
- The firing of GABA neurons inhibit the neurons that inhibit the pain response, leading to a more free flow of the pain response.
- Opioids inhibit the GABA neurons.
- More opioids, less GABA neuron firing, more neuron firing that inhibits pain, less pain

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4708964/

Opioids and the Reward System

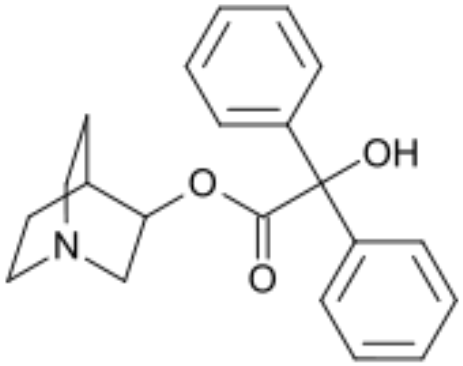
- Dopamine (the feel-good chemical) is a neurotransmitter that has many functions, including stimulating the reward system that reinforces behavior necessary for the survival of the species, such as eating, drinking, and sex.
- GABA neurons inhibit the release of dopamine.
- The inhibition of the GABA neurons by opioids leads to an increase of dopamine in the system.
- More opioids leads to more inhibition of GABA neurons, which leads to more dopamine, which leads to greater reward.

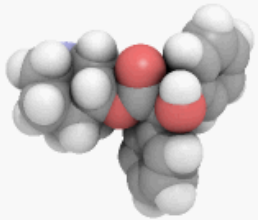
Opioid Fatalities

- Death can arise from the excess inhibition of the neurons that send signals to the diaphragm muscle telling it to contract, causing one to breathe in.
- The antidote naloxone (Narcan®) competes successfully with opioids for their receptor sites.

BZ (QNB)

- **3-Quinuclidinyl benzilate** (BZ) - military incapacitating agent.
- Related to atropine
- Competitive inhibitor of acetylcholine at receptor sites in smooth muscle, exocrine glands, autonomic ganglia, and the brain
- Decreases the effective concentration of acetylcholine seen by receptors at these sites.
- Opposite of effects in nerve agent poisoning.
- Effects include stupor, confusion, and hallucinations.
- Symptoms are delayed but long-lasting

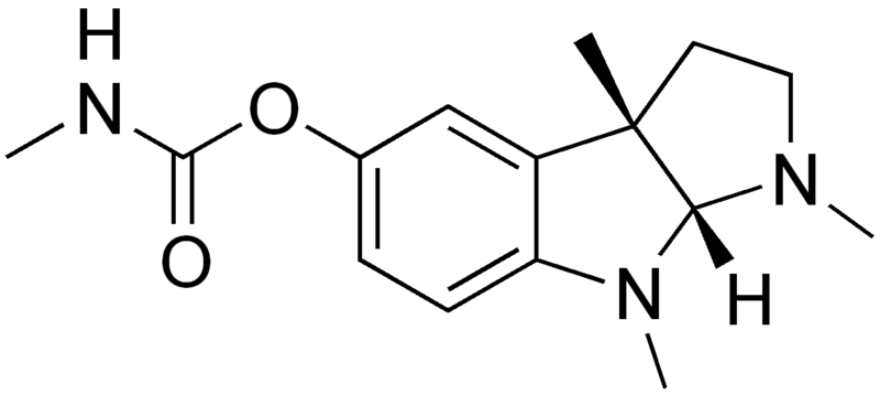




BZ (QNB)

- Crystalline solid
- Can be released into the air as fine particles or as an aerosol created from a solution (BZ dissolved in a solvent)
- Can contaminate water and food
- Schedule 2 of the Chemical Weapons Convention (Once considered a potential incapacitating agent for military applications; now used to treat people with an overactive bladders)

Physostigmine - BZ Antidote



- Anticholinesterase, which temporarily raises acetylcholine concentrations by binding ***reversibly*** to acetylcholinesterase, the enzyme responsible for the breakdown of acetylcholine in the synaptic gap.

Toxins

- A **toxin** is a poisonous substance produced within living cells or organisms.
- Because toxins are chemicals produced by biological organisms, they can be considered chemical or biological weapons, the use of which would be a violation of both the CWC and the BWC (Biological Weapons Convention).
- As modern chemistry can synthesize an ever-growing number of toxins, they fall under the purview of the CWC.
- Two toxins, ricin and saxitoxin, are listed on Schedule 1 of the CWC.

