Science and Technology

Chemical Weapons Part 1

By

Mark Bishop

Chemical Weapons (CW)

- Chemical weapons are, "***Any chemical*** which through its chemical action on life processes can cause death, temporary incapacitation or permanent harm to humans or animals. This includes all such chemicals, regardless of their origin or of their method of production, and regardless of whether they are produced in facilities, in munitions or elsewhere." (OPCW)

Special gas mask for dogs-1917

Types of Chemical Weapons

- Choking agents (e.g. chlorine, phosgene)
- Blistering agents (e.g. sulfur mustard)
- Blood agents (e.g. hydrogen cyanide)
- Nerve agents (e.g. sarin, VX, novichok)
- Toxins (e.g. ricin)
- Tearing agents (e.g. CS)
- Opiate-like agents (e.g. fentanyl)
- Psychochemical Incapacitants (e.g. BZ)

Assignment

- This will begin after the fourth chemistry module lecture.
- You will divide yourselves into groups of four.
- Two people in each group will pretend to be either *terrorists* or a country's *military leaders* and plan a simulated chemical weapons attack.
  - Identify your goal (high lethality, get attention, take over territory, etc.)
  - Choose the target.
  - Choose the chemical weapon
  - Choose the means of dispersal.
  - Determine a source of the chemical weapon.
- Two people in each group will act as the *security team* attempting to stop the attack and minimize damage.

Assignment

- The *terrorists* or *military leaders* will provide subtle clues to the *security people*.
- The *security pair* can tell the *terrorists* what they are looking for, and the *terrorists* will provide clues based on these searches.
- Based on the clues they have received, the security team will develop a plan to stop the attack, and failing that, a plan to minimize the effects of the attack.
- Each group of four will make a 5-minute presentation describing their experience.

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

For terrorists or governments?

- **Terrorist criteria**
  - Either relatively simple to make or obtain in some other way.
  - Relatively simple to disperse
  - Can be lethal or incapacitating
  - Relatively low cost
- **Government with well-developed chemical industry (e.g. North Korea or Syria)**
  - Can be more difficult to make.
  - Can have more sophisticated dispersal techniques.
  - More likely to want lethal
  - Higher cost may be OK

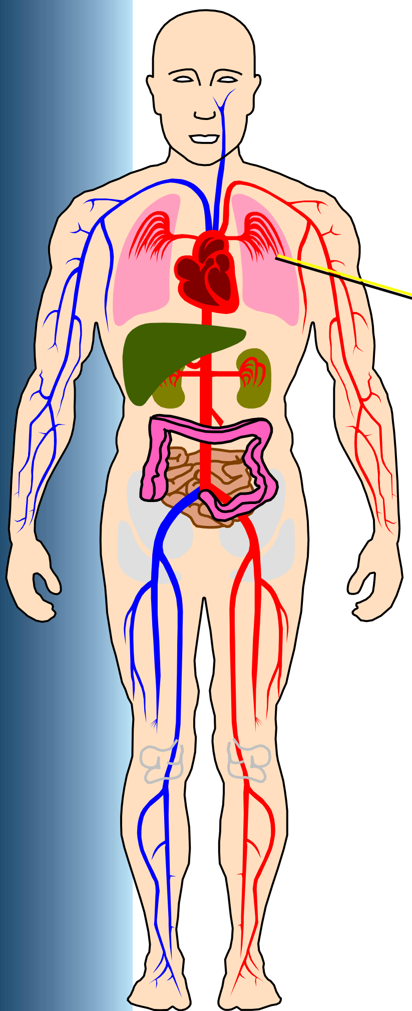
Exam Topics for CW

- For the chemical weapons chlorine, phosgene, sulfur mustard, hydrogen cyanide, sarin, VX, fentanyl, BZ, and ricin, be able to describe each of the following.
  - Identify the chemical structure from a line drawing or Lewis structure (For example, I may give you a structure and ask you which of the chemical agents listed above it represents.)
  - List examples of its use as a chemical weapon, if any.
  - Identify whether it's more likely to be lethal or incapacitating.

Exam Topics for CW (cont.)

- Relative difficulty in obtaining it compared to the other chemical weapons (Issues related to (1) its production, including cost, safety precautions, storage issues, and availability of its precursors, and the necessary equipment and (2) ability to obtain it from the chemical industry)
- Whether or not it has uses other than as a chemical weapon.
- Which CWC schedule it's listed on (if any)
- Its physiological effects
- Its relative persistence on the ground
- Necessary protective gear
- Treatment for exposure
- How it can be destroyed

Choking Agents



- Diphosgene, **phosgene**, **chlorine**, chloropicrin
- Mode of action: inhalation
- Physiological effects
  - Victim can die of oxygen deficiency via different mechanisms
- Form when disseminated: gas
- Required defensive gear: protective mask

1899 International Peace Conference

- At The Hague, Netherlands
- 26 countries, including Germany, signed the treaty
- One section outlawed the use of “projectiles the object of which is the diffusion of asphyxiating or deleterious gases.”

Chlorine and WWI

During peace time a scientist belongs to the world, but during war time he belongs to his country.

Fritz Haber

- In 1914-15, WWI, which was expected to end quickly, was bogged down in trench warfare, so each side was looking for ways to break through the lines.
- Fritz Haber, who won the Nobel Prize for chemistry for helping to develop a way of making ammonia from nitrogen and hydrogen in 1918, suggested loading projectiles with chlorine and shrapnel.
- Germans thought that they could avoid violating the Hague Convention by putting poison gas ***and shrapnel*** in projectiles, based on the interpretation that the convention banned "projectiles, the ***sole*** object of which is the diffusion of asphyxiating or deleterious gases.")

Chlorine as a Chemical Weapon

- Shortage of artillery shells led to use of chlorine from pressurized gas cylinders.
- Used against French troops near Ypres, Belgium, April 22, 1915.
- Wind conditions had to be in the correct direction, strong enough to move the gas to the enemy lines, but not too strong to disperse the gas too quickly.

Chlorine as a Chemical Weapon

- 168 metric tons (megagrams) released from 5730 cylinders
- Cl_2 is more dense than air
- 5-ft cloud moved at 4 mph
- Warmed, expanded to 30-ft yellow-green cloud, causing blindness, coughing, nausea, headache, and chest pain
- Created 4-mile gap in Allied line

Chlorine as a Chemical Weapon

- Reacts with water to form hydrochloric acid and hypochlorous acid, which damage tissues in the lungs and draw water into the lungs.

$$Cl_2 + H_2O \rightarrow HCl + HClO$$

Chlorine Lethality

- Death can come from asphyxia due to at least three possible mechanisms
  - Water in lungs displaces air ("*dry land drowning*").
  - Chlorine is more than twice as dense as air, so it displaces the air in the lungs.
  - Oxidative injury to the airways and lungs.
- Cardiac toxicity can lead to cardiac dysfunction.

Chlorine as a Chemical Weapon

- 600 French and Algerian troops lay blinded and dying.
- Fluid entering the lungs caused men to drown on dry land.
- Within an hour after the clearing of the gas, the Germans captured two villages, took 2000 prisoners, and confiscated 51 artillery pieces.
- German High Command had not expected the attack to work, so they did not place enough troops in the area to exploit the break in the lines, so Ypres remained in Allied hands.
- German press hailed the new innovation, but in other parts of Europe, the use of chlorine gas was condemned.

Reluctance Overcome by Perceived Necessity

I must confess that the commission for poisoning the enemy, just as one poisons rats, struck me as it must any other straightforward soldier; it was repulsive to me. If, however, the poison gas were to result in the fall of Ypres, we would win a victory that might decide the entire campaign. In the view of this worthy goal, all personal reservations had to be silent. So onward, do what must be done. War is necessity and knows no exception.

Berthold von Deimling

Commander of the German XV Army Corps at Ypres

Personal Protection (Military)

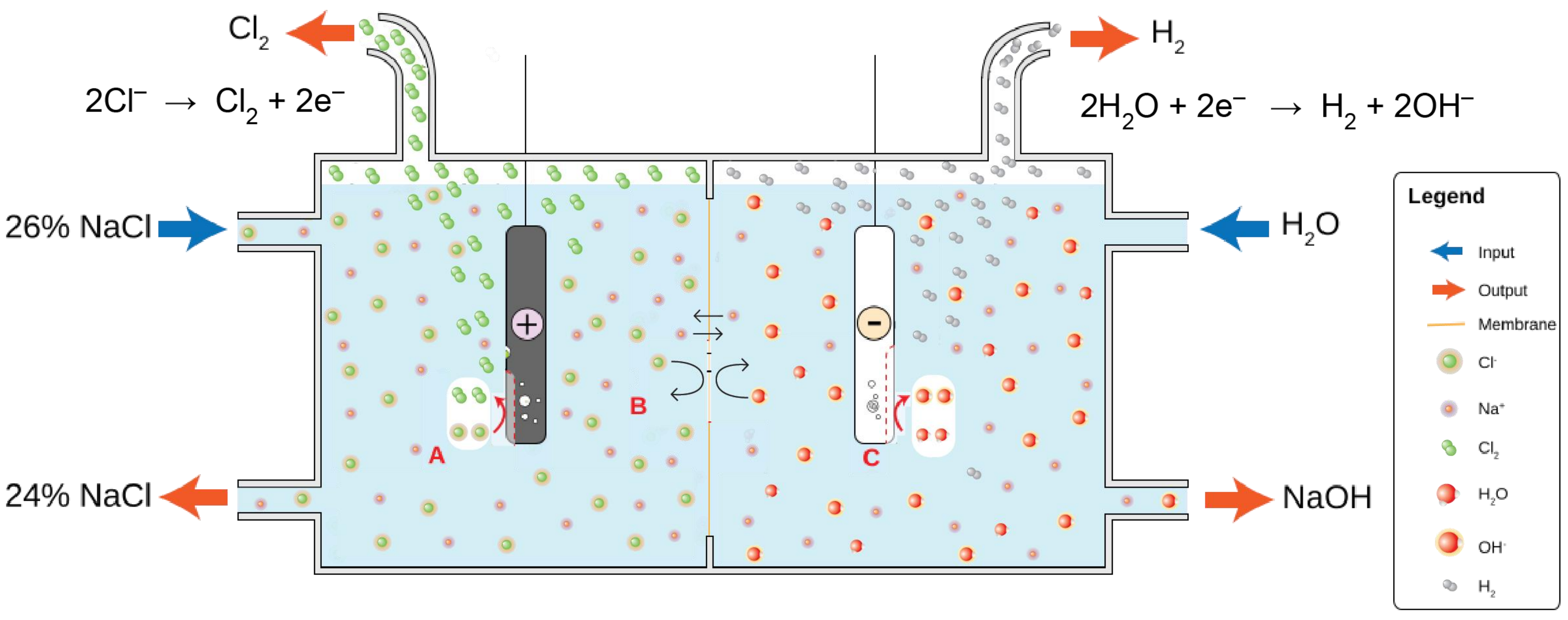
Ways to Obtain Chlorine, Cl_2

- 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.

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



Chlorine from Captured Production Plant

- December 2012 – a chemical plant east of Aleppo, Syria was taken by rebel fighters from the Al-Nusra Front (now part of Hay’at Tahrir al-Sham, Organization for the Liberation of the Levant). The factory produces chlorine among other chemicals.

http://www.france24.com/en/20121208-syria-warns-rebels-may-resort-chemical-weapons-assad-united-nations-islamists/

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

Syrian American Medical Society

- Syrian American Medical Society, a charity that runs 95 medical facilities inside the country, reported the following.
  - 161 chemical attacks from the beginning of the conflict through 2015
  - Used reports and first-hand accounts from physicians and health workers in Syria.
  - SAMS compiled another 133 reported chemical attacks that could not be fully substantiated.
  - Documented chemical attacks have led to at least 1,491 deaths and 14,581 injuries from chemical exposure.

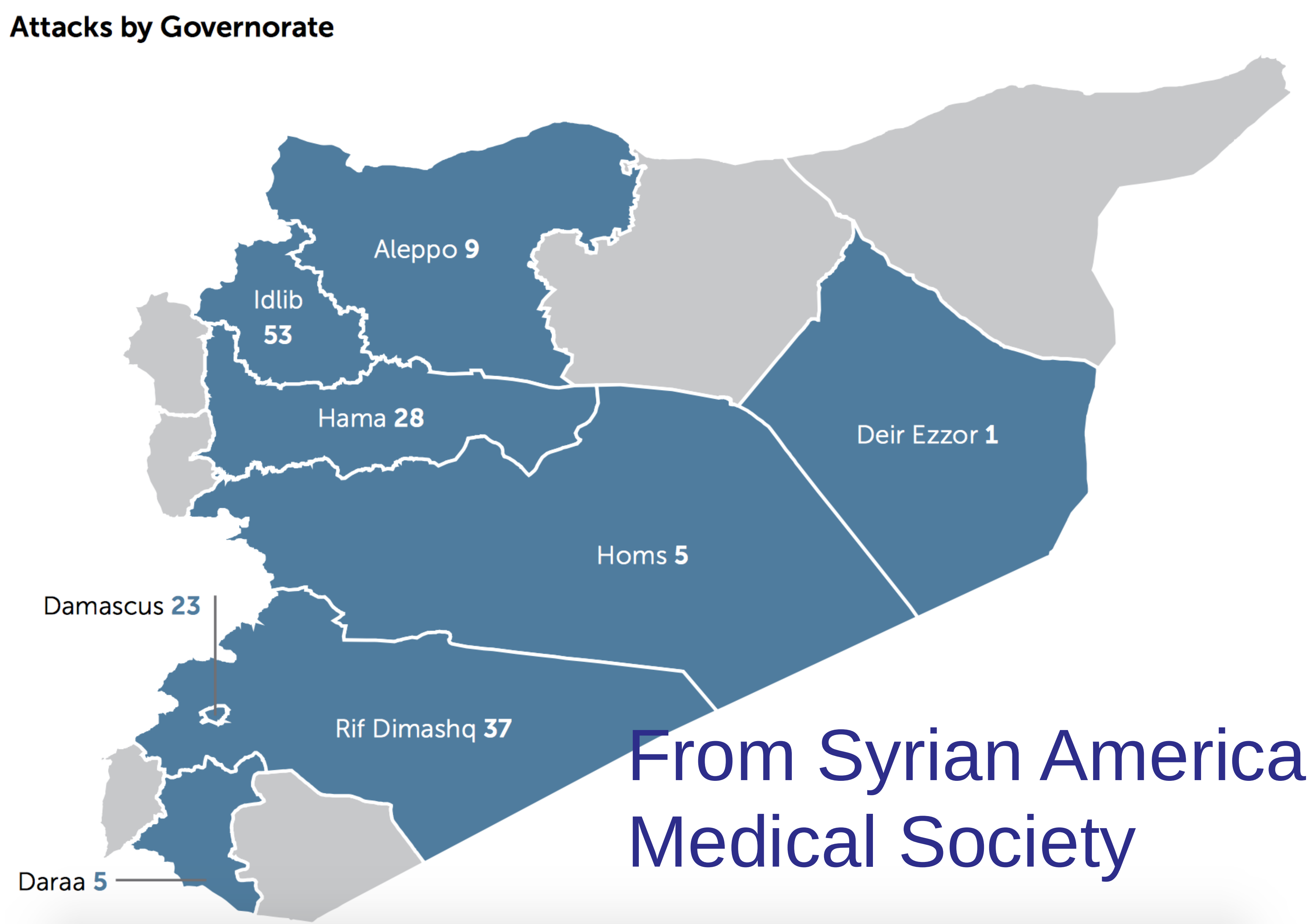
http://www.sams-usa.net/reports/a-new-normal-ongoing-chemical-weapons-attacks-in-syria/

http://www.sams-usa.net/wp-content/uploads/2016/09/A-New-Normal_Ongoing-Chemical-Weapons-Attacks-in-Syria.compressed.pdf

Syrian American Medical Society

- Syrian American Medical Society, a charity that runs 95 medical facilities inside the country, reported the following.
  - Nearly 200 chemical attacks since 2012
  - Used reports and first-hand accounts from physicians and health workers in Syria.
  - By 2015, documented chemical attacks led to at least 1,491 deaths and 14,581 injuries from chemical exposure.

http://www.sams-usa.net/reports/a-new-normal-ongoing-chemical-weapons-attacks-in-syria/
https://www.sams-usa.net/press_release/sams-syria-civil-defense-condemn-chemical-attack-douma/



From Syrian American Medical Society

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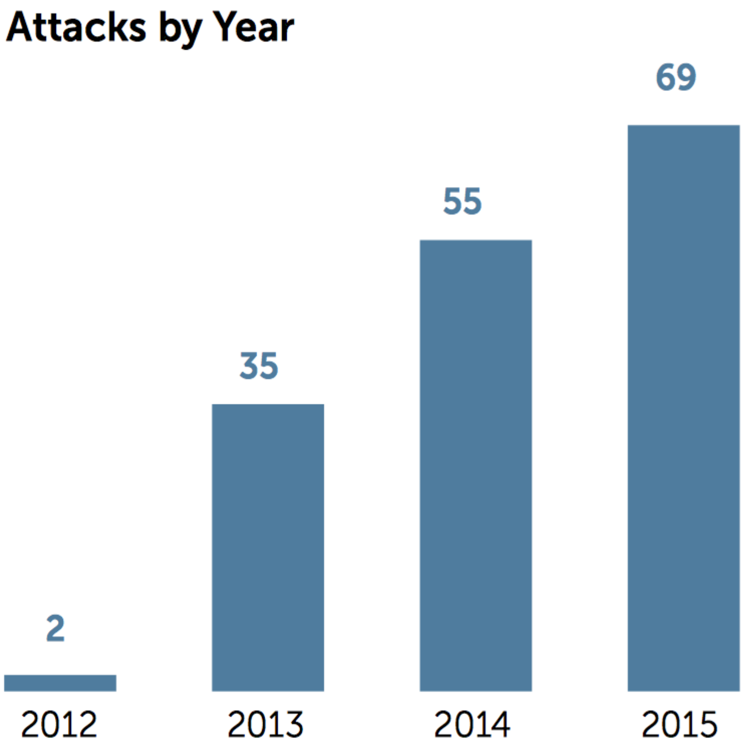
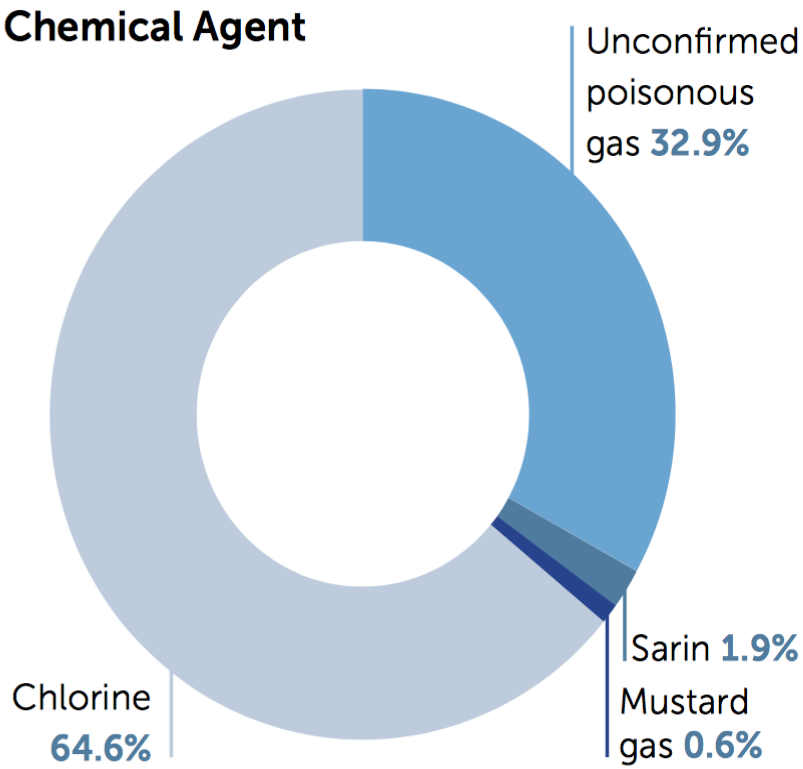
From Syrian American Medical Society





http://www.sams-usa.net/wp-content/uploads/2016/09/A-New-Normal_Ongoing-Chemical-Weapons-Attacks-in-Syria.compressed.pdf

OPCW-UN Fact-Finding Missions (FFM) and Joint Investigative Mechanism (JIM)

- Described the investigations and results of eight cases of possible use of chlorine or a chlorine derivative and one related to the use of sulfur mustard in Syria.
- Reported that there were three incidents where there was either a substance “matching the characteristics of chlorine”, “a canister with traces of chlorine or a chlorine-like substance”, “a significant number of people — up to 150 — may have been exposed to chlorine” and a “canister with traces of chlorine”.
- Two cases with a “toxic substance” used.
- They reported one incident where “there was sufficient information to conclude that Islamic State in Iraq and the Levant (ISIL) was the only entity with the ability, capability, motive and means to use sulfur mustard in Marea on 21 August 2015”.
- For the other incidents, they were unable to confirm the use of chemical weapons.

https://www.un.org/ga/search/view_doc.asp?symbol=S/2016/738

OPCW-UN FFM and JIM

https://unoda-web.s3.amazonaws.com/wp-content/uploads/2013/12/report.pdf

http://www.the-trench.org/wp-content/uploads/2016/01/OPCW-FFM-20140616-1st-Chlorine-investigation-report.pdf

http://www.the-trench.org/wp-content/uploads/2016/01/OPCW-FFM-20140910-2nd-Chlorine-investigation-report.pdf

http://www.the-trench.org/wp-content/uploads/2016/01/OPCW-FFM-20141218-3rd-Chlorine-investigation-report.pdf

http://www.the-trench.org/wp-content/uploads/2016/01/OPCW-FFM-20151217-Syria-request-Rev1.pdf

http://www.the-trench.org/wp-content/uploads/2016/01/OPCW-FFM-20151029-Idlib-Governorate.pdf

http://www.the-trench.org/wp-content/uploads/2016/01/OPCW-FFM-20151029-Marea.pdf

http://www.securitycouncilreport.org/atf/cf/%7B65BFCF9B-6D27-4E9C-8CD3-CF6E4FF96FF9%7D/s_2016_142.pdf

http://www.un.org/en/ga/search/view_doc.asp?symbol=S/2016/530

https://www.un.org/ga/search/view_doc.asp?symbol=S/2016/738

Islamic State and Chlorine Gas

- There is some evidence that the Islamic State has used chlorine gas in roadside bombs.

http://www.bbc.com/news/world-middle-east-31847427

http://www.rt.com/news/198796-isis-chlorine-attack-report/

http://www.telegraph.co.uk/news/worldnews/middleeast/syria/11978627/Chemical-weapons-experts-confirm-Islamic-State-use-of-mustard-gas-in-Syria.html

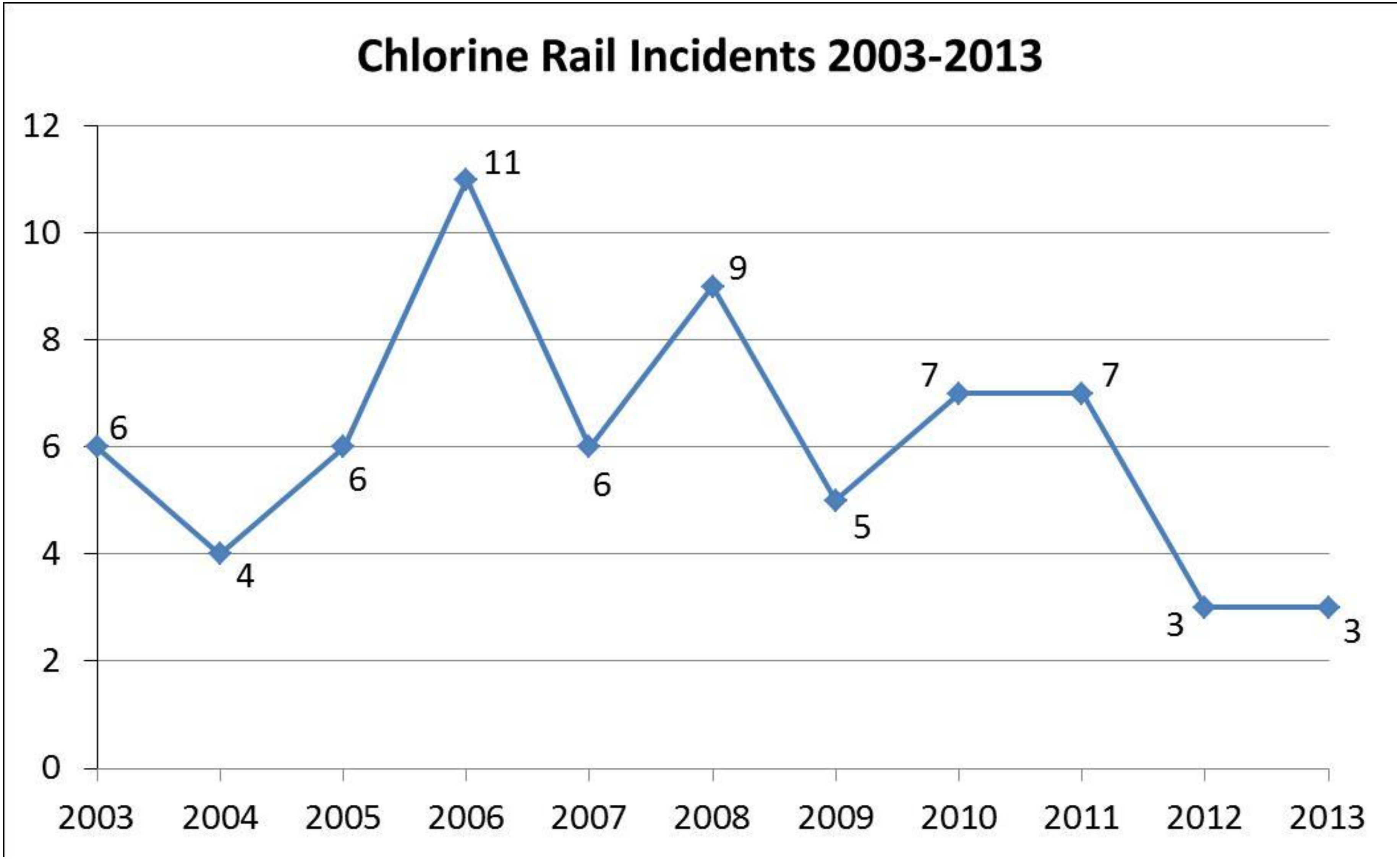
http://www.ibtimes.com/what-isis-chemical-weapons-stockpile-islamic-state-group-has-recruited-experts-across-2192871

Chlorine, Cl_2, is still a threat today.

- The United States produces approximately *1 billion pounds of chlorine* a year for use in water treatment facilities.
- Potential vulnerability of chlorine-filled rail tank cars, by which chlorine is primarily transported (accident, sabotage)

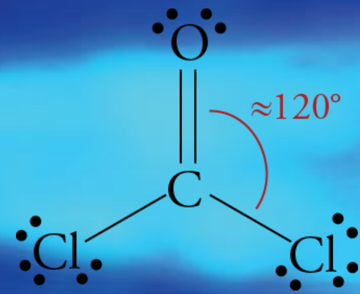
Chlorine rail-car derailment, South Carolina, 2005

Chlorine, Cl_2, Accidents in U.S.



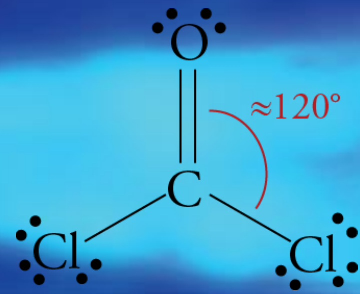
http://www.chlorineinstitute.org/transportation/incident-statistics.cfm

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, $COCl_2$

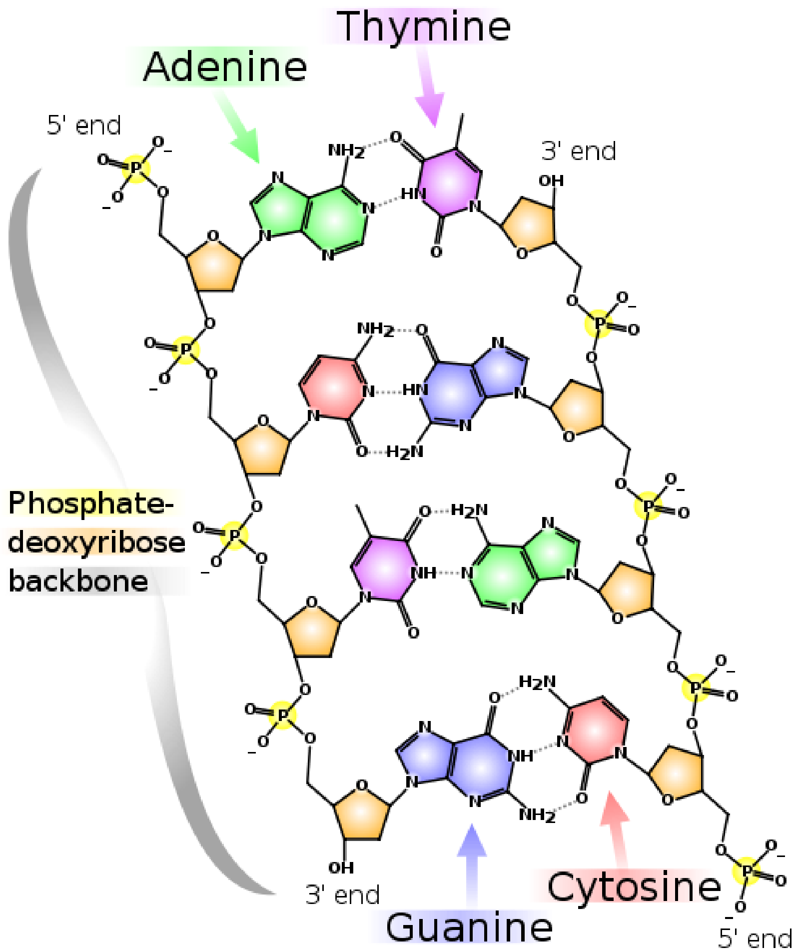


- More difficult to make than chlorine. Produced by passing purified carbon monoxide and chlorine gas through a bed of porous activated carbon, which serves as catalyst. The reactor must be cooled to prevent phosgene from decomposing.

  $$CO + Cl_2 \rightarrow COCl_2$$

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

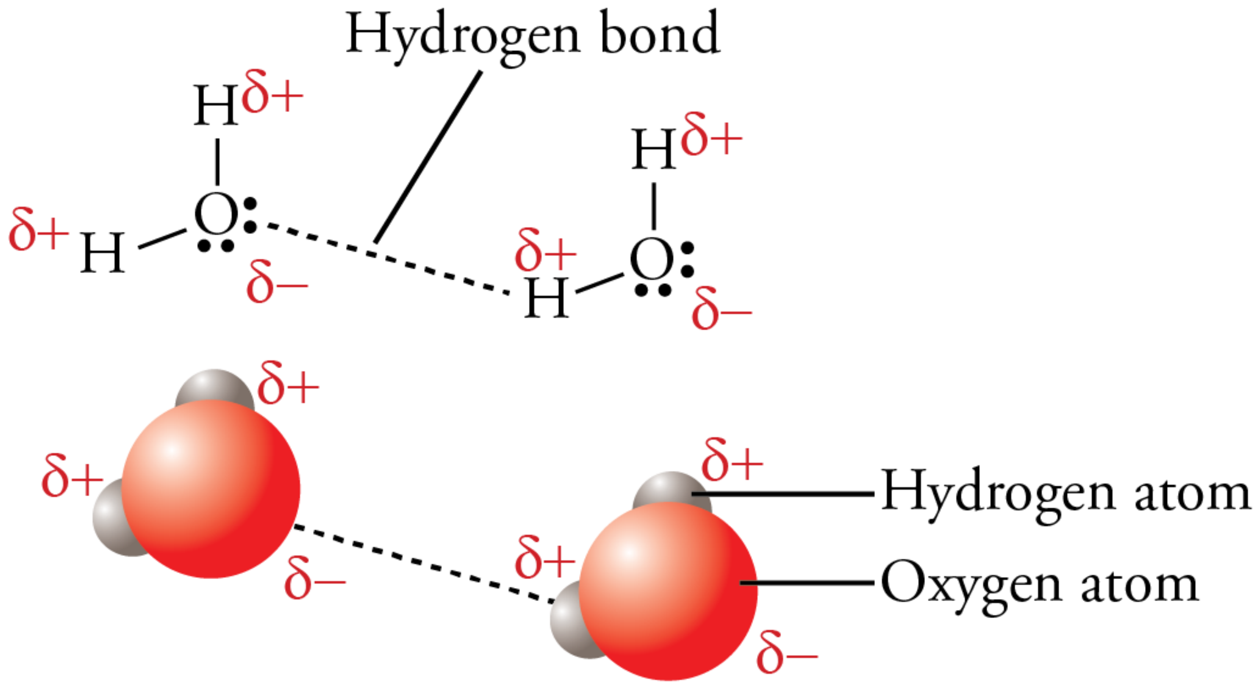
DNA Segment



Thymine
Adenine
5' end
3' end
Phosphate-
deoxyribose
backbone
3' end
Cytosine
Guanine
5' end

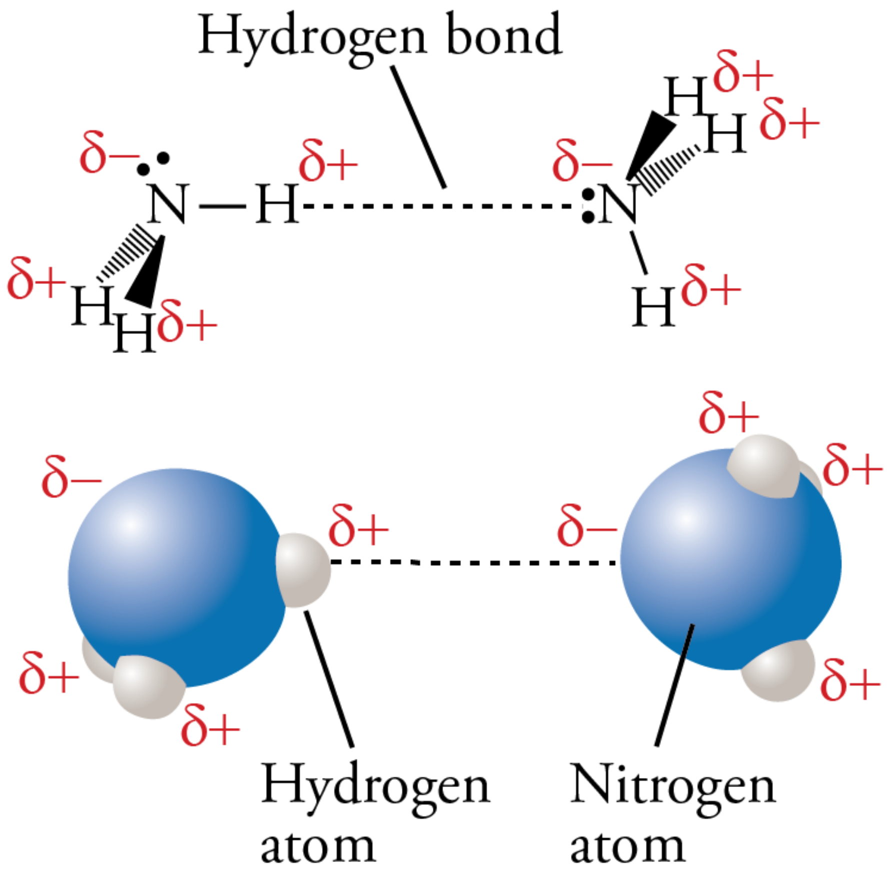
Hydrogen Bonds in Water

In H_2O, the hydrogen bond is between a partial positive H of one H_2O molecule and the partial negative O of another H_2O molecule.