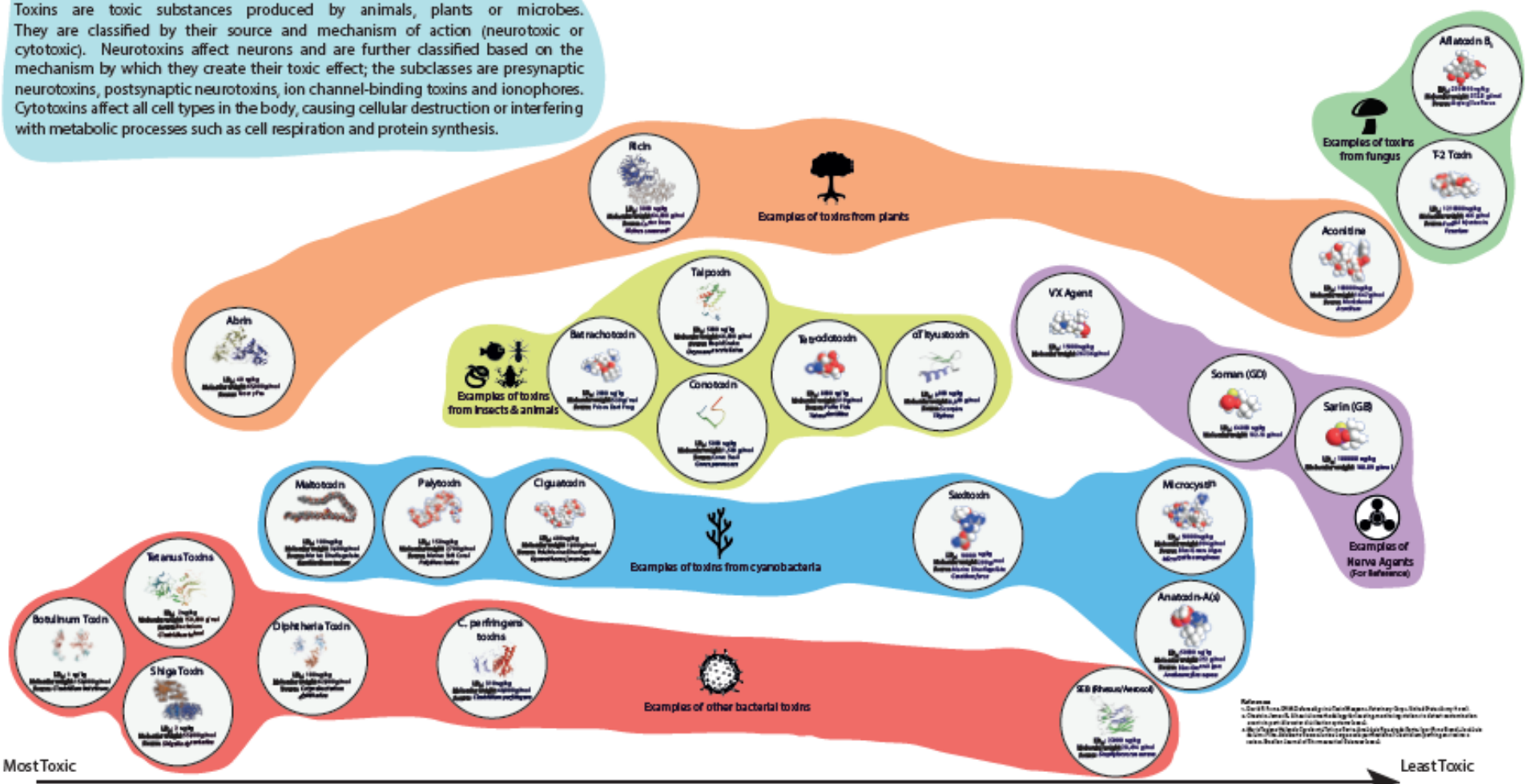
ORGANISATION FOR THE PROHIBITION OF CHEMICAL WEAPONS

Working Together for a World Free of Chemical Weapons

Biological Toxins and their Relative Toxicity

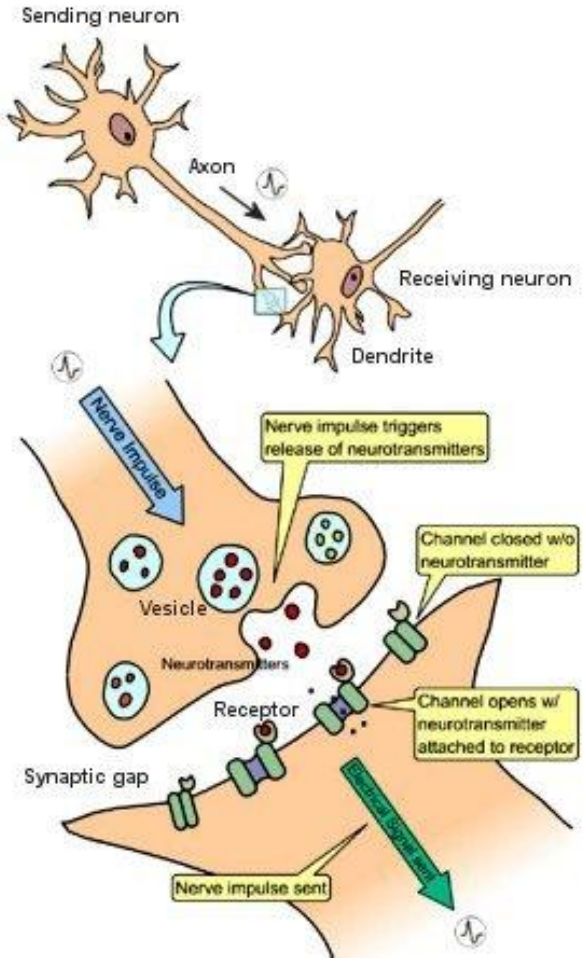
What are Toxins?

Toxins are toxic substances produced by animals, plants or microbes. They are classified by their source and mechanism of action (neurotoxic or cytotoxic). Neurotoxins affect neurons and are further classified based on the mechanism by which they create their toxic effect; the subclasses are presynaptic neurotoxins, postsynaptic neurotoxins, ion channel-binding toxins and ionophores. Cytotoxins affect all cell types in the body, causing cellular destruction or interfering with metabolic processes such as cell respiration and protein synthesis.



Neuron Transfer

- Acetylcholine triggers flow of positive charge into neuron 2 through Na^+/K^+ gates.
- This causes an excess of plus charge inside neuron 2 and an excess of negative charge outside the neuron.
- When the charge imbalance gets large enough, it causes the firing of an electrical impulse through neuron 2, repeating the process.

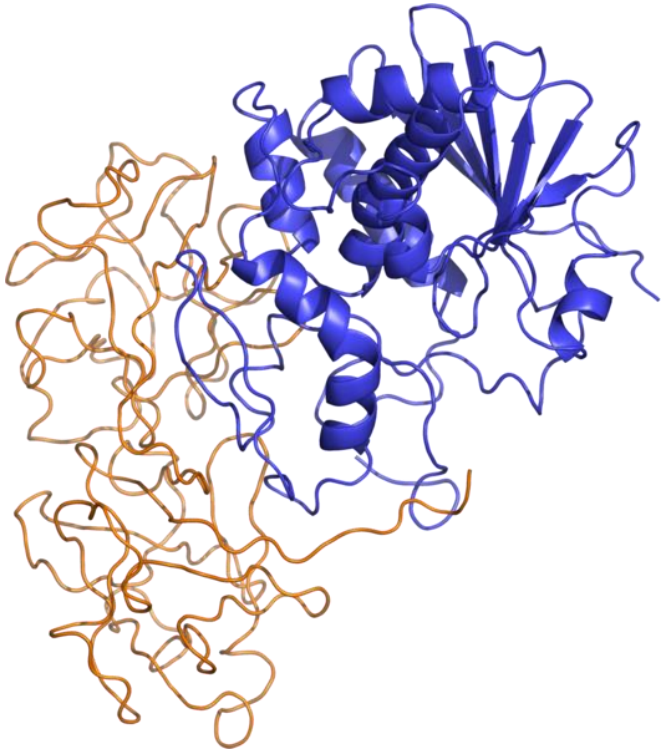


Botulinum Toxin

- Botulinum toxin (Botox) blocks the release of acetylcholine at the neuromuscular junction, which slows the contraction of muscles and can lead to paralysis of muscles, including those in the face.
- This process is reversible, and the muscle gradually regains function over time.

Ricin

- Naturally occurring protein, white powder
- Can be released into the air as a fine powder.
- Can contaminate water and food
- Symptoms arise after a few hours or days
- Can be extracted from castor beans
- Low thermal stability makes it useless in munitions.
- Ricin is listed as a Schedule 1 controlled substance in the CWC.



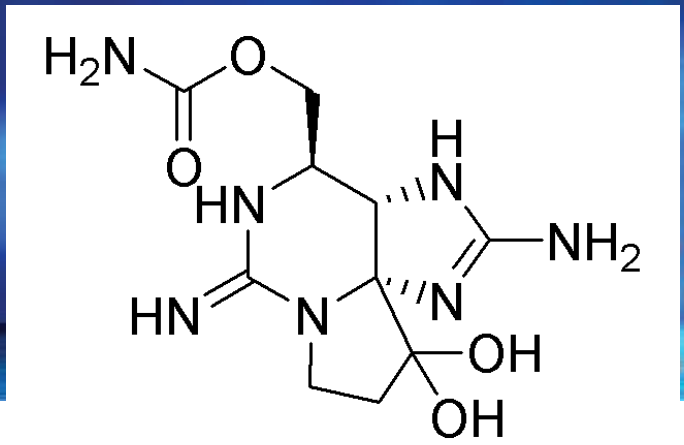
Ricin

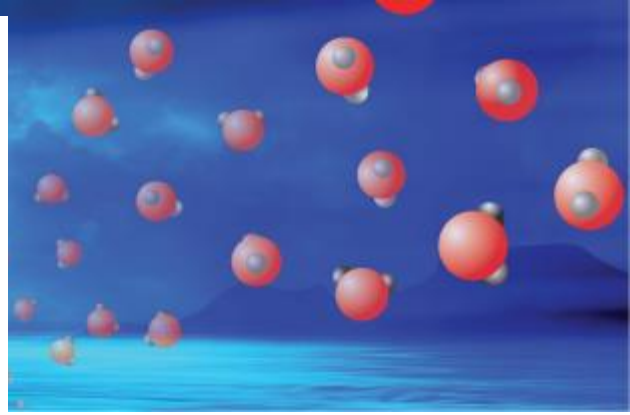
- The LD_{50} of ricin is around 22 micrograms per kilogram in humans if exposure is from injection or inhalation.
- Oral lethal dose is 20–30 milligrams per kilogram.
- The major reason ricin is a public health threat is that it is easy to obtain. (More than 1 million metric tons of castor beans are processed each year.)

Ricin Physiological Effects

- Reacts with ribosomal RNA, deactivates the ribosome, and disrupts protein synthesis.
- Symptoms may take anywhere from hours to days to appear. Death typically occurs within 3–5 days of exposure.
- **Symptoms from inhalation**: respiratory distress (difficulty breathing), fever, cough, nausea, and tightness in the chest. Heavy sweating may follow as well as fluid building up in the lungs (pulmonary edema). Finally, low blood pressure and respiratory failure may occur, leading to death.
- **Symptoms from ingestion**: vomiting and diarrhea that may become bloody. Severe dehydration, followed by low blood pressure….hallucinations, seizures, and blood in the urine. Within several days, the person's liver, spleen, and kidneys might stop working, and the person could die.

Saxitoxin





- **Saxitoxin** (**STX**) is the most well-known paralytic shellfish toxin (PST)
- STX has been found in at least 12 marine puffer fish species.
- Saxitoxin is a neurotoxin that acts as a **selective sodium channel blocker**. It acts on the voltage-gated sodium channels of nerve cells, preventing normal cellular function and leading to paralysis.
- Can potentially be produced in a chemical laboratory.
- The oral LD_{50} for humans is 5.7 µg/kg, therefore approximately 0.5 mg of saxitoxin is lethal if ingested and the lethal dose by injection is about one-tenth of the oral dose.

http://en.wikipedia.org/wiki/Saxitoxin

Saxitoxin

- Saxitoxin is about 1,000 times more toxic than the nerve agent sarin.
- The United States military isolated saxitoxin and assigned it the chemical weapon designation TZ.
- U-2 pilot Francis Gary Powers was issued with a hollow silver dollar containing a tiny, saxitoxin-impregnated needle, to be used to commit suicide in case of capture by enemy forces.
- Saxitoxin is listed in Schedule 1 of the CWC.
- Although there are other ways to obtain saxitoxin, it takes 8 tons of clams to extract 1 gram of toxin.

http://en.wikipedia.org/wiki/Saxitoxin

Comparison of Toxins and Chemical Agents

Toxins	**Chemical Agents**
Natural Origin	Human-made
Difficult, small-scale production	Large-scale industrial production
None volatile	Many volatile
Many are more toxic	Less toxic than many toxins
Mostly not dermally active	Can be dermally active
Legitimate medical use	Almost no medical uses
Odorless and tasteless	Noticeable odor or taste
Diverse toxic effects	Fewer types of effects
Many are effective immunogens	Poor immunogens
Aerosol delivery	Mist/droplet/aerosol delivery

1925 Geneva Protocol

- Protocol on the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare
- **Banned first use of chemical and biological weapons but not their production and stockpiling**
- Adopted by the League of Nations
- Within ten years, it was ratified by forty countries, including most of the major powers except the U.S. and Japan.
- U.S. signed with reservations 50 years later (General Fries lobbied against it, aided by a coalition of veterans' groups, the chemical industry, and the American Chemical Society.)
- A number of countries reserved the right to retaliate and therefore stockpiled chemical weapons.

Chemical Weapons Convention (CWC)

- **A disarmament agreement that bans the production, stockpiling, transferring, and use of chemical weapons.**
- Approved by the U.N. General Assembly in November, 1992.
- Open for signature in 1993
- The U.S. ratified CWC in 1997.

http://www.cwc.gov/

http://www.opcw.org/chemical-weapons-convention//

http://www.opcw.org/news-publications/publications/history-of-the-chemical-weapons-convention/

CWC General Obligations

1. Each State Party to this Convention undertakes never under any circumstances:

(a) To develop, produce, otherwise acquire, stockpile or retain chemical weapons, or transfer, directly or indirectly, chemical weapons to anyone;

(b) To use chemical weapons;

(c) To engage in any military preparations to use chemical weapons;

(d) To assist, encourage or induce, in any way, anyone to engage in any activity prohibited to a State Party under this Convention.

CWC General Obligations (cont.)

2. Each State Party undertakes to **destroy chemical weapons it owns or possesses**, or that are located in any place under its jurisdiction or control, in accordance with the provisions of this Convention.

3. Each State Party undertakes to **destroy all chemical weapons it abandoned** on the territory of another State Party, in accordance with the provisions of this Convention.

4. Each State Party undertakes to **destroy any chemical weapons production facilities** it owns or possesses, or that are located in any place under its jurisdiction or control, in accordance with the provisions of this Convention.

5. Each State Party undertakes not to use riot control agents as a method of warfare.

Organisation for the Prohibition of Chemical Weapons (OPCW)

- Model of multilateralism - 193 member states that contain 98% of the world's population.
- 4 nonmember states
  - Signatory states that have not ratified the CWC
    - Israel
  - States that have neither signed nor ratified the CWC
    - Egypt
    - North Korea
    - South Sudan

States Outside CWC

- Israel
  - Analysts believe that Israel initiated a CW program between mid-1950s and mid-1980s.
  - Refuses to ratify CWC until there's more regional participation.
  - Israel's chemical industry is advanced and diverse.
  - Although Israel is capable of creating CW weapons, there is insufficient information available to reconstruct their CW program.

States Outside CWC

- Egypt
  - Used CW in North Yemen
  - Thought to have inherited mustard agent and phosgene from British forces when they withdrew in 1954
  - May have nerve agents
  - Refuses to join CWC until Israel joins the Nuclear Nonproliferation Treaty (NPT)
  - Thought to have helped Iraq get CW production capabilities

States Outside CWC

- North Korea
  - Thought to have 2500-5000 metric tons of phosgene, hydrogen cyanide, mustard agent, and sarin
  - Has capable but aging chemical industry

https://en.wikipedia.org/wiki/North_Korea_and_weapons_of_mass_destruction#:~:text=North%20Korea%20possesses%20various%20types,anthrax%2C%20smallpox%2C%20and%20cholera.

States Outside CWC

- South Sudan
  - *THE HAGUE, Netherlands—29 November 2023—During the Twenty-Eighth Session of the Conference of the States Parties to the Chemical Weapons Convention (CSP-28), the Head of South Sudan's Delegation, Ambassador Santino Fardol Watod Dicken, also Deputy Head of Mission of the Embassy of South Sudan in Brussels, addressed the Conference* ***announcing South Sudan's readiness to accede to the Chemical Weapons Convention.*** *South Sudan is one of the four countries yet to join the Convention.*

https://www.opcw.org/media-centre/news/2023/11/south-sudan-announces-new-step-accession-procedure-chemical-weapons

CWC Definitions

- **Toxic Chemical** = Any chemical which through its chemical action on life processes can cause death, temporary incapacitation or permanent harm to humans or animals.
- **Precursor** = Any chemical reactant which takes part at any stage in the production by whatever method of a toxic chemical.
- **Key Component** of Binary or Multicomponent Chemical System = The precursor which plays the most important role in determining the toxic properties of the final product and reacts rapidly with other chemicals in the binary or multicomponent system.