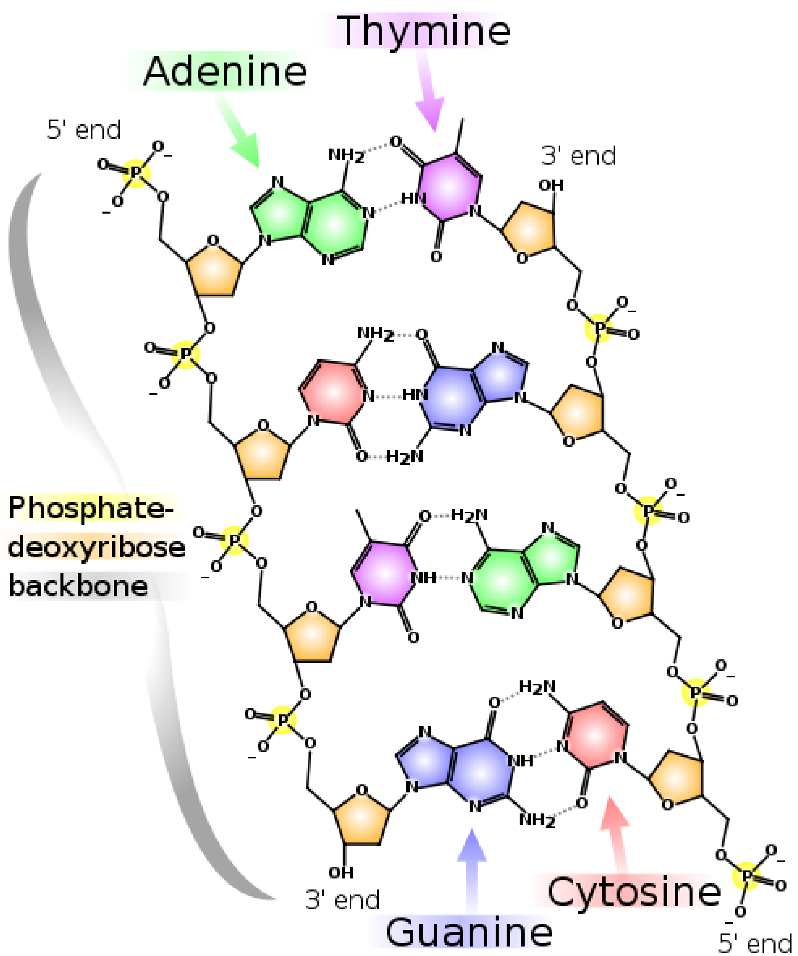


Hydrogen Bonds in Ammonia

In NH_3, the hydrogen bond is between a partial positive H of one NH_3 molecule and the partial negative N of another NH_3 molecule.



DNA Segment

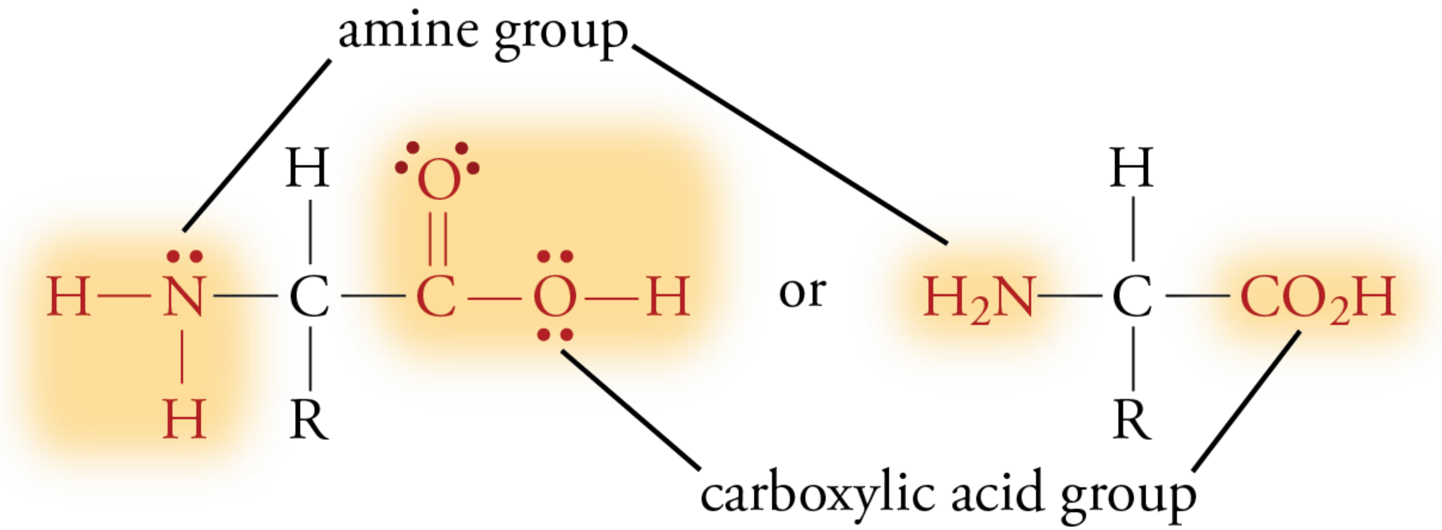


Thymine
Adenine
5' end
3' end
OH
Phosphate-
deoxyribose
backbone
OH
3' end
Cytosine
Guanine
5' end

Protein Synthesis

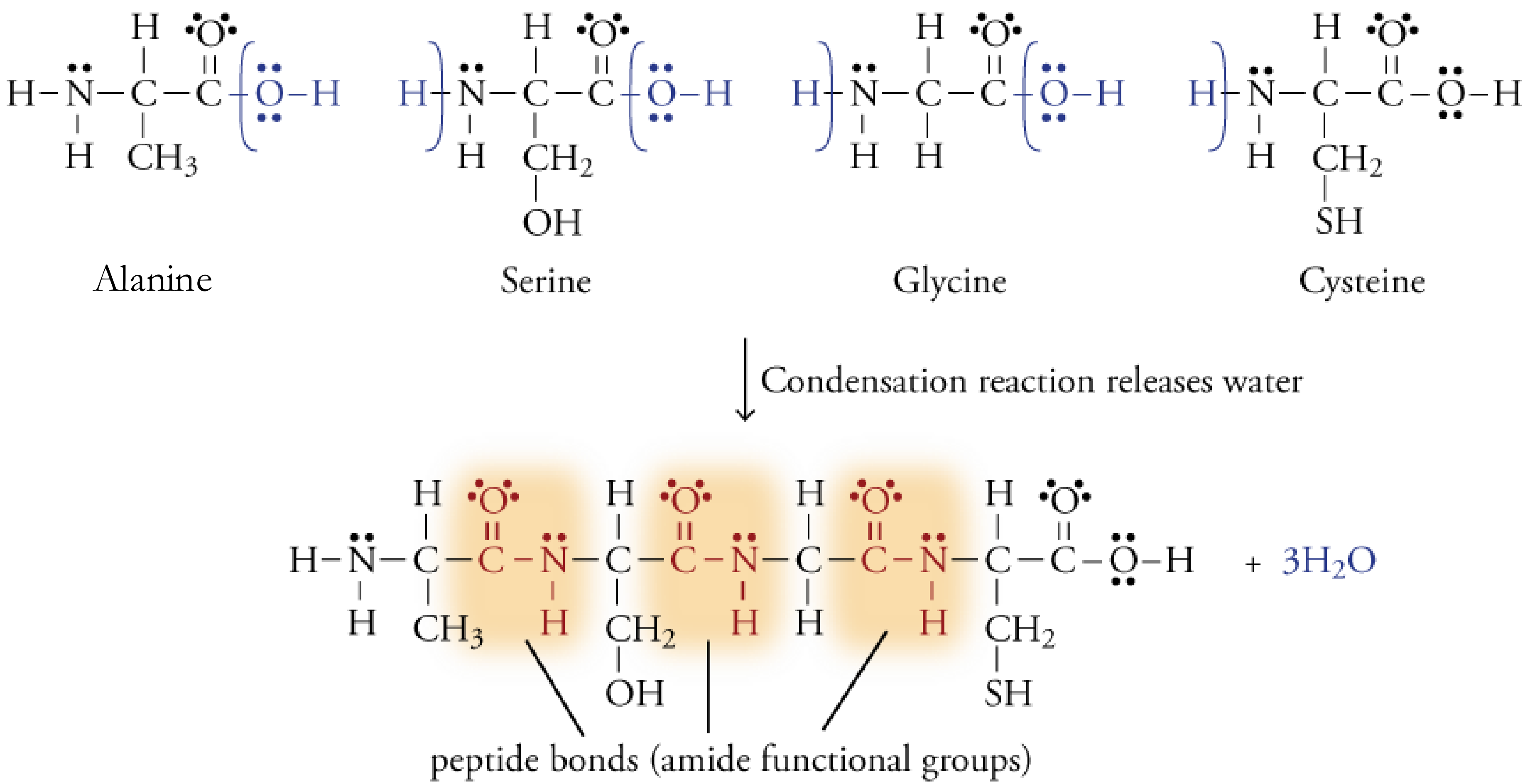
- DNA stays in the nucleus.
- The sequence of bases that contains information necessary to build a protein molecule is transcribed to a sequence of similar bases in a messenger RNA, mRNA, molecule that migrates out of the nucleus to a ribosome in the cell.
- The sequence of bases in the mRNA guides the formation of a protein with a specific sequence of amino acids.

Amino Acids



amine group
H
O
H—N—C—C—O—H
H R
or
H
H_2N—C—CO_2H
R
carboxylic acid group

Formation of Ala-Ser-Gly-Cys



COVID-19 mRNA Vaccines

- COVID-19 mRNA vaccines give instructions for our cells to make a harmless piece of what is called the “spike protein.”
- The spike protein is found on the surface of the virus that causes COVID-19.
- COVID-19 mRNA vaccines are given in the upper arm muscle.
- Once the instructions (mRNA) are inside the cells, the cells use them to make the protein piece.
- After the protein piece is made, the cell breaks down the instructions and gets rid of them.

COVID-19
mRNA Vaccines

- Next, the cell displays the protein piece on its surface.
- Our immune systems recognize that the protein doesn't belong there and begin building an immune response and making antibodies, like what happens in natural infection against COVID-19.

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html

Polypeptides and Proteins

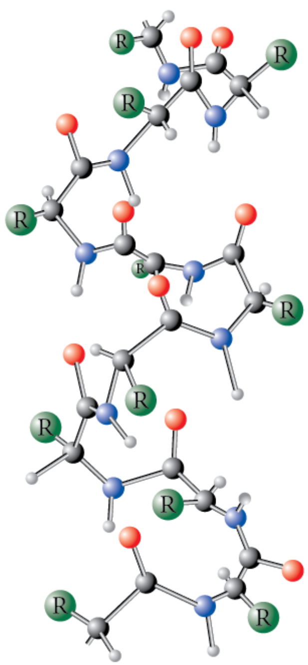
- A chain of amino acids linked by peptide bonds would be called a **polypeptide** or often just a peptide.
- If the polypeptide has more than about 50 amino acids, we called it a **protein**.

Primary and Secondary Protein Structures

- ***Primary Structure*** = the sequence of amino acids in the protein
- The arrangement of atoms that are close to each other in the polypeptide chain is called the ***secondary structure*** of protein.
  - Three types
    - α-helix
    - β-sheet
    - irregular

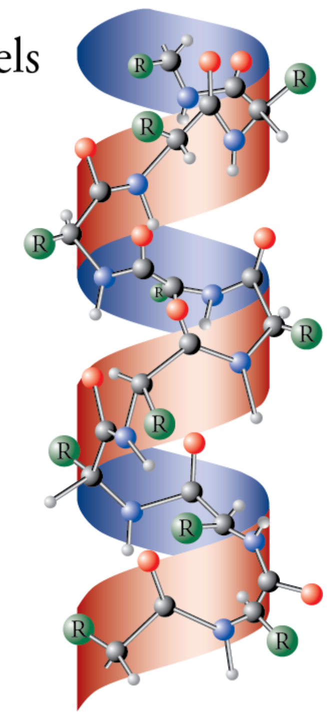
α-helix – Secondary Structure

Ball-and-stick model of a portion of the α-helical secondary structure of a protein molecule

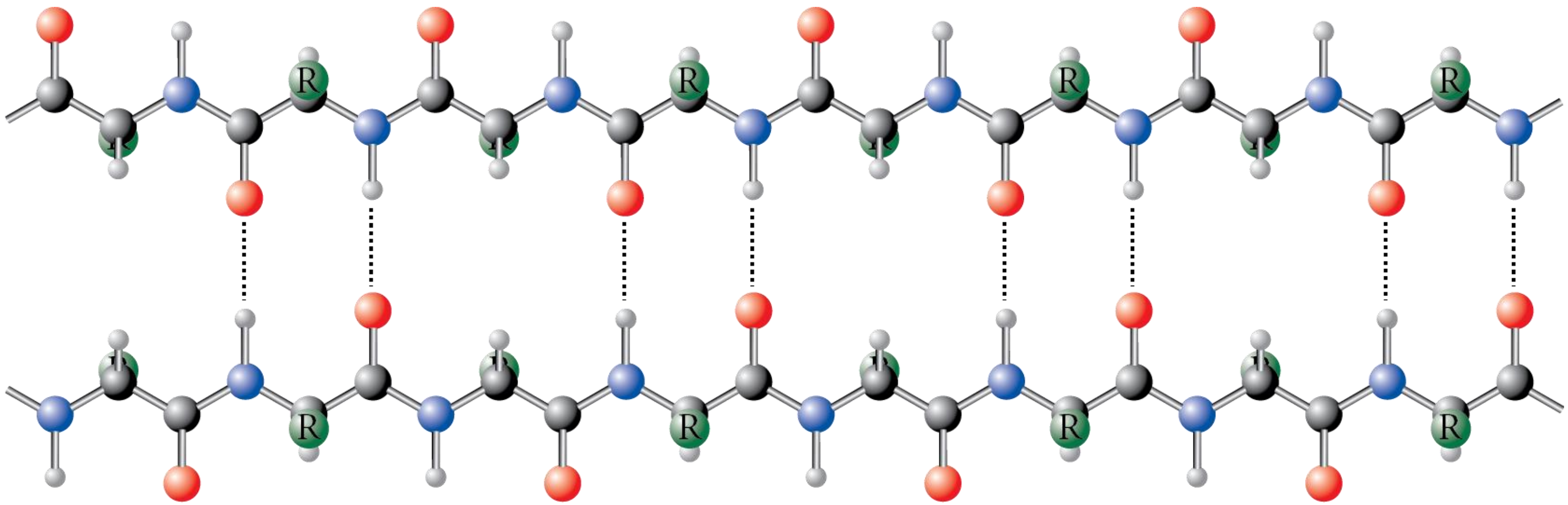


This ribbon model shows the general arrangement of atoms in a portion of the α-helical secondary structure of a protein molecule.