CWC Schedule 1

http://www.opcw.org/chemical-weapons-convention/annex-on-chemicals/a-guidelines-for-schedules-of-chemicals/

- Schedule 1 chemicals have few or no uses other than as chemical weapons agents or to arm chemical weapons.
- Examples include the nerve agents, sulfur mustards, nitrogen mustards, and lewisite
- They are the most highly regulated of all chemicals.

http://www.cwc.gov/index_chemicals_sch1.html

CWC Schedule 2

- Schedule 2 chemicals are chemicals that could be used as weapons or to make weapons, but also have legitimate small-scale uses.
- Examples include Amiton (a V-series nerve agent) and BZ.

http://www.cwc.gov/index_chemicals_sch2.html

CWC Schedule 3

- Schedule 3 chemicals have large-scale uses other than chemical weapons.
  - Chemical plants producing more than 30 Mg per year must report to the Organisation for the Prohibition of Chemical Weapons (OPCW).
  - The plants can be inspected, and there are restrictions on export to countries that have not signed the CWC.
  - Phosgene and hydrogen cyanide are examples.

http://www.cwc.gov/index_chemicals_sch3.html

CWC Parts A and B

- Each schedule is divided into
  - Part A – toxic chemicals themselves
  - Part B – their precursors (chemicals used to produce the toxic chemicals)

Organisation for the Prohibition of Chemical Weapons (OPCW)

- Intergovernmental organization located in The Hague, Netherlands
- *"…**implementing body of the [CWC]…**given the mandate to achieve the object and purpose of the Convention, to **ensure the implementation of its provisions**, including those for **international verification of compliance** with it, and to provide a **forum for consultation and cooperation among States Parties**."*

http://www.opcw.org/about-opcw/
http://www.opcw.org/

OPCW Tasks

- Bring all States into the CWC
- Verifying the destruction of declared chemical weapons, including those in abandoned CW weapons
  - The CWC is unique among disarmament treaties in having a verification regime.
- Verifying the destruction or conversion of CW plants
- Monitoring future compliance with CWC

OPCW Fact Finding Missions

- Collection of evidence
  - Environmental samples
  - Biomedical samples
  - Chain-of custody
  - Interviews
  - Photos, video
- On-site detectors, on-site analysis
- OPCW designated laboratory network
- Report results

Science for Diplomats 17 March 2015
www.opcw.org/fileadmin/OPCW/Science_Technology/Diplomats_Programme/Science_for_Diplomats_at_the_OPCW_2014_2015.pdf

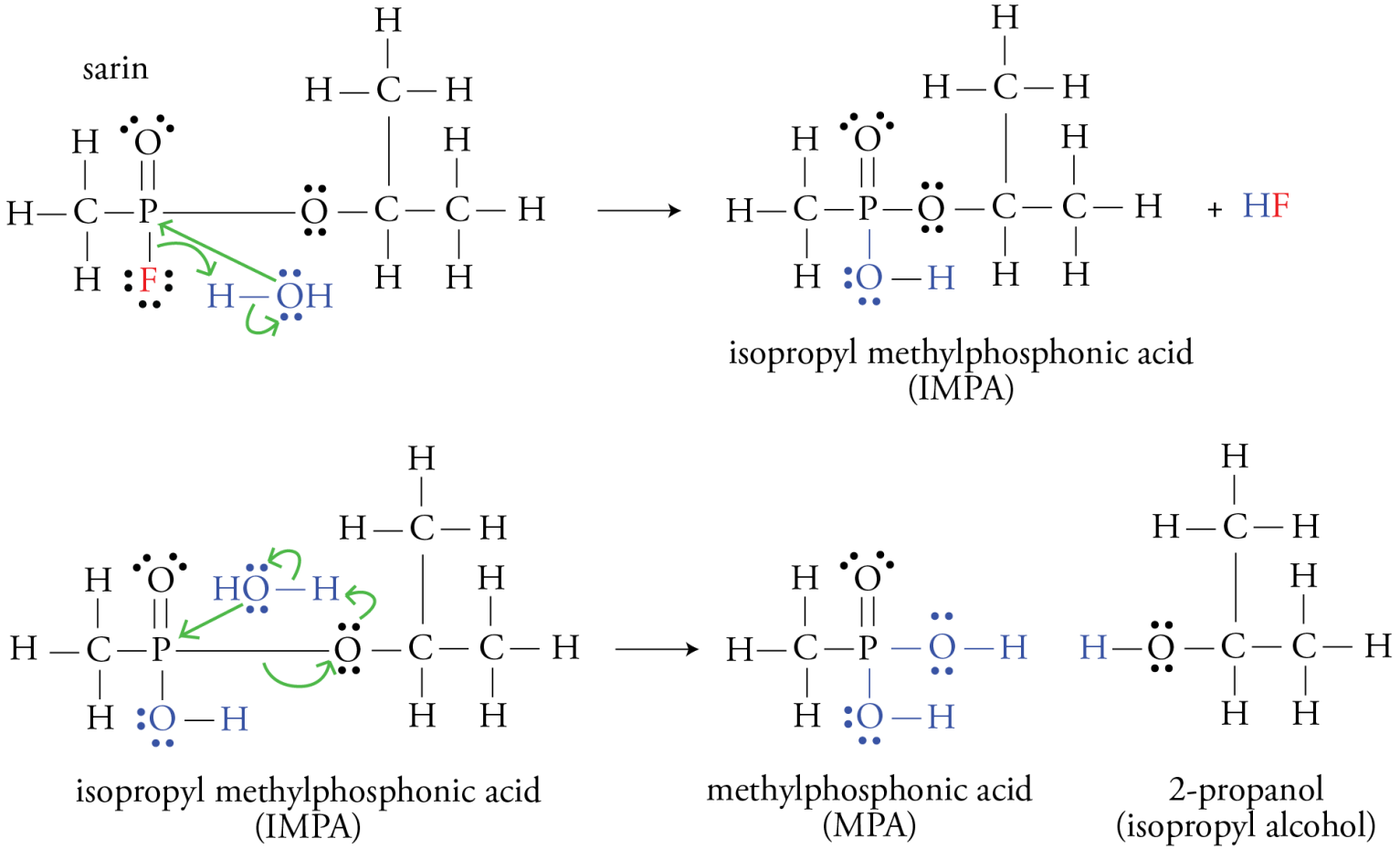
Sample Types and Assumed Concentrations

- Environmental samples
  - “Neat” agent from a reactor or bomb
  - Residue from a reaction or waste container
  - Contaminated clothing, hair, soil, water, etc.
  - Concentrations usually expected >1 µg/g (ppm)
  - Survey analysis is possible
- Biomedical samples
  - Urine, blood, plasma, tissue, etc.
  - Intact chemical agent likely not present (degradation/reaction product or metabolite)
  - Concentration levels quite low, < 5 ng/g (ppb)
  - Survey analysis not possible; must use targeted analysis

Science for Diplomats 17 March 2015
www.opcw.org/fileadmin/OPCW/Science_Technology/Diplomats_Programme/Science_for_Diplomats_at_the_OPCW_2014_2015.pdf

Hydrolysis of Sarin

Each arrow represents the movement of a pair of electrons as covalent bonds are broken and made.



Detection of Sarin Use

- The product of the first step in the hydrolysis of sarin, isopropyl methylphosphonic acid (IMPA), is a chemical that is not commonly found in nature, so if it is found at the site of a chemical weapons attack, it's an indication of the use of sarin.
- IMPA was detected in 20 of 42 reported environmental samples taken by the OPCW team in Ghouta, Syria.
- The final products of the hydrolysis of sarin are formed from the hydrolysis of other organophoshates.

How does a GC/MS work?