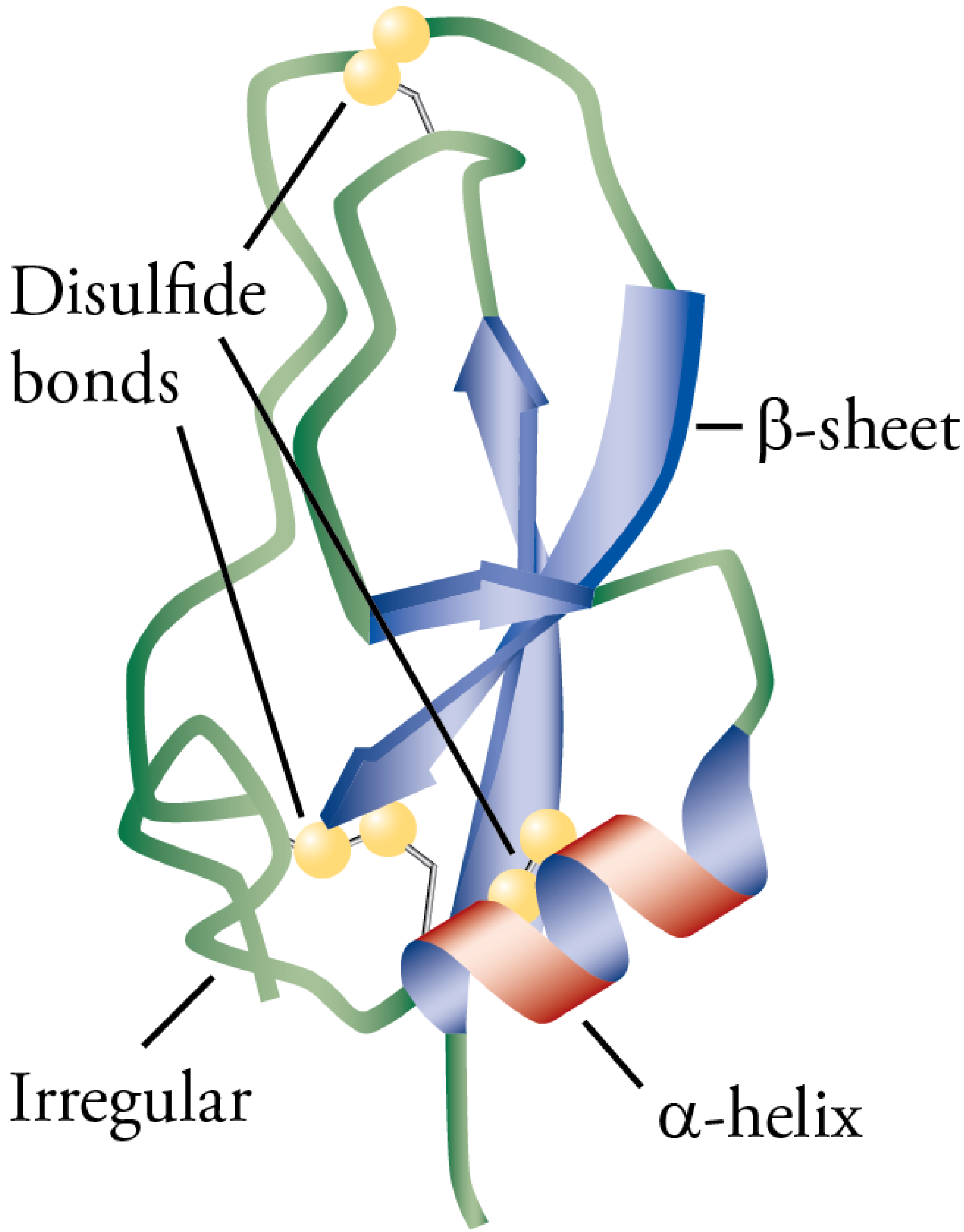
The two models superimposed



β-Sheet
Secondary Structure



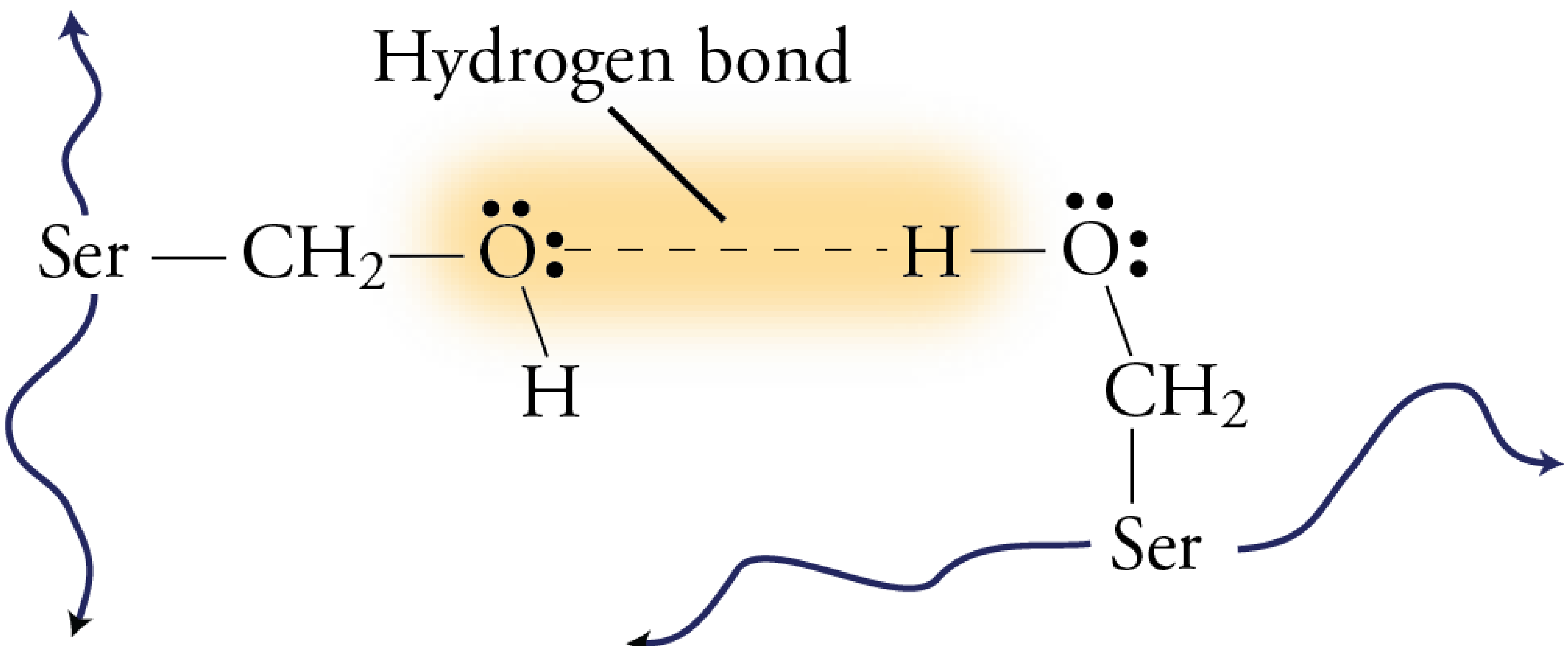
The Ribbon Structure of the Protein BPTI



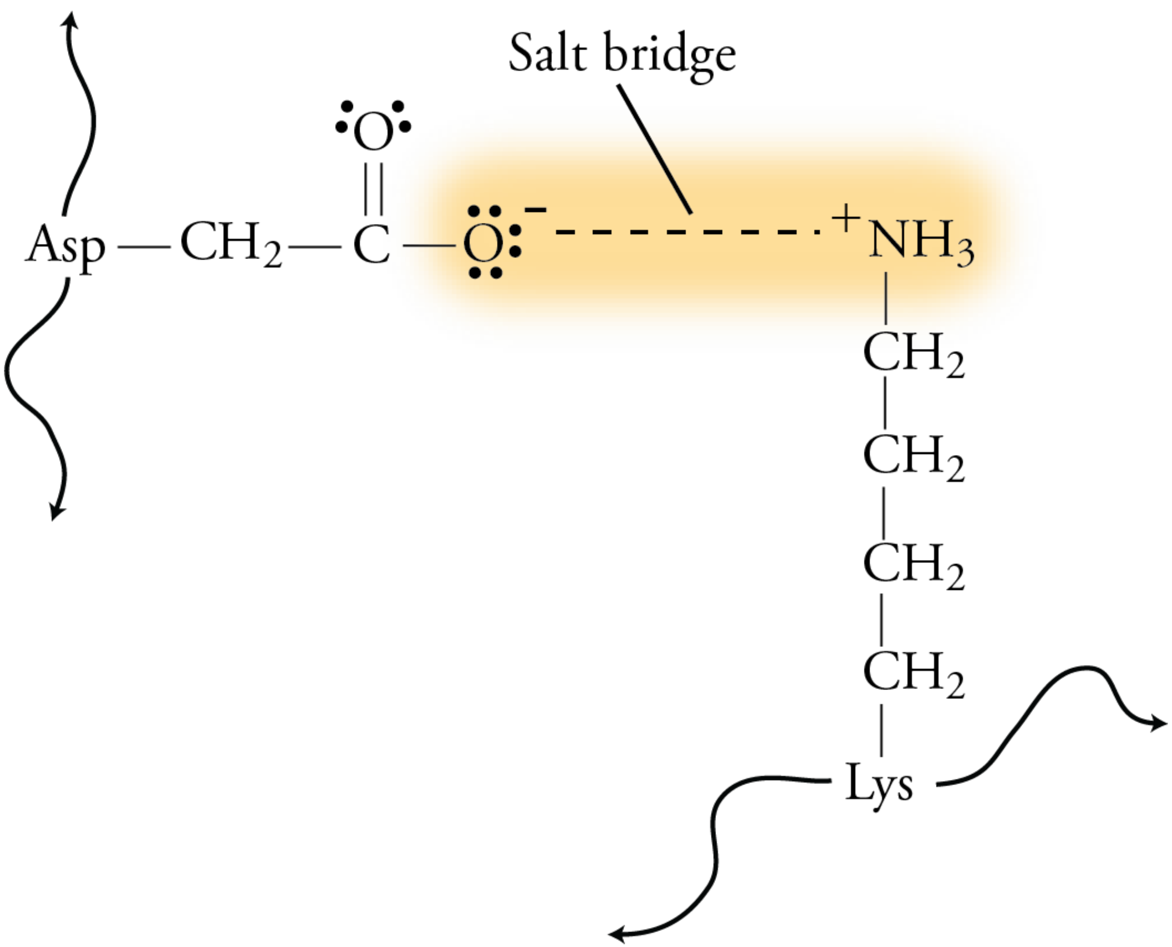
Tertiary Protein Structure

- The very specific overall shape of the protein called its ***tertiary structure***.
- The protein chain is held in its tertiary structure by interactions between the side chains of its amino acids.
  - Hydrogen bonds
  - Salt bridges
  - Disulfide bonds

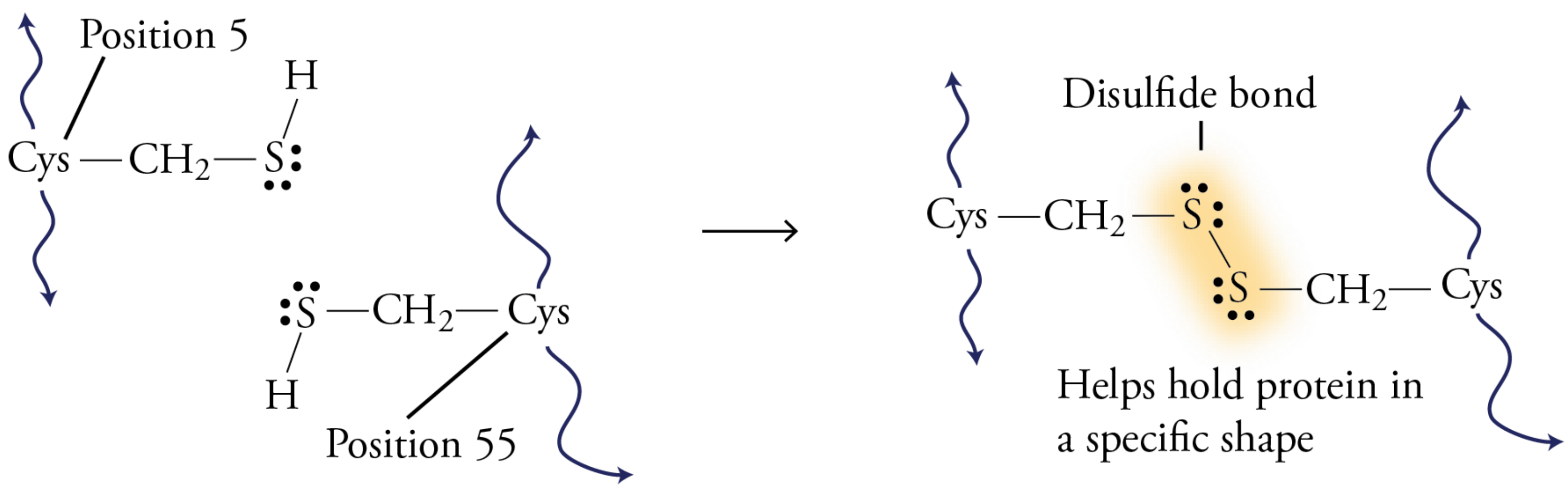
Hydrogen Bonding in Proteins



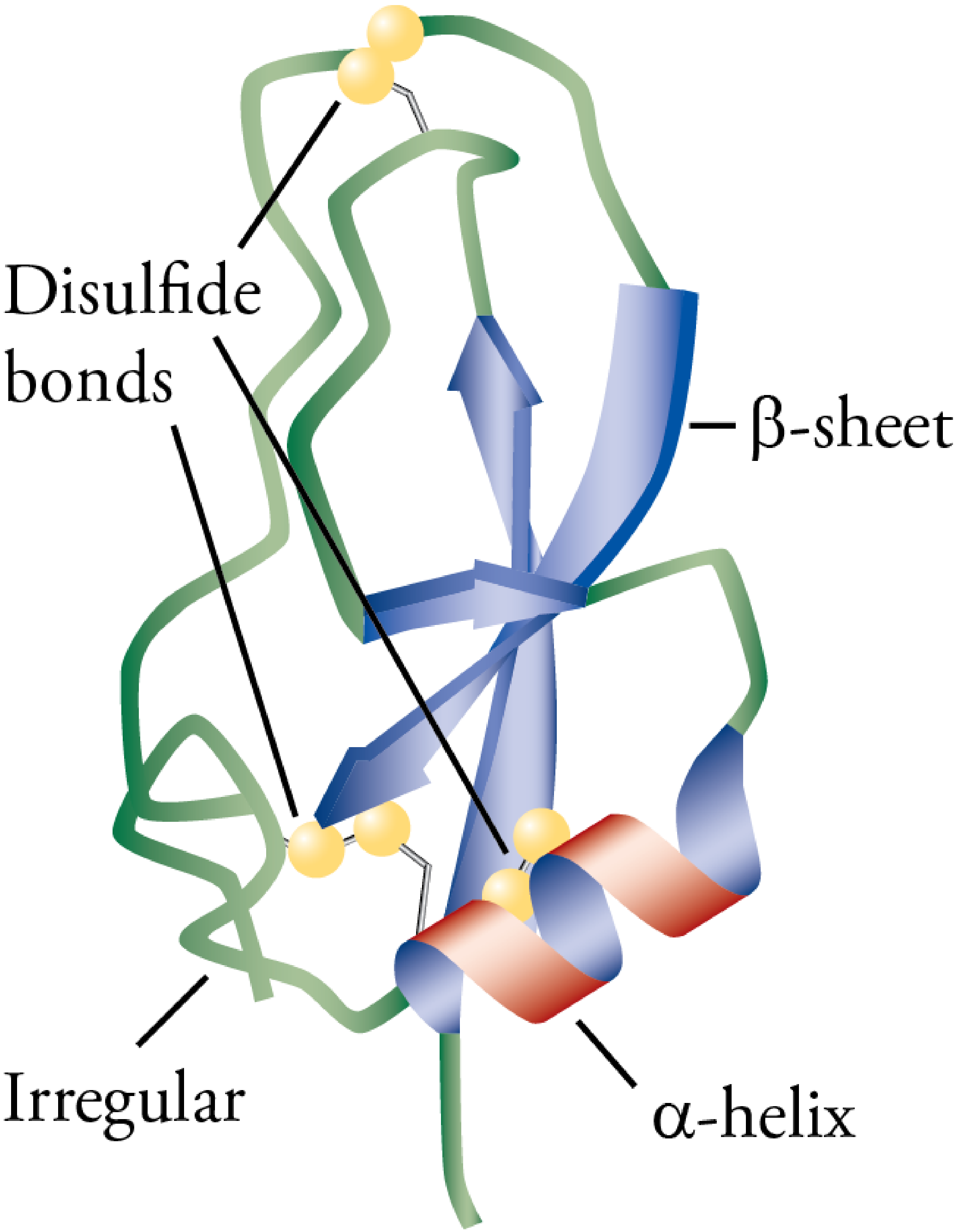
Salt Bridge in Proteins



Disulfide Bonds in Proteins

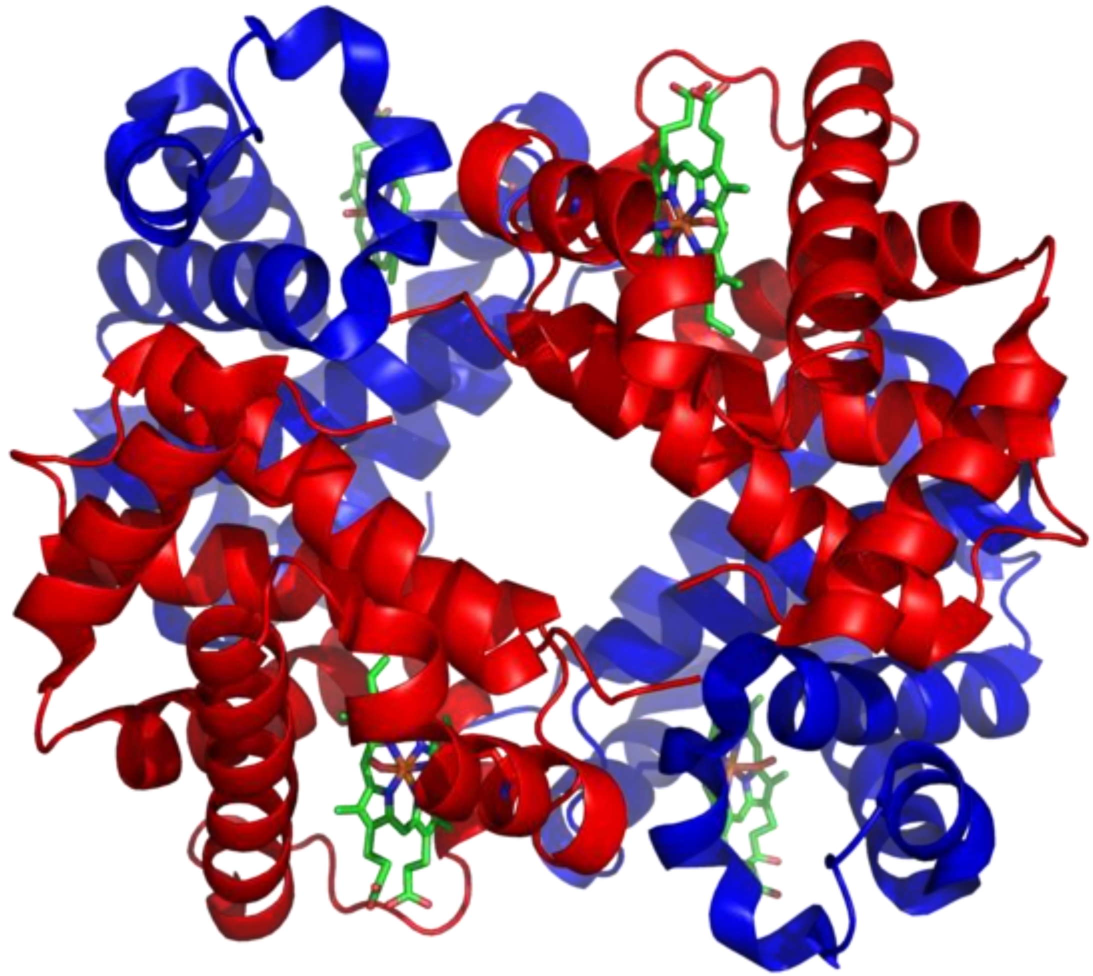


The Ribbon Structure of the Protein BPTI



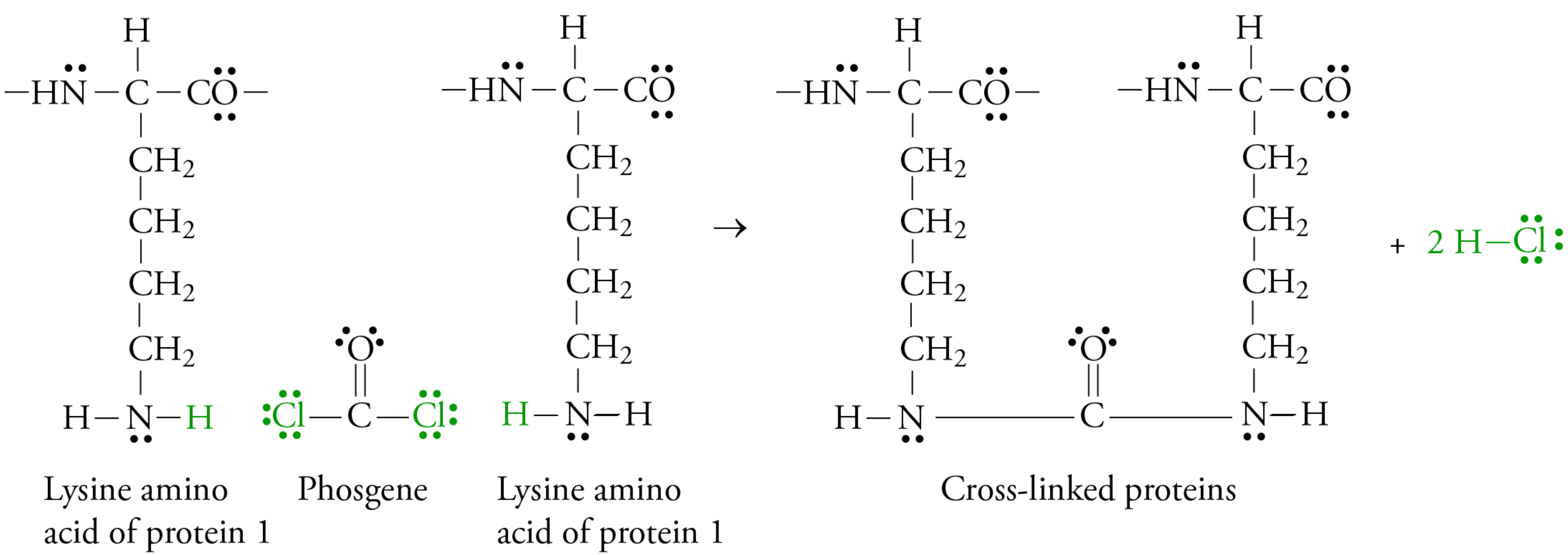
Hemoglobin

- The protein hemoglobin carries oxygen in the blood.



Phosgene Reactions with Protein

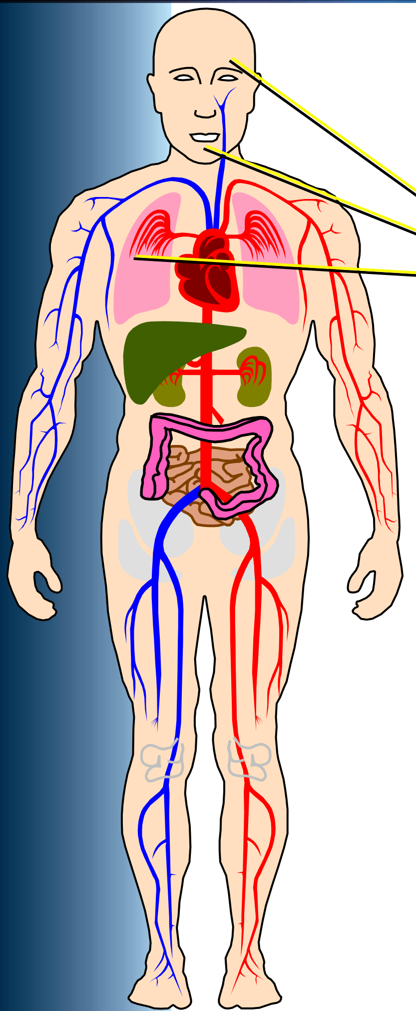
- Phosgene reacts with amino acids in proteins by acylation, adding an acyl group (a group with a CO double bond).
- It reacts with the amines of the proteins, linking protein together.
- The altered proteins no longer function in their normal way.



Dual Use

- A small-scale malicious chemical program can easily be hidden behind a normal industrial/research chemistry front.
  - Chlorine is used for water purification and to make many other compounds.
  - Phosgene is used to make important compounds, including pharmaceuticals and plastics.

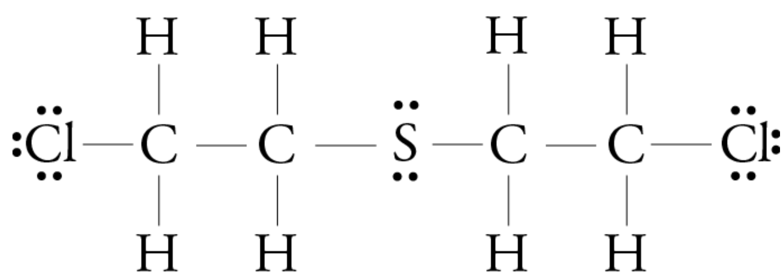
Blister Agents (Vesicants)

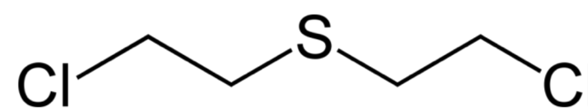


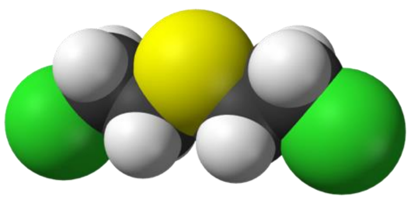
- **Sulfur mustard**, nitrogen mustard, phosgene oxime, Lewisite
- Mode of action: inhalation, skin contact
- Physiological effects
  - Damages skin, mucous membranes, and eyes, causing large water blisters on exposed skin
  - Causes damage to upper airways
  - Primarily causes medical casualties, but can be lethal when large amounts are inhaled
- Form when disseminated: liquid, **aerosol**, vapor, dust
- Required defensive gear: protective mask & clothing

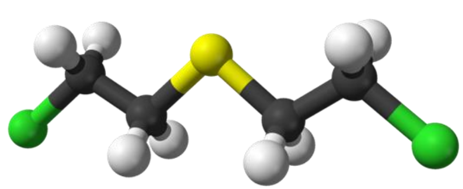
Sulfur Mustard, H or HD

- 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.

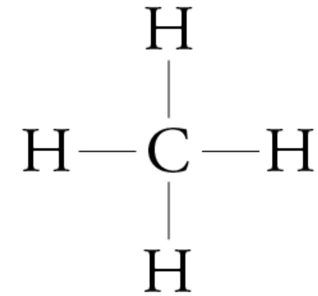


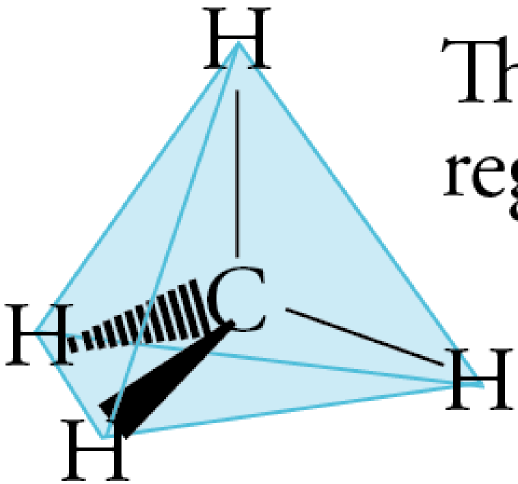




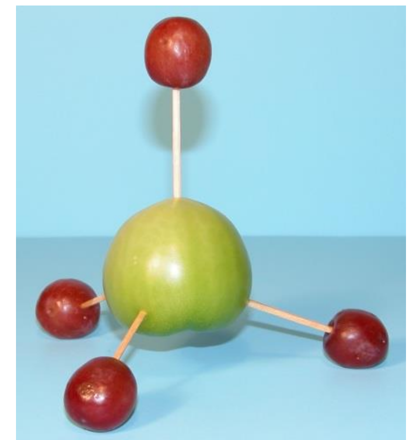


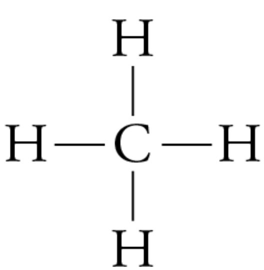
Methane, CH_4



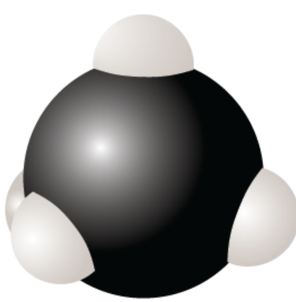


The shaded shape is a regular tetrahedron.

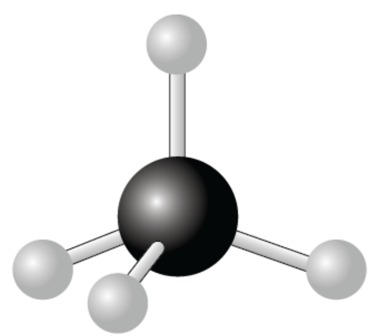




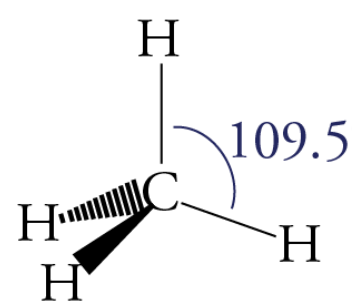
Lewis structure



Space-filling model



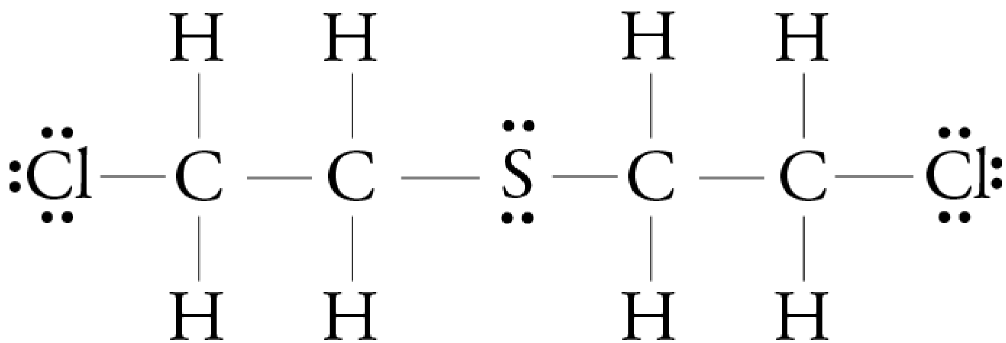
Ball-and-stick model



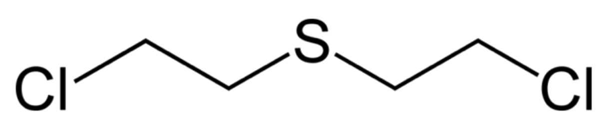
Geometric Sketch

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.

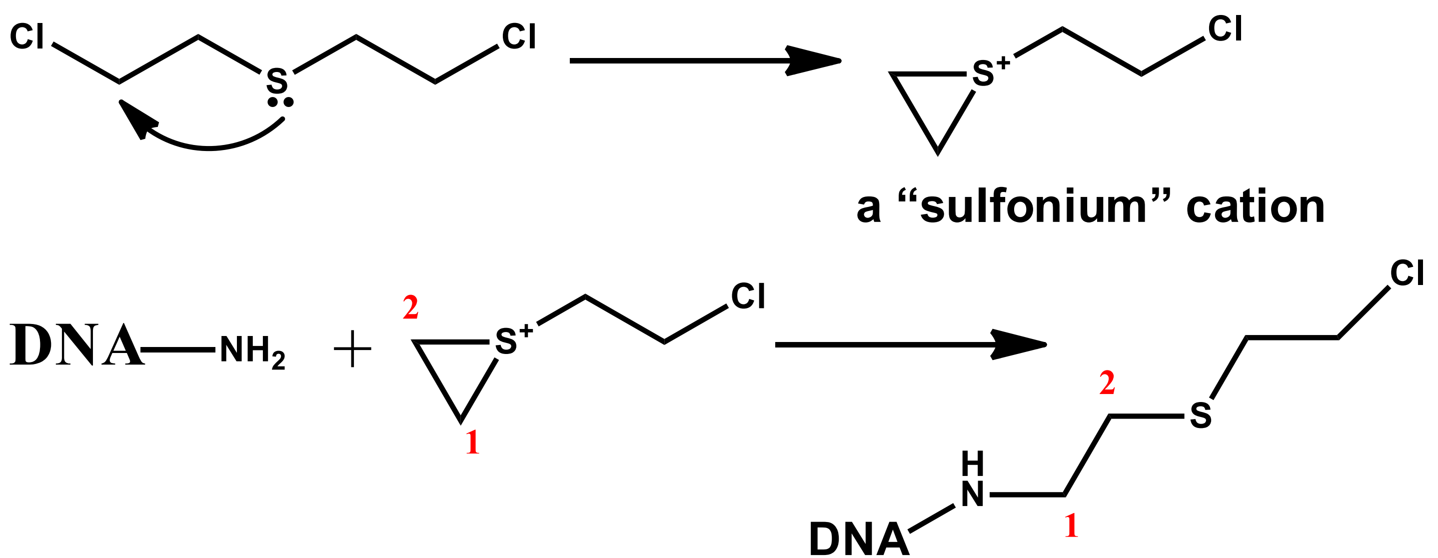
Sulfur Mustard (cont.)