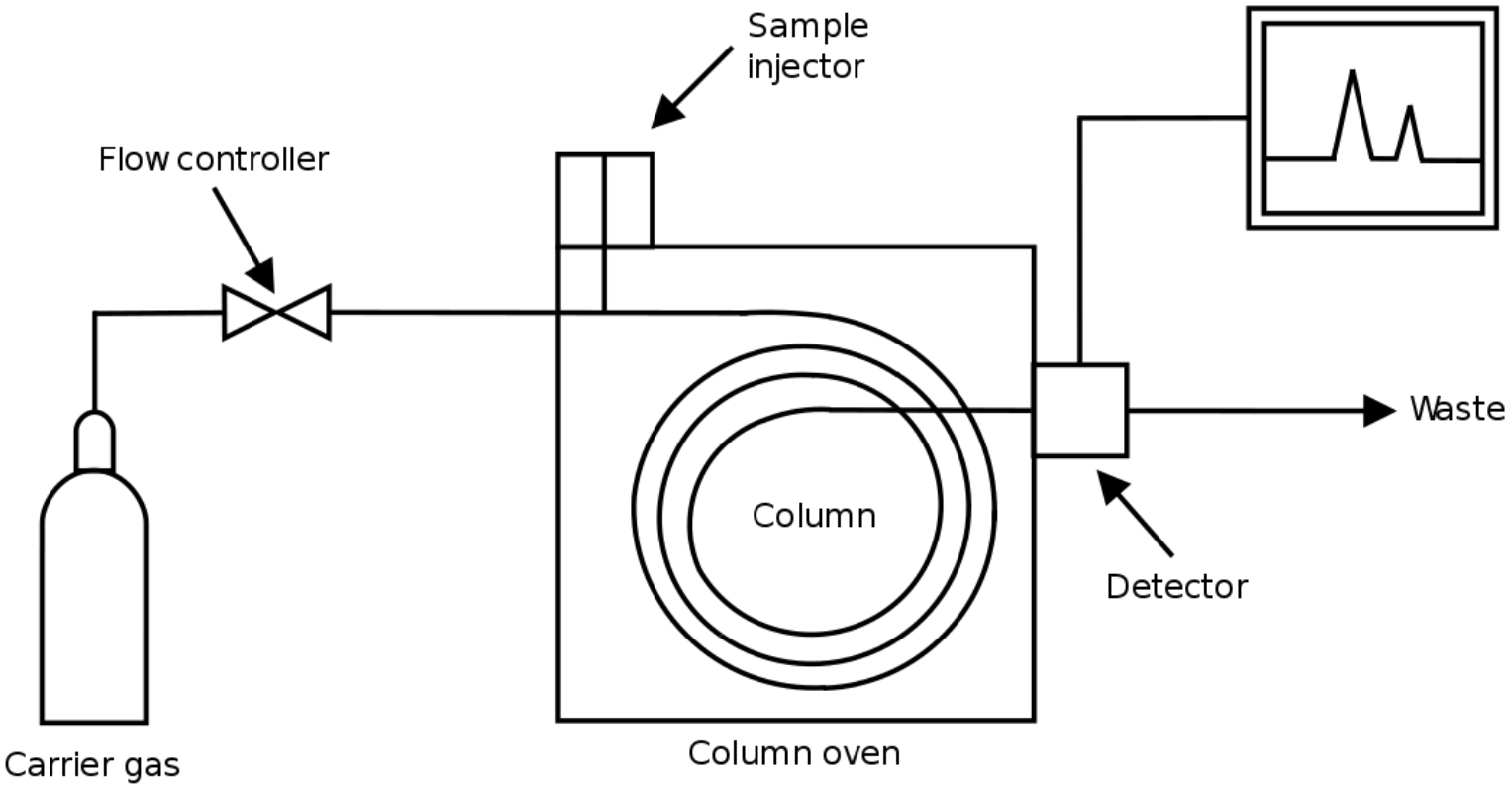
(1) Autosampler:
Injects a small amount (1 µL) of sample into the Gas Chromatograph

(2) Gas Chromatograph:
Separates chemical species and creates a chromatogram of all the species in the sample.

(3) Mass Spectrometer:
Creates a spectrum or "fingerprint" of each compound as it comes from the GC

Science for Diplomats 17 March 2015
www.opcw.org/fileadmin/OPCW/Science_Technology/Diplomats_Programme/Science_for_Diplomats_at_the_OPCW_2014_2015.pdf

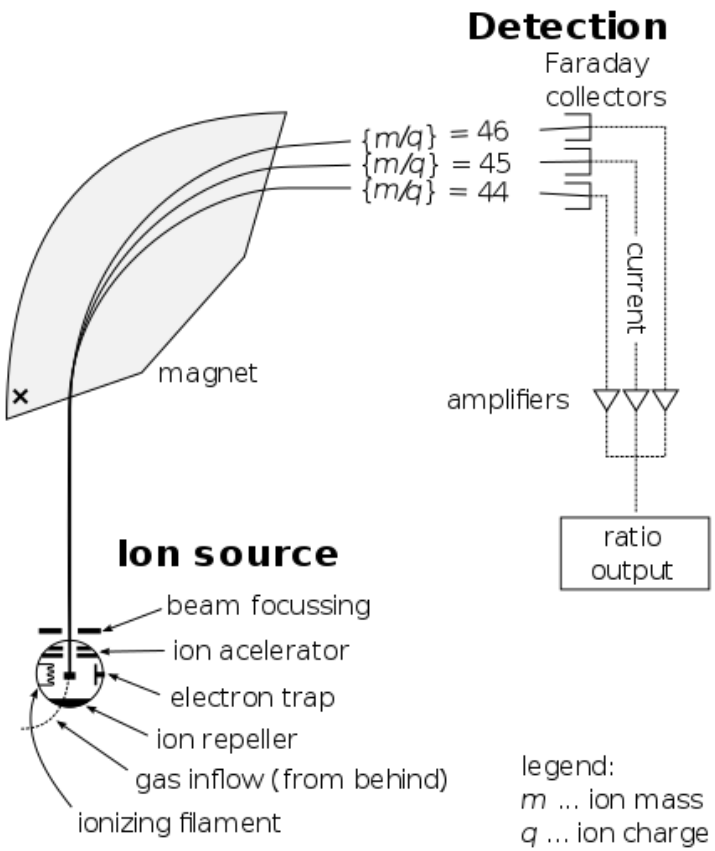
Gas Chromatograph



Gas Chromatograph

- Volatile sample injected.
- Carried by an inert or unreactive gas (e.g. helium or nitrogen) through column with solid coated with thin layer of liquid or a polymer.
- Substances move back and forth between moving in the gas and stationary on liquid or polymer.
- Different substances have different volatilities and different attractions to liquid or polymer, so they spend different amounts of time moving in gas.
- Substances are separated because they come out of the column at different times