- “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

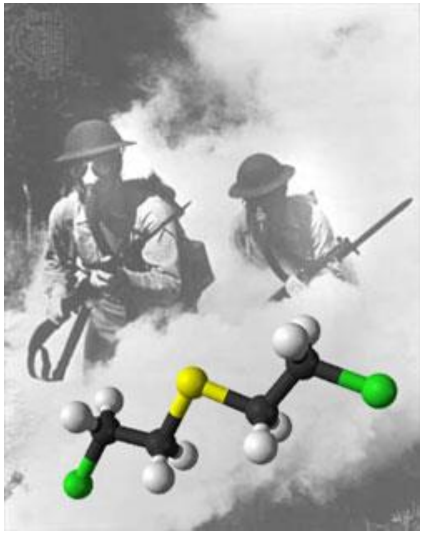
- After initial treatment, patients with blisters are treated in the same way that any burn victim would be treated.
- Because the symptoms do not appear for hours, it is less likely that the treatments would be done in time to avoid problems.
- Fatal in about 2% of exposures in WW1, so mostly used as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

Difference Between Theoretical and Actual Effects

- The ability of CW agents to kill or hurt people depends on a number of factors, such as:
  - Quality of agent
  - Means of delivery
  - Environmental factors
- *Illustration:* In theory, less than a teaspoon of mustard agent can kill if it is inhaled into the lungs. Yet in WW I, more than 60 pounds of mustard agent were used for each man killed or wounded by it. Only 2% of the people affected by mustard agent actually died.

Sulfur Mustard Military History

- Used first by Germans in WWI in 1917.
- Captured mustard agent shells used by Allies in 1917.
- Later dispersed as an aerosol, in aerial bombs, land mines, mortar rounds, artillery shells, and rockets.
- Adolf Hitler claimed he was exposed to mustard agent in 1918 and temporarily blinded. He may have been trying to cover up hysterical blindness.



Sulfur Mustard Military History

- 1919: United Kingdom against the Red Army
- 1921-27: Spain and France against insurgents in Morocco
- 1935-40: Italy against Abyssinia (now Ethiopia)
- 1937-45: Japanese against China
- 1963-67: Egypt against North Yemen
- 1983-88: Iraq against Iran and the Kurds
- 1995, 1997: Possibly Sudan against insurgents in their civil war

World War I
Casualties from CW

Total Amount of Chemical Agents Used – 112,000 Tons			
Nations	Non-fatal	Deaths	Total Casualties
Commonwealth Forces (Britain, Canada, Australia, New Zealand, India,...)	180,597	8,109	188,706
France	182,000	8,000	190,000
United States	71,345	1,462	72,807
Italy	55,373	4,627	60,000
Russia	419,340	56,000	475,340
Germany	191,000	9,000	200,000
Austria - Hungary	97,000	3,000	100,000
Others	9,000	1,000	10,000
Total	1,205,655	91,198	1,296,853

CW Use in Interwar Period

- Italian Use of CW in Ethiopia 1935-1936
  - sprayed mustard from planes and dropped aerial bombs with sulfur mustard
  - Italy argued that the protocol did not prohibit the use of chemical weapons in retaliation for war crimes.
  - estimated 15,000 casualties

CW Use in Interwar Period

- Japanese against Chinese 1937-1945
  - Over 1,000 assaults with blister and incapacitating agents
  - Estimated 10,000 fatalities (99% military)
  - Estimated 84,000 casualties (80% military)
- Japan began shipping CW to Manchuria in 1935.
- In 1940, shipped 100,000 munitions to fight Soviets.
- In 1945, retreating Japanese units dumped or buried CW stocks.
  - Under the CWC, Japan is obligated to clean up the abandoned CW that they left behind in China.
  - That operation is still on-going today.

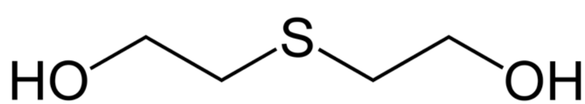
Factors Affecting the Ability to Make CW

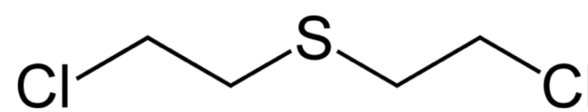
- Scientific and industrial expertise
- Availability of precursors
- Availability of equipment
- Money available
- Desired quantity
- Desired purity
    - For a variety of reasons, products of chemical reactions are rarely pure, so after the initial reactions, steps are taken to purify the product.
-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

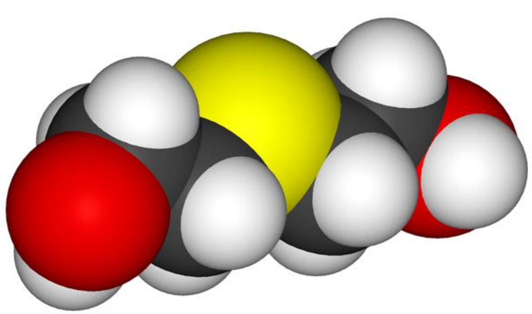
Production of Sulfur Mustard

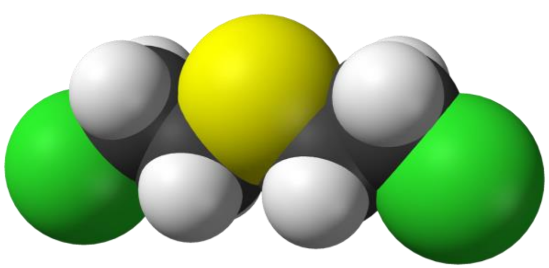
- There are many ways to make sulfur mustard.
- The simplest way is combining thiodiglycol and concentrated hydrochloric acid.

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









Chemical Weapons Convention (CWC)

- **A disarmament agreement that bans the production, stockpiling, transferring, and use of chemical weapons.**
- 193 States committed to the Chemical Weapons Convention, 98% of the global population live under the protection of the Convention, and 100% of the chemical weapons stockpiles declared by possessor States have been verifiably destroyed.

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
Schedule 1

https://www.opcw.org/chemical-weapons-convention/annexes/annex-chemicals/annex-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.

https://www.opcw.org/chemical-weapons-convention/annexes/annex-chemicals/schedule-1

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 for potential chemical weapons and thiodiglycol for a precursor.

https://www.opcw.org/chemical-weapons-convention/annexes/annex-chemicals/schedule-2

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.

https://www.opcw.org/chemical-weapons-convention/annexes/annex-chemicals/schedule-3

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)

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.

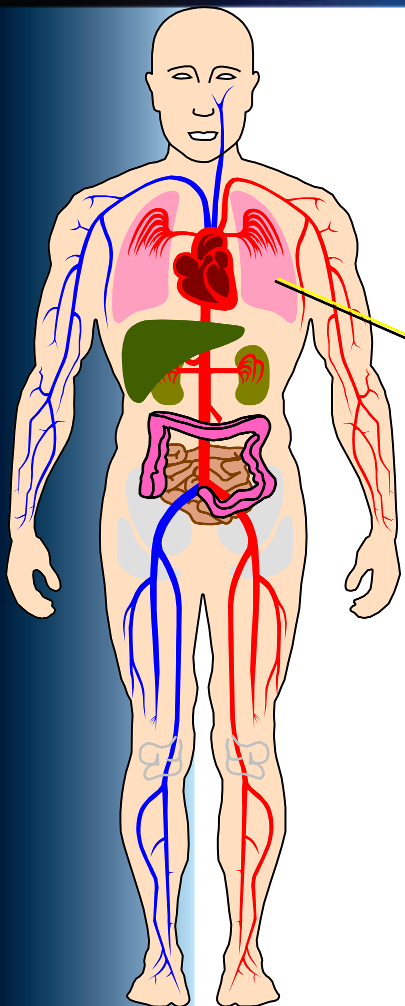
Destruction of U.S. Chemical Weapons

- Pueblo, Colorado
  - All of the 2613.2 tons of mustard agent in approximately 780,000 munitions was destroyed by neutralization (hydrolysis).
  - Started March 2015, finished 6/22/23

https://www.cma.army.mil/pcd/

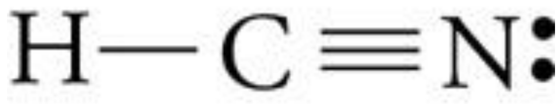
https://www.peoacwa.army.mil/pcapp/

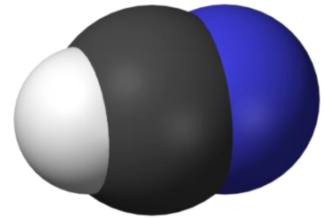
Blood Agents



- **Hydrogen cyanide**, cyanogen chloride, **sodium or potassium cyanide**, and arsine
- Mode of action: inhalation, skin and eye contact, or ingestion
- Physiological effects of cyanide
  - Disrupts cellular respiration by deactivating a key enzyme in the process.
- Form when disseminated: gas, aerosol, or solution
- Required defensive gear: full mask and suit

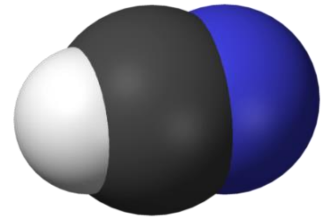
Hydrogen Cyanide, HCN





- 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.

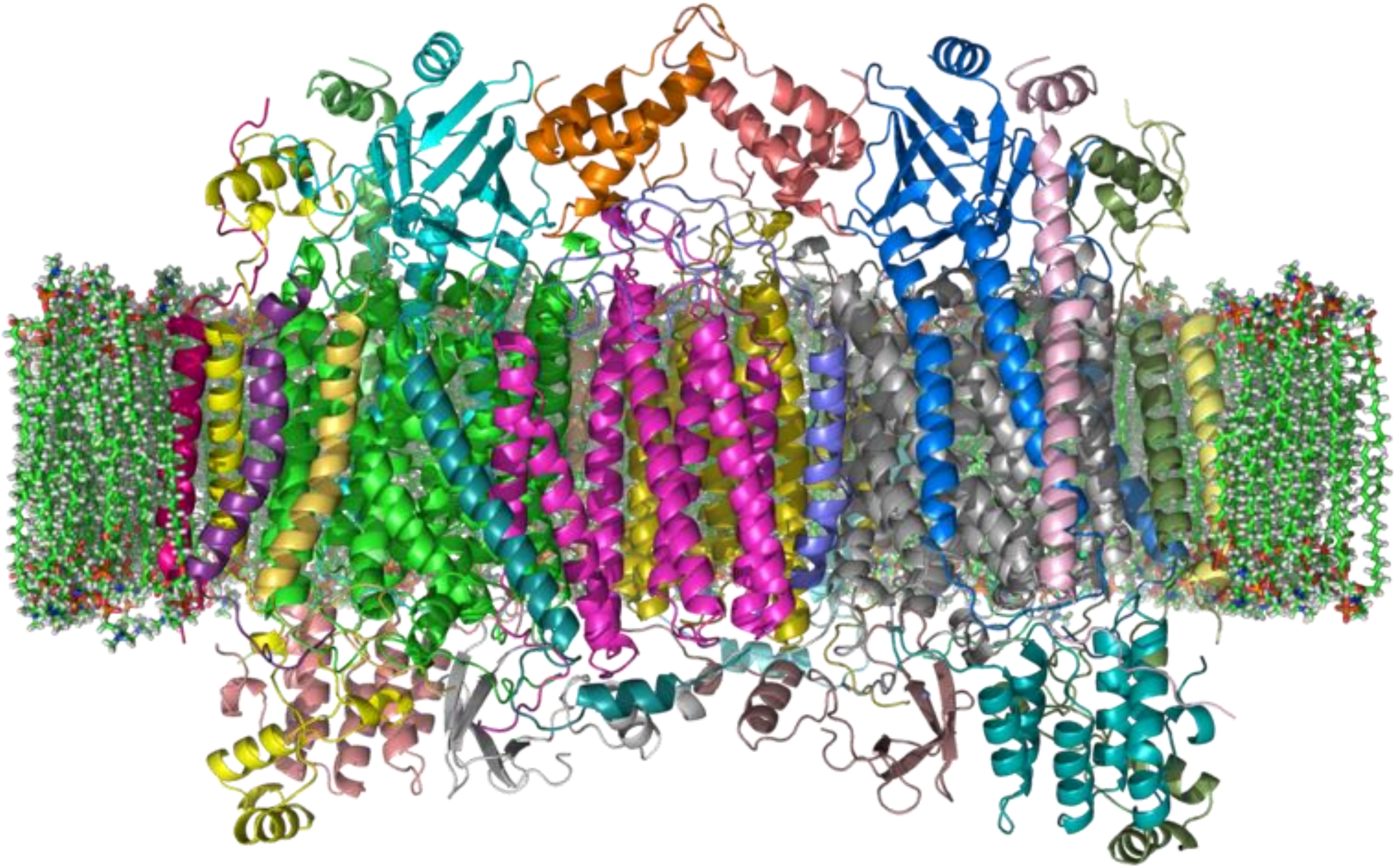
Cellular Respiration

- 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



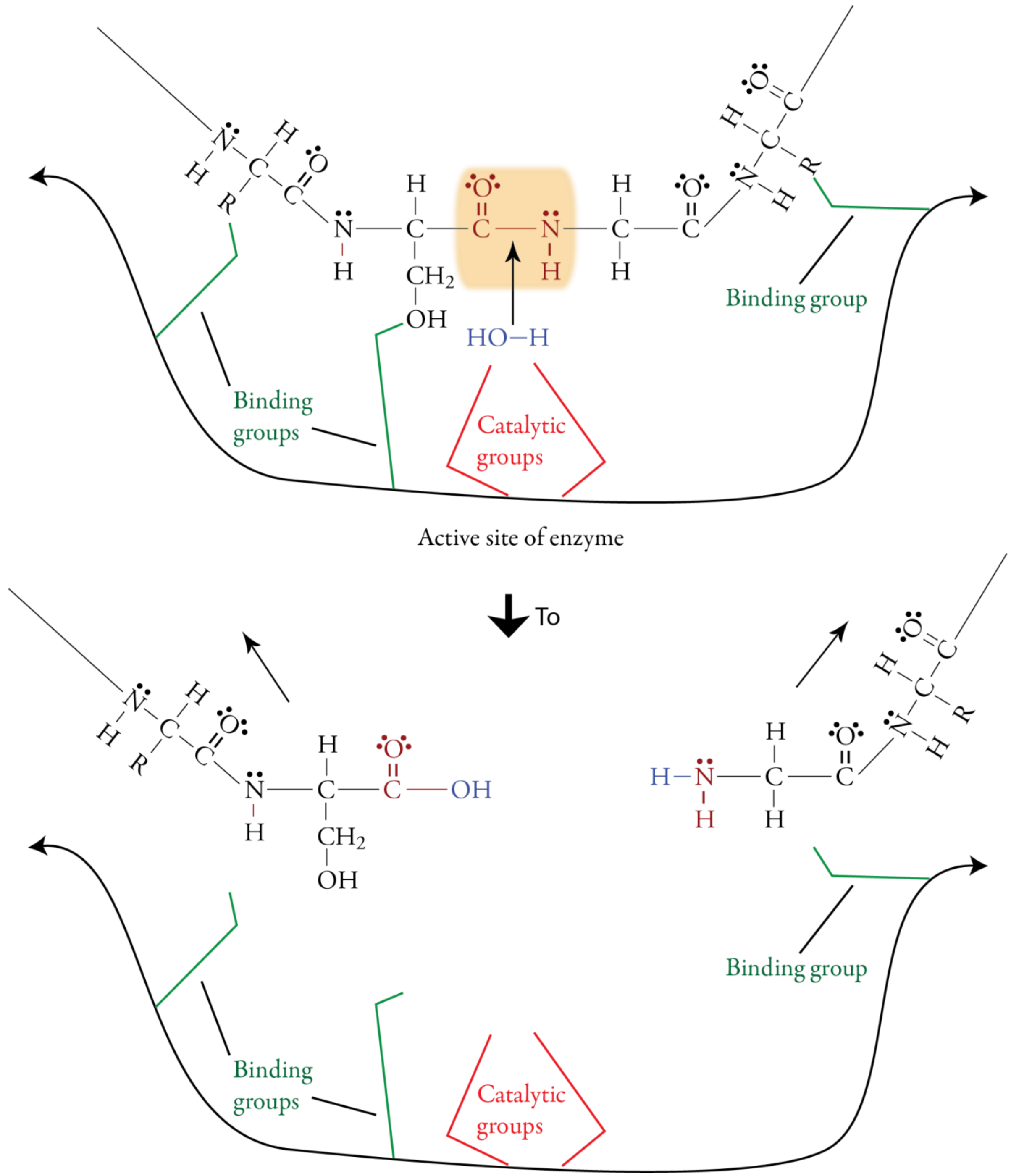
Cellular Respiration

- 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.

Enzymes

- ***Catalysts*** speed chemical changes without being permanently altered themselves.
- ***Enzymes*** are naturally occurring catalysts, primarily composed of protein.
- The chemicals that they act on are called ***substrates***.