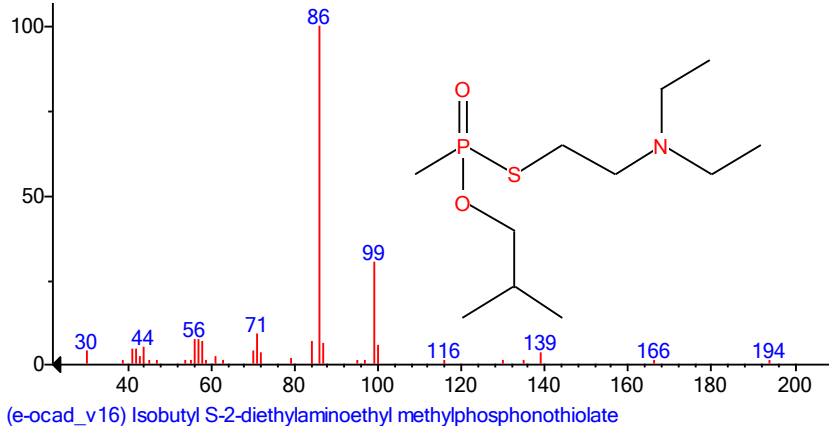
Mass Spectrometer

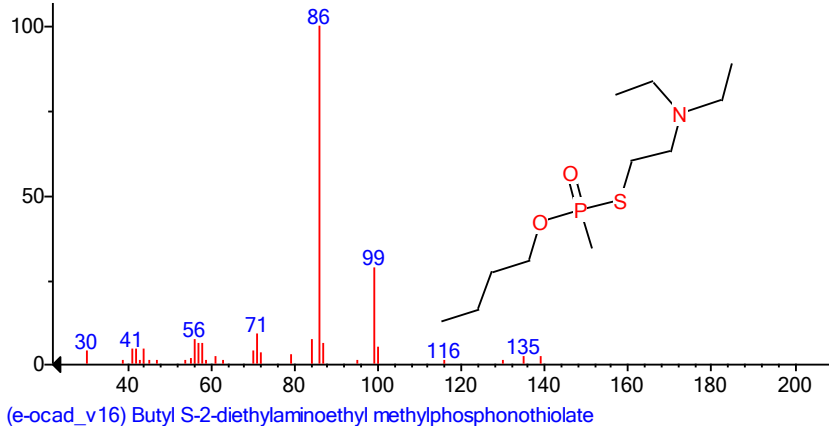


Mass Spectrometer

- Substance is ionized and broken into fragments by an electron beam.
- Ions are accelerated into a magnetic field.
- Moving ions create a magnetic field that interacts with the external magnetic field, causing the ions to be deflected.
- The more massive the particle is, the more difficult it is to deflect it, so the less it is deflected.
- Detector finds the ions at different positions, and a mass spectrum is created based on the amount of deflection and the intensity of the ion beam at different degrees of deflection.
- Each substance yields a unique mass spectrum, and comparison of a mass spectrum to mass spectrums of known substances can be done to identify substances.

GC/MS Results: Spectra Match to Library



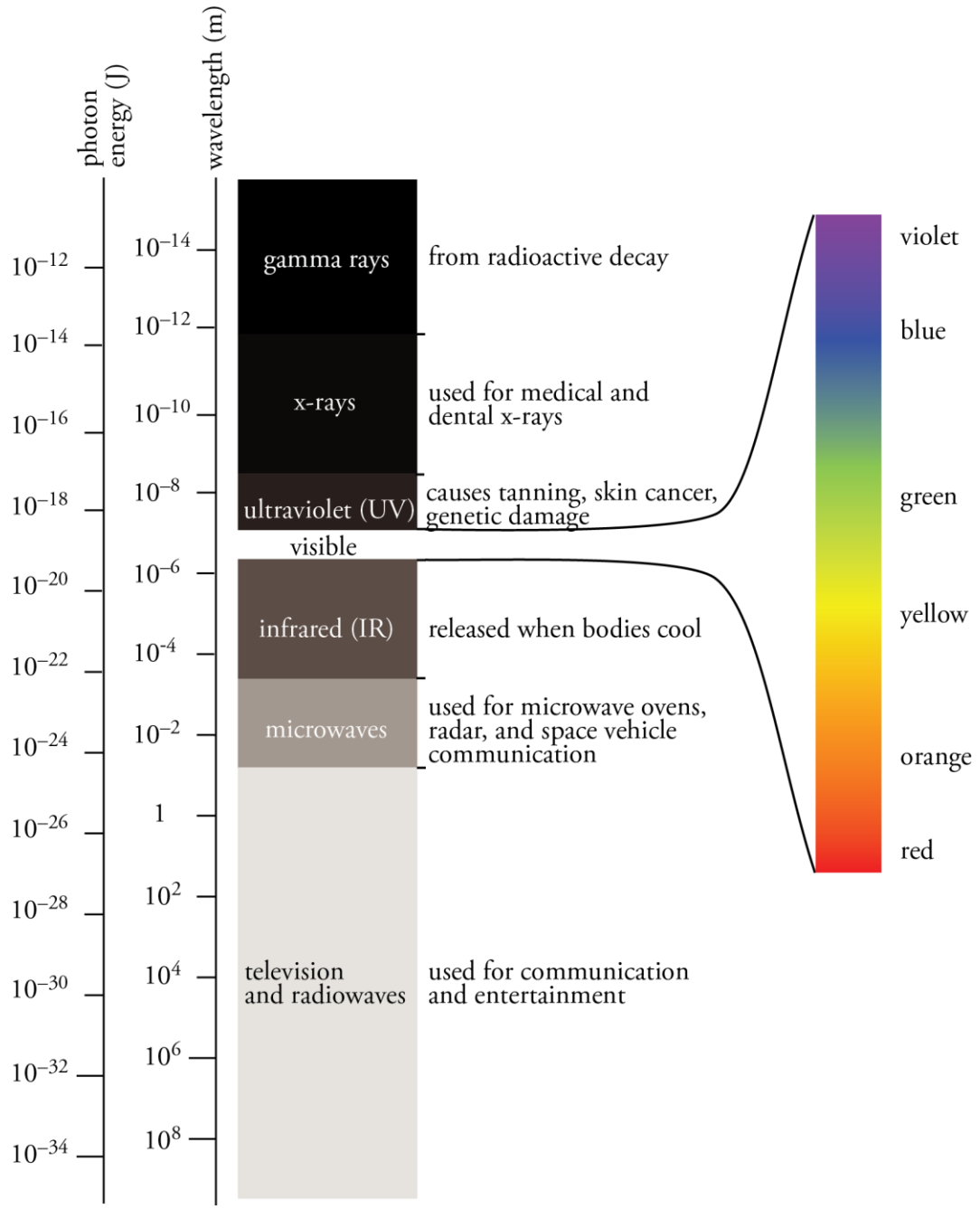


- Small differences in mass spectra indicate different structures
- Both are V-agents

Science for Diplomats 17 March 2015
www.opcw.org/fileadmin/OPCW/Science_Technology/Diplomats_Programme/Science_for_Diplomats_at_the_OPCW_2014_2015.pdf

Infrared (IR) Radiation

- Infrared radiation is longer wavelength and lower energy than visible light.
- There is a range of energies within the IR region of the radiant energy spectrum.