Enzyme Active Site



Enzymes

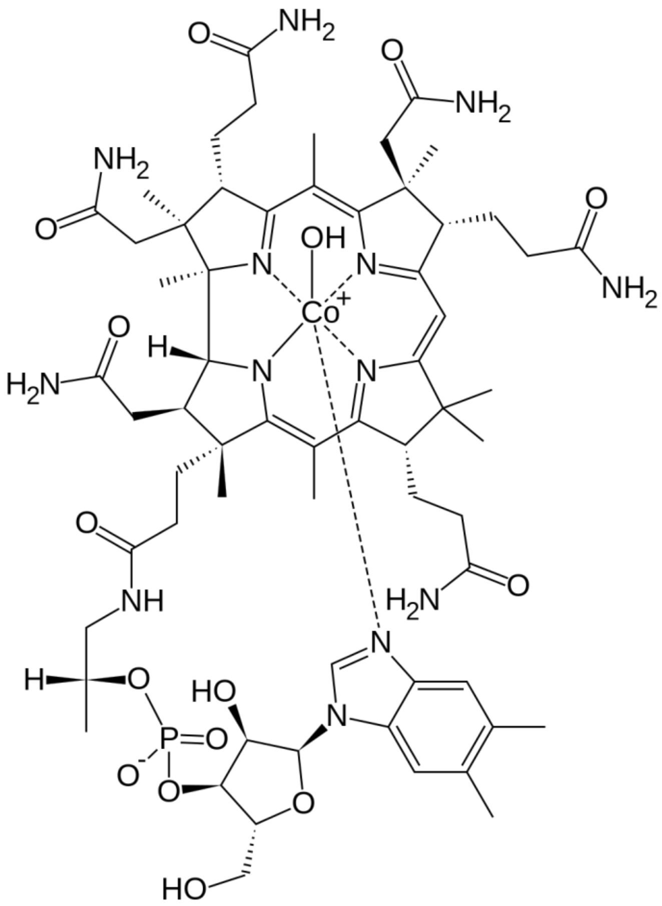
- Very specific due to
  - Substrate shape – “Lock and Key”
  - Positions of binding groups, which attract substrates to the active site.
  - Positions of the catalytic groups that speed the reaction.
- Speed chemical reactions because
  - Provide a different path to products that has more stable intermediates and therefore requires less energy.
  - Give the correct orientation every time.

One HCN Antidote

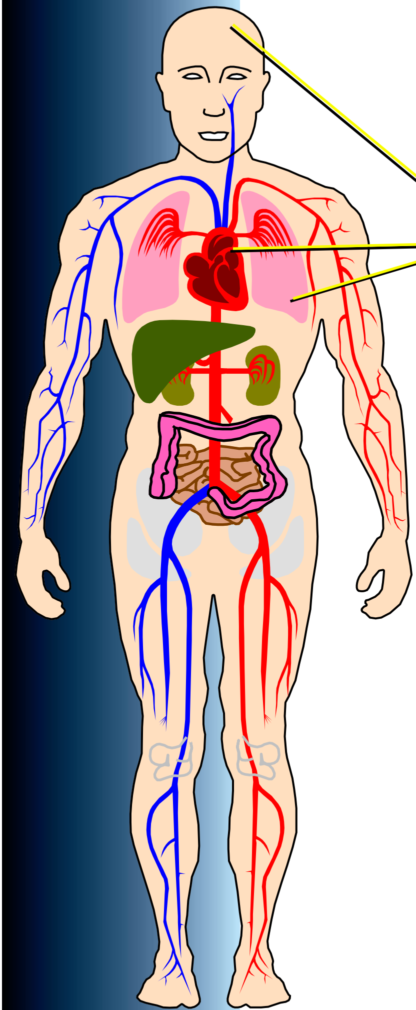
- Best administered by health professional
- First - a small inhaled dose of amyl nitrite
  - Nitrites oxidize some of hemoglobin's iron from the Fe^{2+} state to the Fe^{3+} state, converting the hemoglobin into methemoglobin.
  - Cyanide preferentially bonds to methemoglobin rather than the cytochrome 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.

Destruction of U.S. Chemical Weapons

- Blue Grass Army Depot - Richmond, Kentucky
  - As of 7/7/23, all of the 523.4 tons of nerve agents (sarin and VX) and mustard agent in projectiles, warheads, and rockets were destroyed by hydrolysis followed by supercritical water oxidation.

https://www.cma.army.mil/bluegrass/

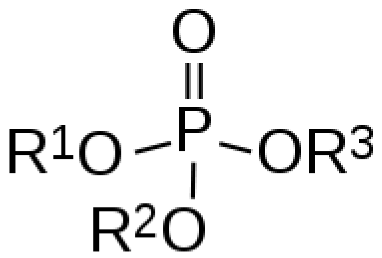
https://www.peoacwa.army.mil/bgcapp/

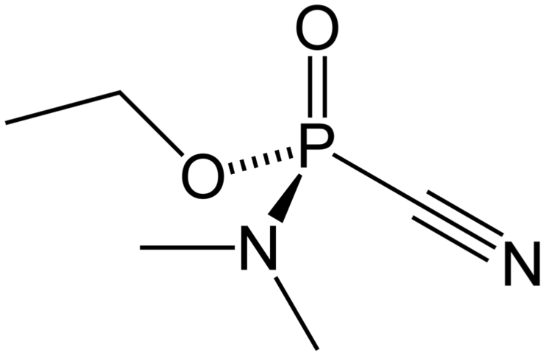
Nerve Agents – Three Series

- G-series
  - Produced by Germans
  - 1936 – GA (tabun)
  - 1939 – GB (sarin)
  - 1944 – GD (soman)
  - 1949 – GF (cyclosarin)
  - GA and GB less persistent after dispersal
- V-series
  - More persistent after dispersal
  - VX most important…first produced by the British in the 1950s
- Novichoks

Nerve Agents

- Discovered accidentally by German chemists developing pesticides.
  - Germany had the world's most advanced chemical industry.
  - Searching for new organophosphate pesticides
- Made many variations of the structure and tested them for potency.
- One compound found to be very dangerous and therefore considered "taboo" (tabu in German)…called Tabun.



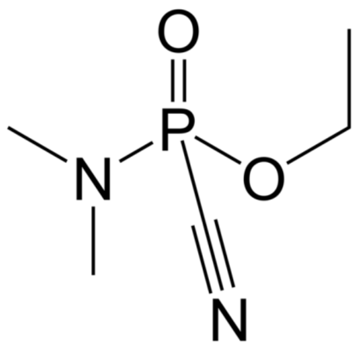


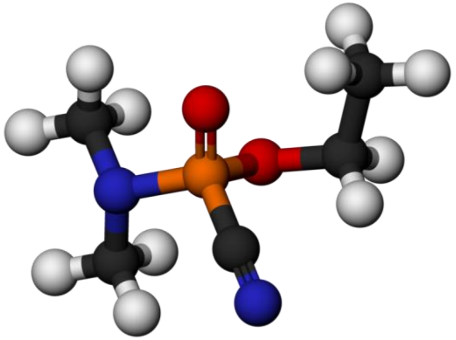
One Way to Do Science

- Trial-and-error based on previous experience.
- Steps taken by the German Gerhard Schrader working for the IG Farben chemical company and trying to make new pesticides.
  - Some fluorine compounds are known to be toxic, so synthesized many different organic compounds with fluorine and tested them for toxicity to insects and safety for humans.
  - After no luck, tried adding first sulfur, then phosphorus, making a series of “organophosphate” compounds with promising characteristics.
  - To make the organophosphates more toxic, he added the cyanide group, which was known to be toxic, leading to tabun.
  - Noticed the adverse effects on himself after making it in the laboratory.

Tabun (GA)

- First synthesized in 1936
- Faint fruity odor…harder to detect than chlorine, phosgene, mustard agent, and hydrogen cyanide, which have more distinctive odors…troops less likely to put on gas masks
- Not very volatile, which created problems with distribution
- Not as stable as later nerve agents
- Easier to produce than the other G-series agents (more later)

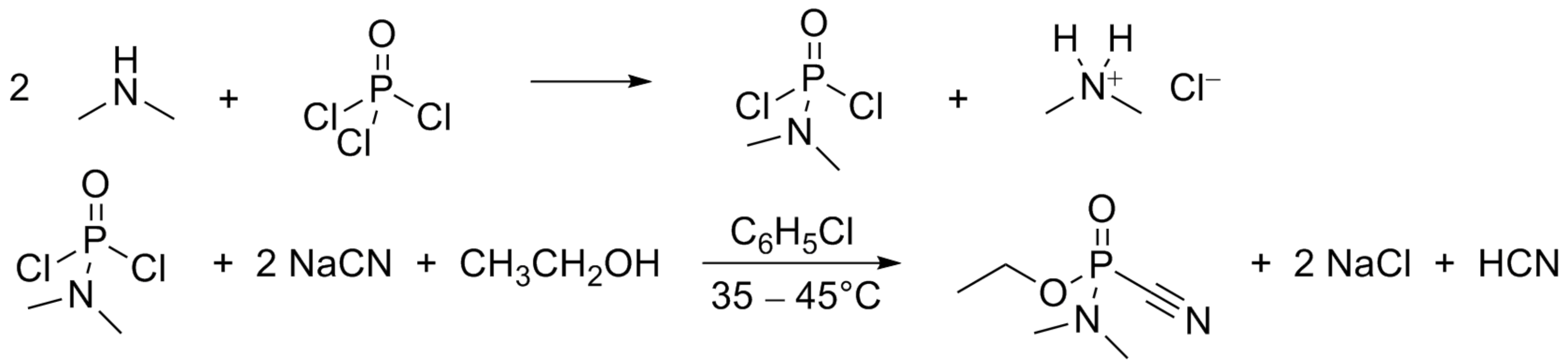




http://chemapps.stolaf.edu/jmol/jmol.php?model=N%23CP%28%3DO%29%28OCC%29N%28C%29C

Production of Tabun

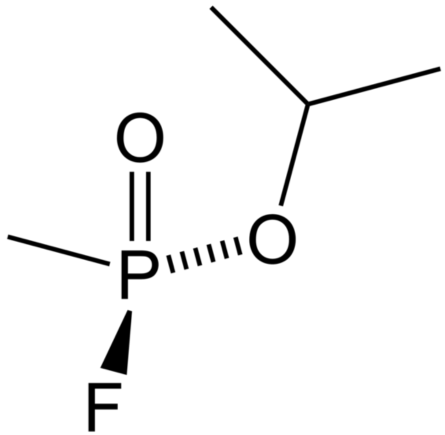
- Made from widely available phosphorus oxychloride ($POCl_3$), which is on Schedule 3, Part B of the CWC, sodium cyanide (NaCN), dimethyl amine ($NH(CH_3)_2$), and ethanol (C_2H_5OH). All are used to make other substances, including pharmaceuticals, pesticides, missile fuels, and gasoline additives.
- Must handle highly toxic HCN gas.
- Does not require use of corrosive materials and does not produce highly reactive intermediates.

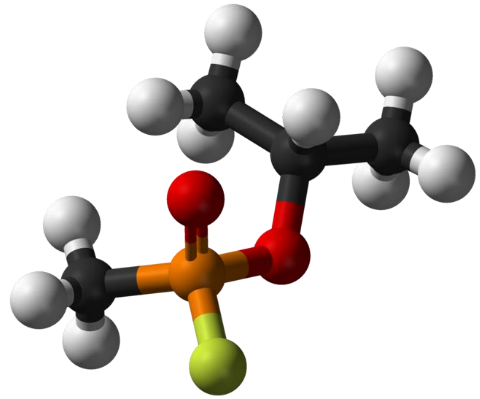


Sarin (GB)

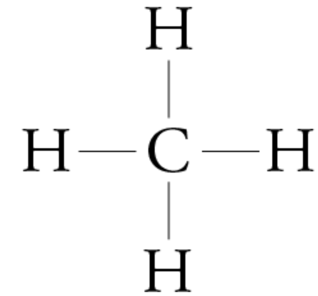
- Developed by the Germans in 1939
- Adopted as the standard nerve agent for the U.S. in 1948.
- Odorless and colorless liquid
- Relatively stable when stockpiled
- Relatively volatile
- Can cause death in minutes
- Breaks down fairly rapidly in the environment
- Has antidotes
- Hard to make

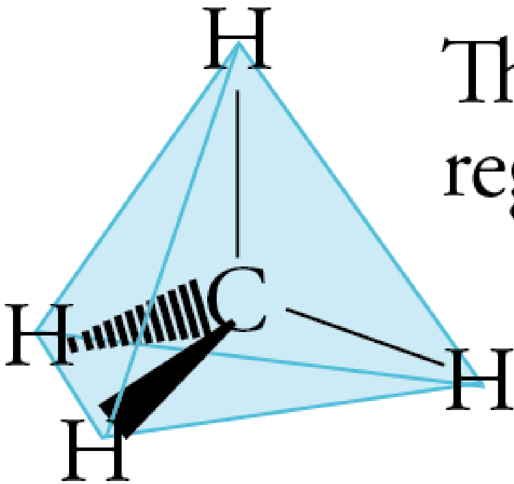
http://chemapps.stolaf.edu/jmol/jmol.php?model=FP%28%3DO%29%28OC%28C%29C%29C



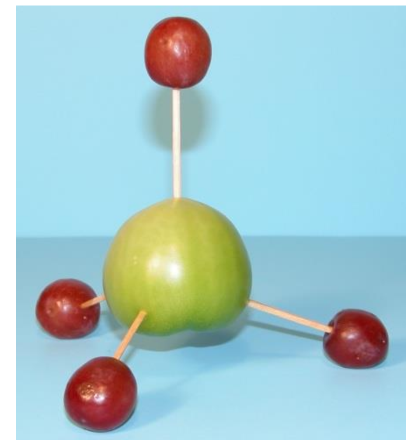


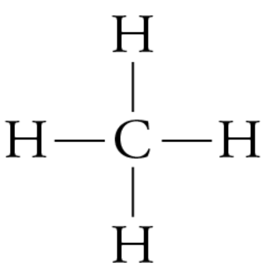
Methane, CH_4



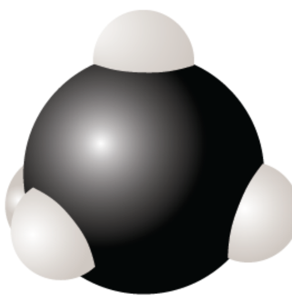


The shaded shape is a regular tetrahedron.

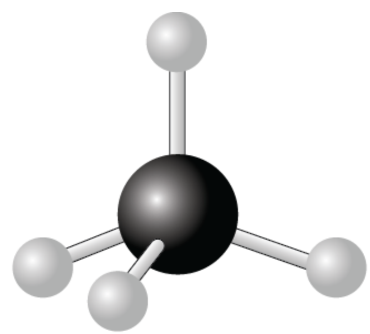




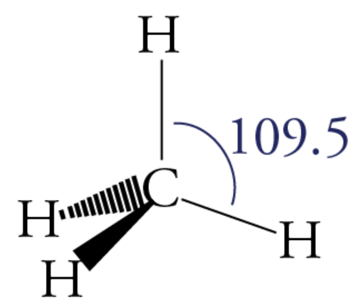
Lewis structure



Space-filling model



Ball-and-stick model



Geometric Sketch

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

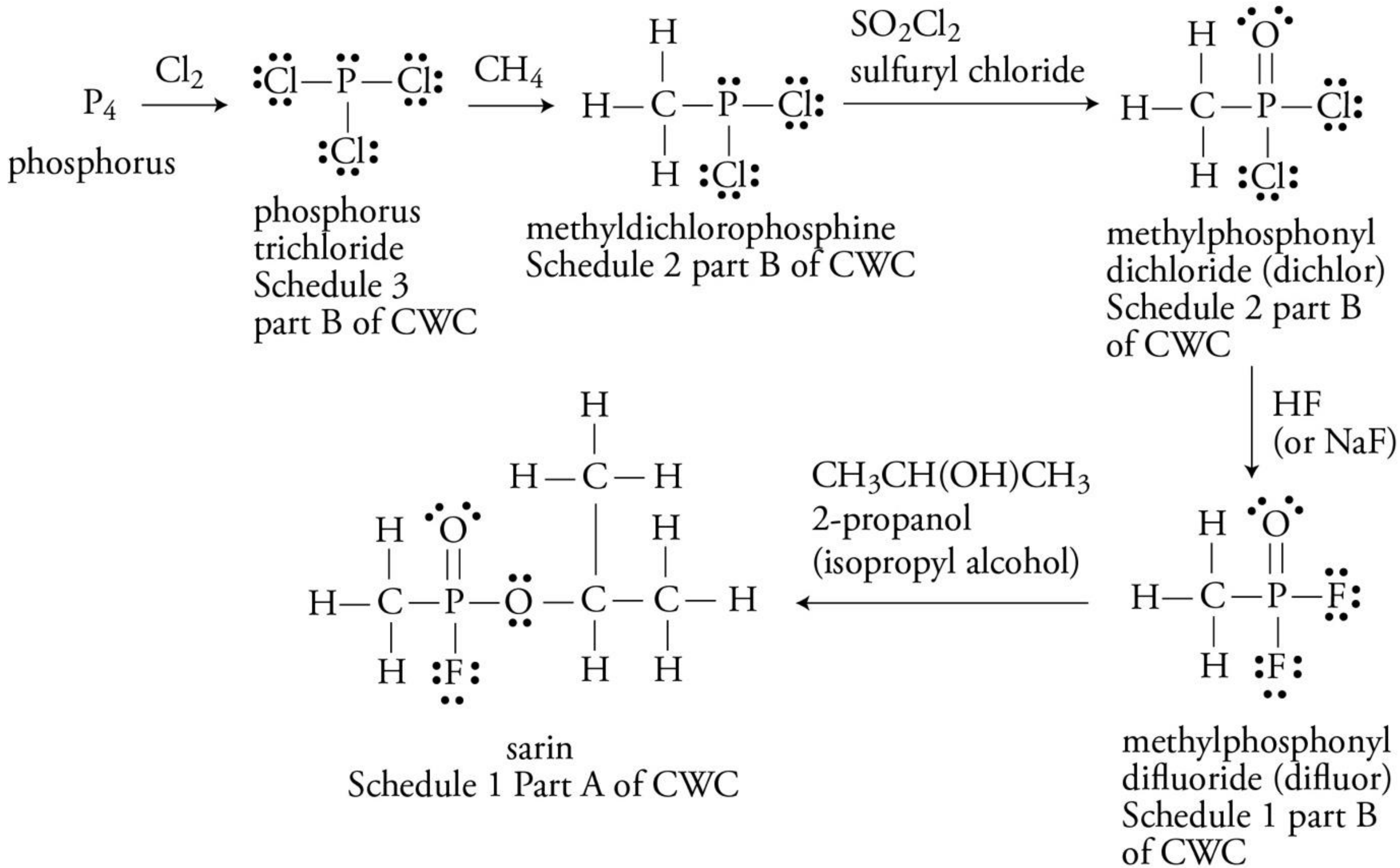
Factors Affecting the Ability to Make Chemical Weapons

- 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



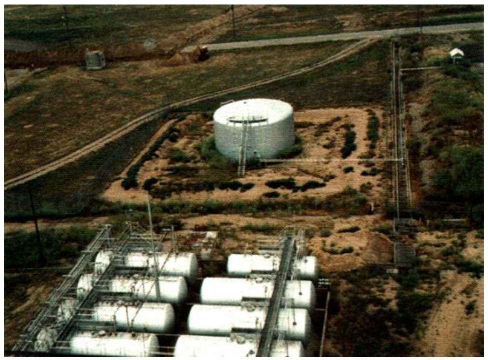
Production of Sarin

- Most easily prepared from methylphosphonyl difluoride and isopropyl alcohol.