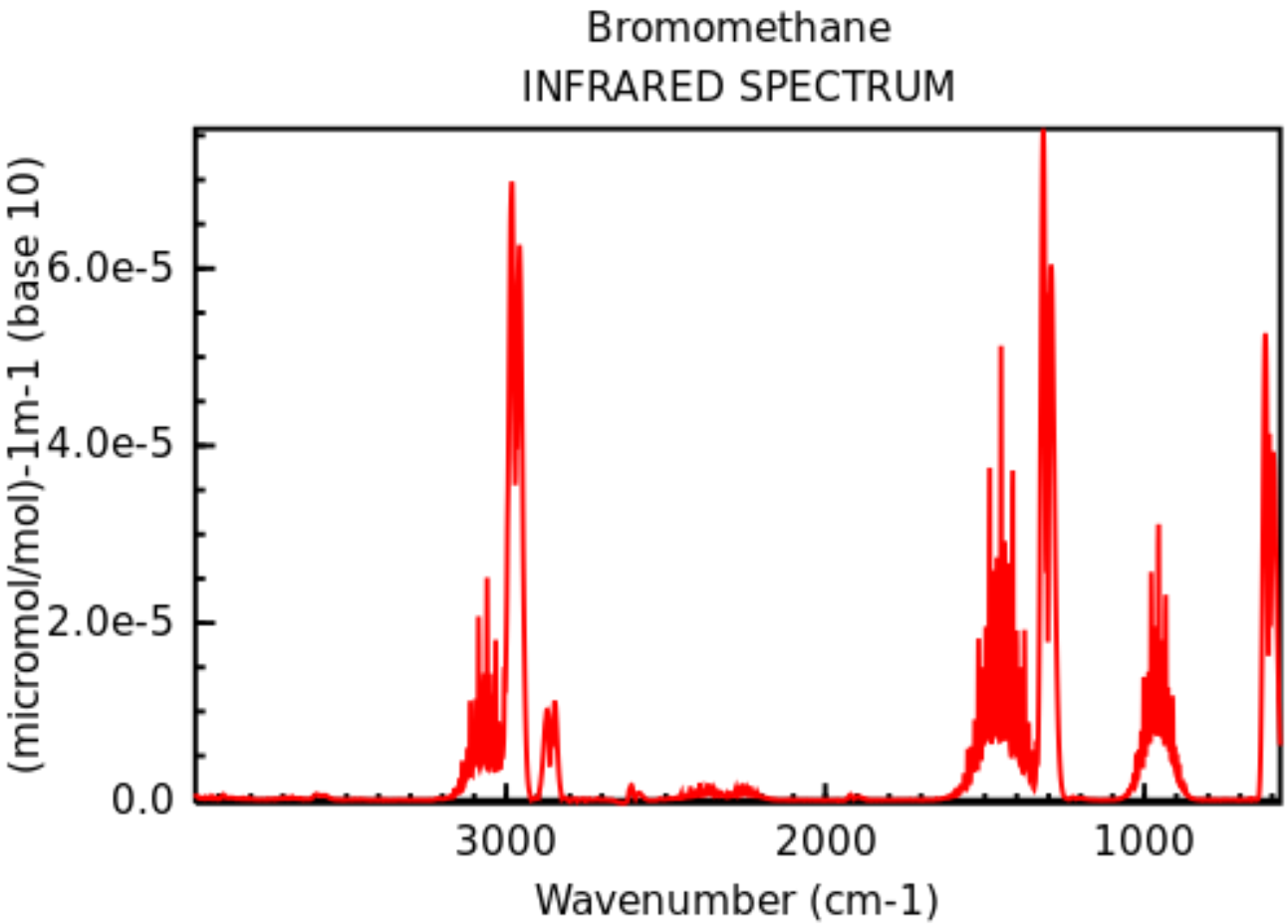


Infrared (IR) Radiation and Vibrations and Rotations

- Each molecule has a unique set of most stable (ground state) and less stable (excited state) vibrational and rotational energies.
- The molecules can be excited from a ground state to an excited states by infrared radiation.
- Because each substance has a unique set of differences in energy between ground and excited states, each substance absorbs a unique set of IR wavelengths and energies, which can be used to identify substances.

http://www2.ess.ucla.edu/~schauble/MoleculeHTML/CO2_html/CO2_page.html

IR Spectrum


Bromomethane
INFRARED SPECTRUM
(micromol/mol)-1m-1 (base 10)
6.0e-5
4.0e-5
2.0e-5
0.0
3000
2000
1000
Wavenumber (cm-1)
NIST Chemistry WebBook (http://webbook.nist.gov/chemistry)

OPCW Member State Obligations

- *Each country that belongs to the OPCW must:*
  - *destroy all chemical weapons it owns or possesses;*
  - *destroy all chemical weapons it may have abandoned in another country; and*
  - *destroy facilities it owns or possesses which were involved in the production of chemical weapons.*

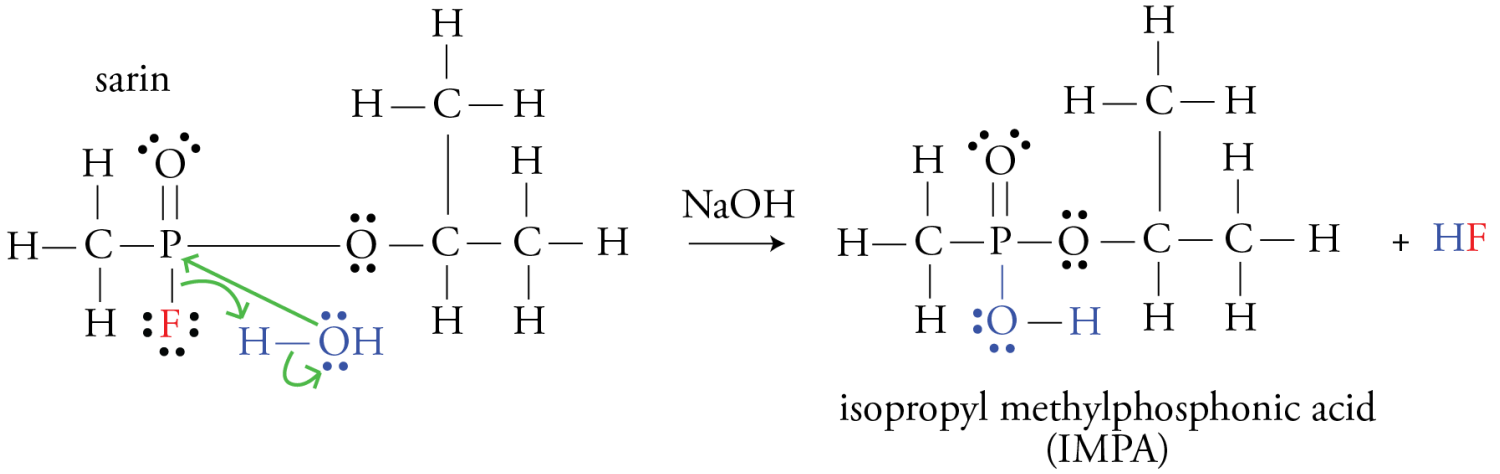
https://www.opcw.org/our-work/demilitarisation/destruction-of-chemical-weapons/

Three Ways of Disposing of Chemical Weapons

- Ocean dumping (no longer done)
- Incineration
- Hydrolysis (chemical neutralization) followed by various further treatments (now favored)

Hydrolysis of Sarin

Each arrow represents the movement of a pair of electrons as covalent bonds are broken and made.



Common CW Precursors

- Most precursors have legitimate commercial uses.
- Dual-use nature impedes detection of CW programs.
- Trade in precursors is monitored and controlled.

Chemical Compound	***Commercial Uses***	***CW Agent***
Thiodiglycol	plastics, textile dyes, ink	Mustard agent
Phosphorus trichloride	plasticizers, insecticides	Sarin
Sodium cyanide	dyes & pigments, nylon, metal hardening	HCN
Phosphorus pentasulfide	insecticides, lubricants, pyrotechnics	VX

Origins of the Australia Group

- *"In early 1984, a United Nations investigation team found that Iraq had used chemical weapons (CW) in the Iran-Iraq war in violation of the 1925 Geneva Protocol, and that at least some of the precursor chemicals and materials for its CW program had been sourced through legitimate trade channels. In response, several countries introduced export controls on certain chemicals that could be used to manufacture CW."*
- *These controls suffered from a lack of uniformity, and it soon became apparent that attempts were being made to circumvent them. This led Australia to propose a meeting of the countries with export controls with the aim of harmonising their national licensing measures and enhancing cooperation.*

https://www.dfat.gov.au/publications/minisite/theaustraliagroupnet/site/en/origins.html

Australia Group

- Established 1985
- *"The principal objective of Australia Group participants' is to use licensing measures to ensure that exports of certain chemicals, biological agents, and dual-use chemical and biological manufacturing facilities and equipment, do not contribute to the spread of CBW. The Group achieves this by harmonising participating countries' national export licensing measures. The Group's activities are especially important given that the international chemical and biotechnology industries are a target for proliferators as a source of materials for CBW programs."*

http://www.australiagroup.net/en/objectives.html

Australia Group

- The Australia Group lists some chemical weapons precursors that are not listed on CWC Schedules.

  https://www.dfat.gov.au/publications/minisite/theaustraliagroupnet/site/en/precursors.html

- They have a list of dual-use chemical manufacturing facilities and equipment and related technology and software that could be used to make chemical weapons.

  https://www.dfat.gov.au/publications/minisite/theaustraliagroupnet/site/en/dual_chemicals.html

Australia Group
43 Participants

- European Union (1985), Germany (1985), United States (1985), United Kingdom (1985), Italy (1985), Japan (1985), France (1985), Spain (1985), Sweden (1991), Poland (1994), Switzerland (1987), Netherlands (1985), Argentina (1993), Republic of Korea (1996), Australia (1985), Latvia (2004), Austria (1989), Lithuania (2004), Belgium (1985), Luxembourg (1985), Bulgaria (2001), Malta (2004), Canada (1985), Mexico (2013), Croatia (2007), New Zealand (1985), Republic of Cyprus (2000), Norway (1986), Czech Republic (1994), Denmark (1985), Portugal (1985), Estonia (2004), Romania (1995), Slovak Republic (1994), Finland (1991), Slovenia (2004), Greece (1985), Hungary (1993), Republic of Turkey (2000), Iceland (1993), Ukraine (2005), Ireland (1985), India (2018)

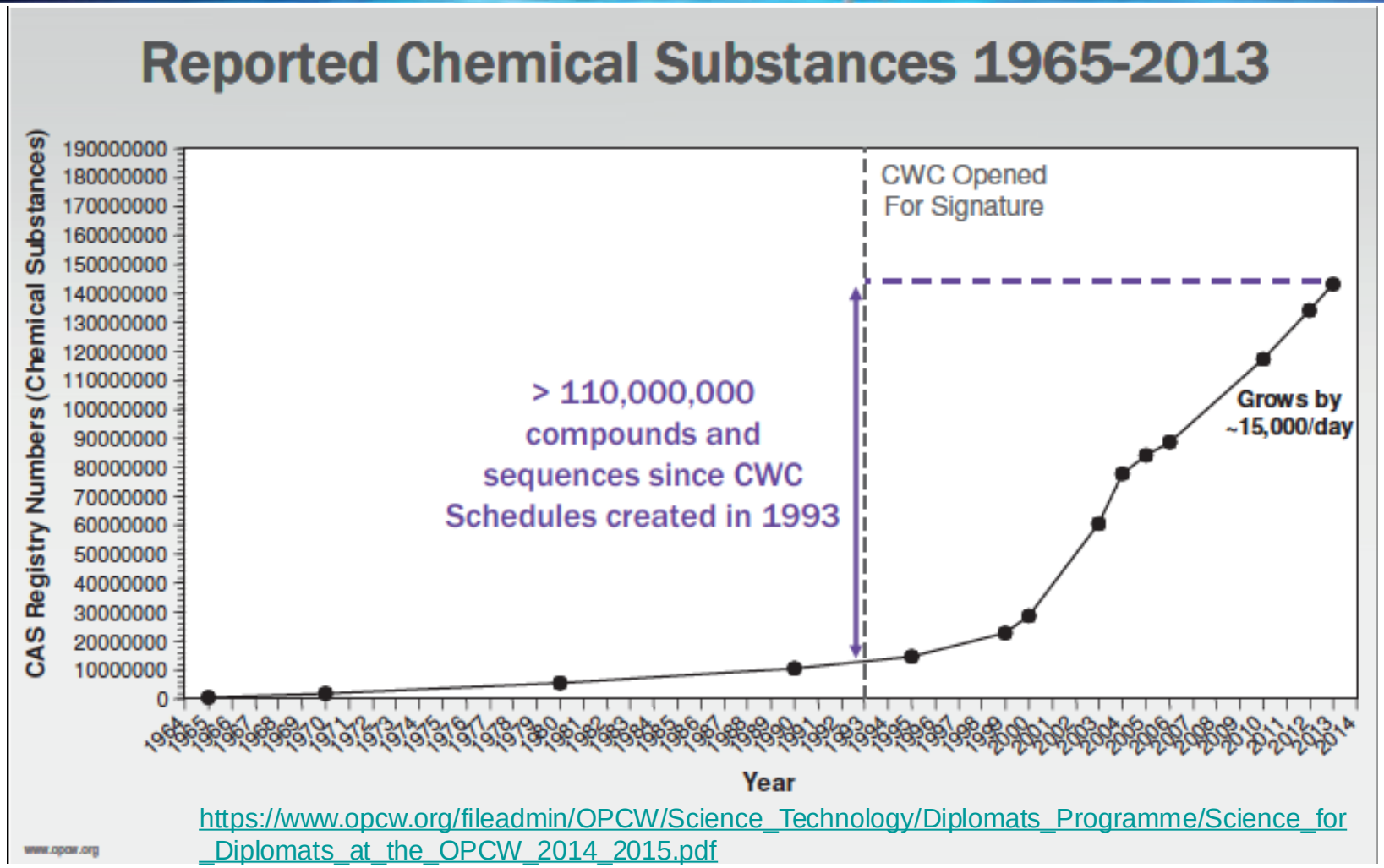
http://www.australiagroup.net/en/participants.html

Top 10 Chemical-Producing Countries

- In Australia Group:
  - 1. USA
  - 2. Germany
  - 5. Japan
  - 6. United Kingdom
  - 7. Italy
  - 8. France
  - 9. India
- Not in Australia Group:
  - 3. Russia
  - 4. China
  - 10. Brazil

http://www.australiagroup.net/en/participants.html

Many New Substances Created



https://www.opcw.org/fileadmin/OPCW/Science_Technology/Diplomats_Programme/Science_for_Diplomats_at_the_OPCW_2014_2015.pdf

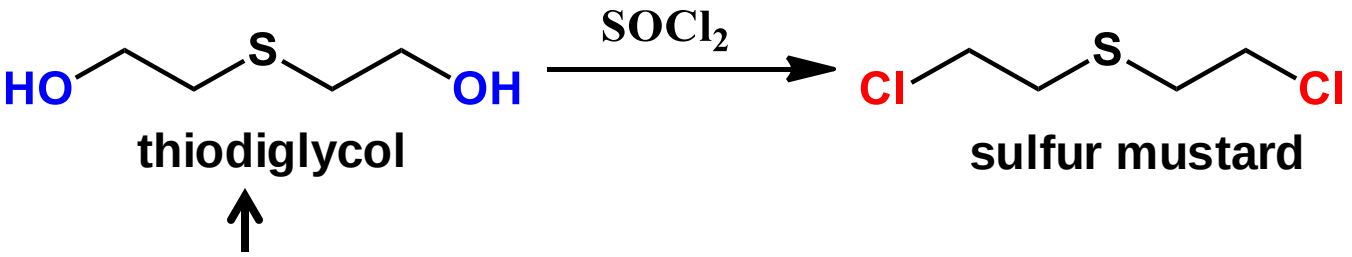
Ways to Circumvent Export Controls on Precursors

- Substitute uncontrolled chemical for controlled one.
- Purchase relatively small quantities from multiple sources
- Produce precursors from simpler, uncontrolled substances.
  - There are at least 9 ways to make sulfur mustard documented in the chemical literature, and some of these involve uncontrolled substances.

http://www.cwc2013.info/RG2013-by-doc/6/AG-precursors.pdf

Iraqi Sulfur Mustard Program

Synthesizing precursor compounds from simpler ones that are not export controlled or are available from domestic sources



Embargo placed on this by Western Countries in early 80's