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

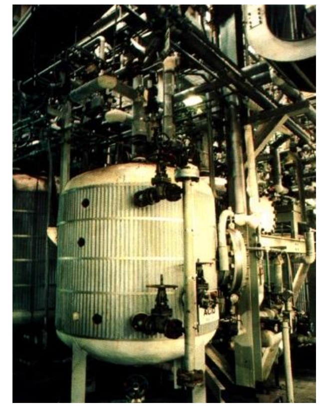
- Three technical hurdles when making from simpler substances.
  - Involves corrosive hot hydrochloric acid, HCl, and hydrogen fluoride, HF, so need corrosion resistant equipment, e.g. vessels and pipes of an alloy that is 40% nickel…Monel and Hastalloy.
  - Alkylation reaction in which a methyl, $-CH_3$,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

Production Process (Simplified)



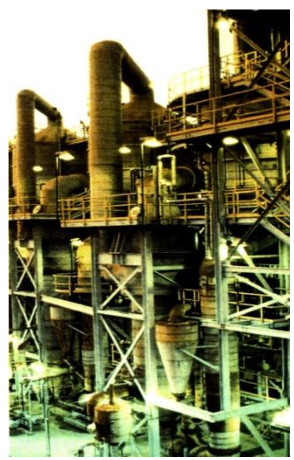
Precursors stockpiled

Piped to chemical processing area



Combined in reactor under controlled conditions, often with catalysts

Precursors react to form new compounds

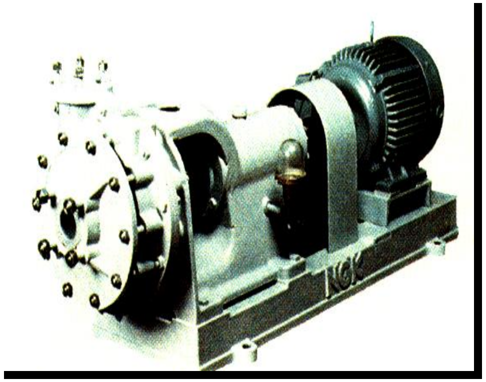


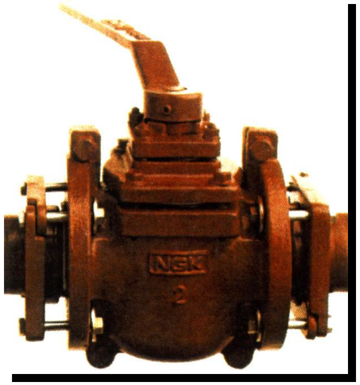
Distillation & filtration separates & purifies agents and byproducts

Agents are stored until filled into munitions

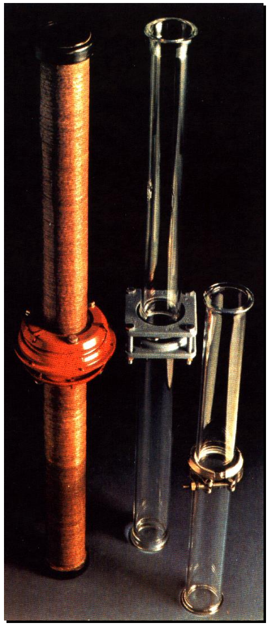
Equipment

- Standard chemical process equipment could be suitable for a clandestine CW program, but specialized equipment is preferable.
  - corrosion resistance (high nickel content)
  - equipment designed for handling extremely toxic substances (e.g. double seal pumps)
- Safety equipment (incinerators, toxic gas monitors, etc.) also has dual-uses.





Hastelloy pumps & valves



Glass lined pipes

Large-Scale Chemical Reactors

CW Agents Production Equipment

Jacketed Pipe Heat Exchanger- *keeps reactions at proper temps*

Glass Lined Pipe & Fittings- *Good for corrosive chemicals*

Glass Lined Steel Cyclones – *used to separate large batches of chemicals*

It's not that easy. Example: Aum Shinrikyo

- $2 BILLION assets; 40,000 members, government deference
- $10 million plant; 100 scientists/engineers
- Goals: sarin - 2 tons/day; 70 ton arsenal; small targets
- Achieved: ~2 kg sarin/attack
  - Auditorium (Feb 1994)
  - Dormitory (June 1994)
  - Subway (March 1995)
- Casualties: 17 total killed

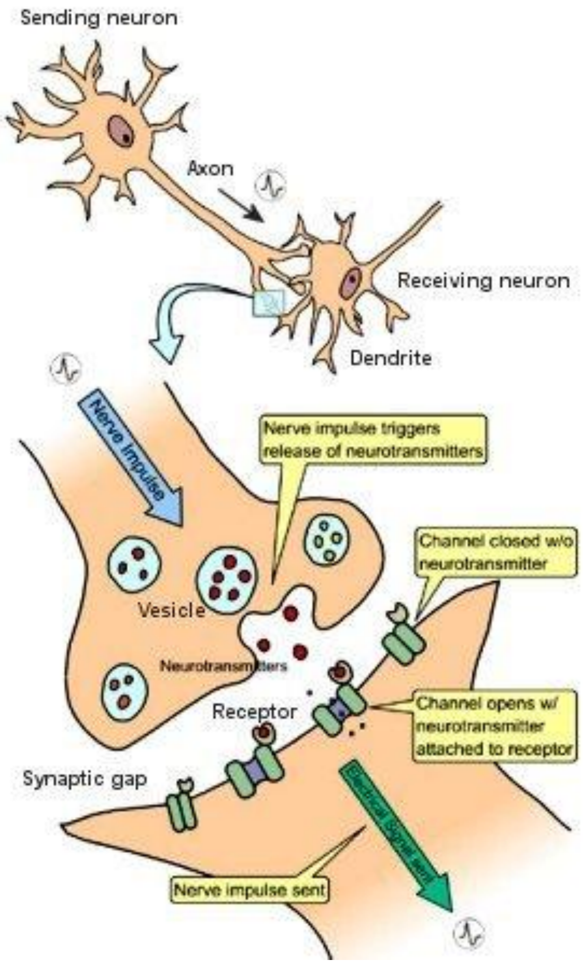
Other Necessary Components

- Containment and waste treatment.
- Additives to stabilize and augment the effects of CW agent
- Design and produce munitions
  - Designed to convert liquid or powdered agent into an aerosol (tiny droplets that stay suspended in air for several hours)
- Filling of munitions…very dangerous, so requires sealed building and controlled atmosphere
- Storage and transportation

Neurotransmitters

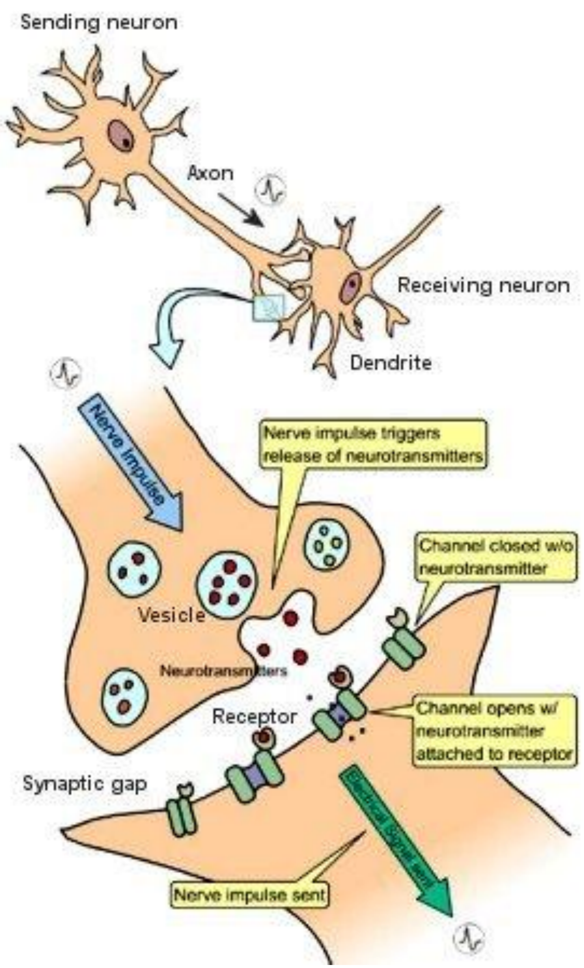
- Neurotransmitters cause nerve cells to fire.

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



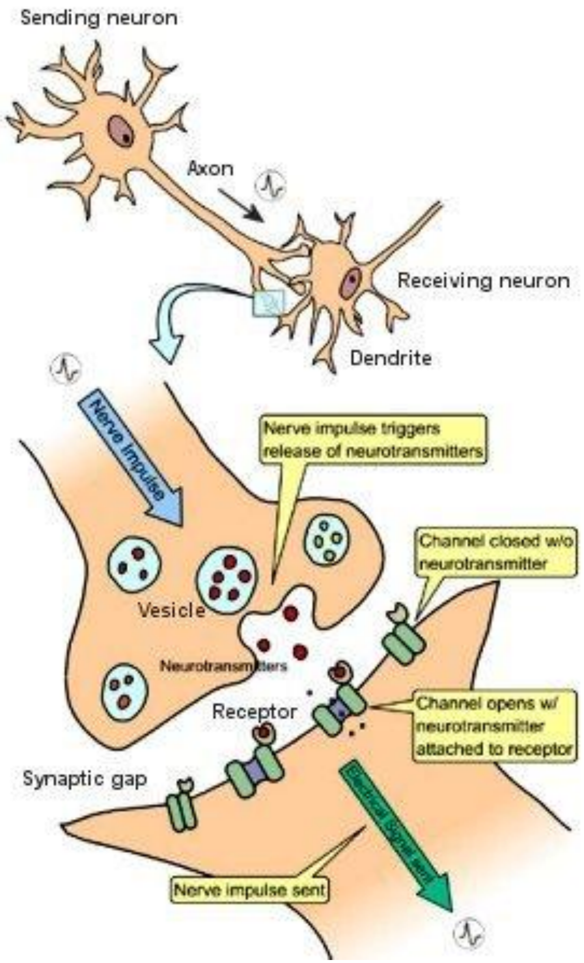
Neuron Transfer

- 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.



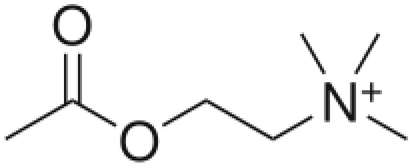
Neuron Transfer

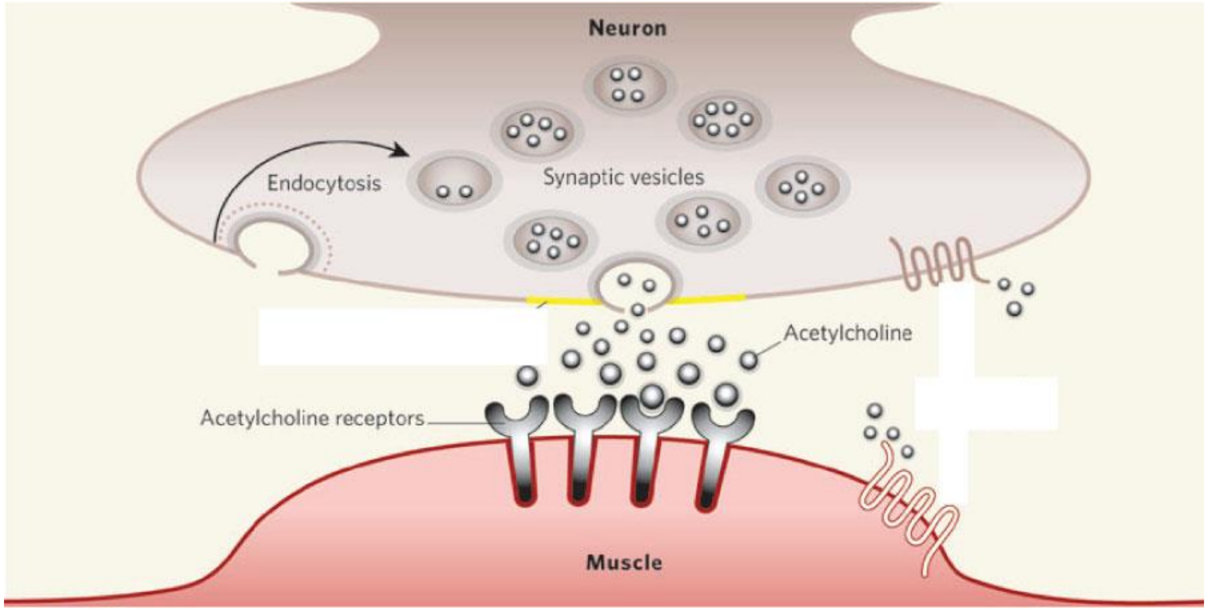
- Acetylcholine triggers flow of positive charge into neuron 2 through Na^+/K^+ gates.
- This causes an excess of plus charge inside neuron 2 and an excess of negative charge outside the neuron.
- When the charge imbalance gets large enough, it causes the firing of an electrical impulse through neuron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

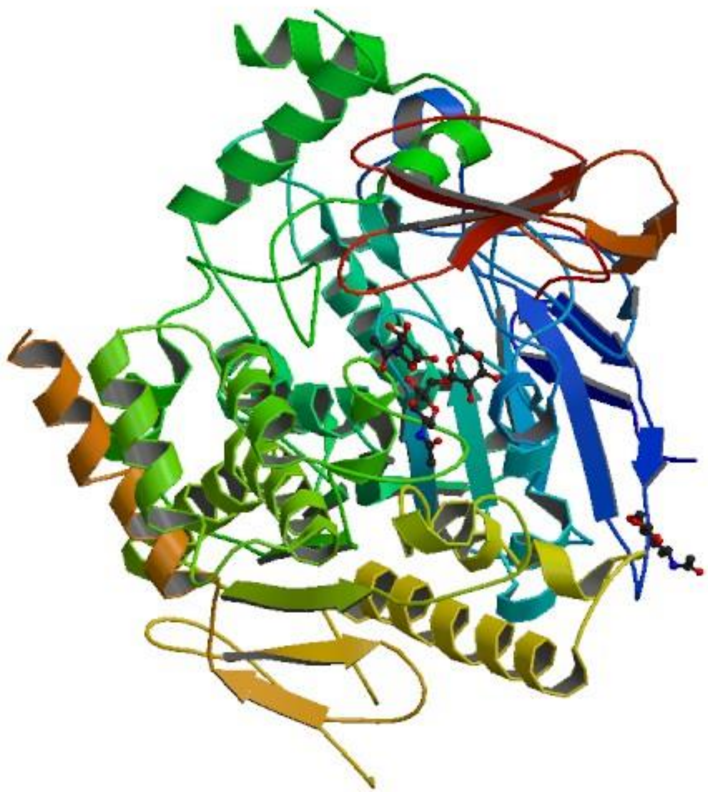




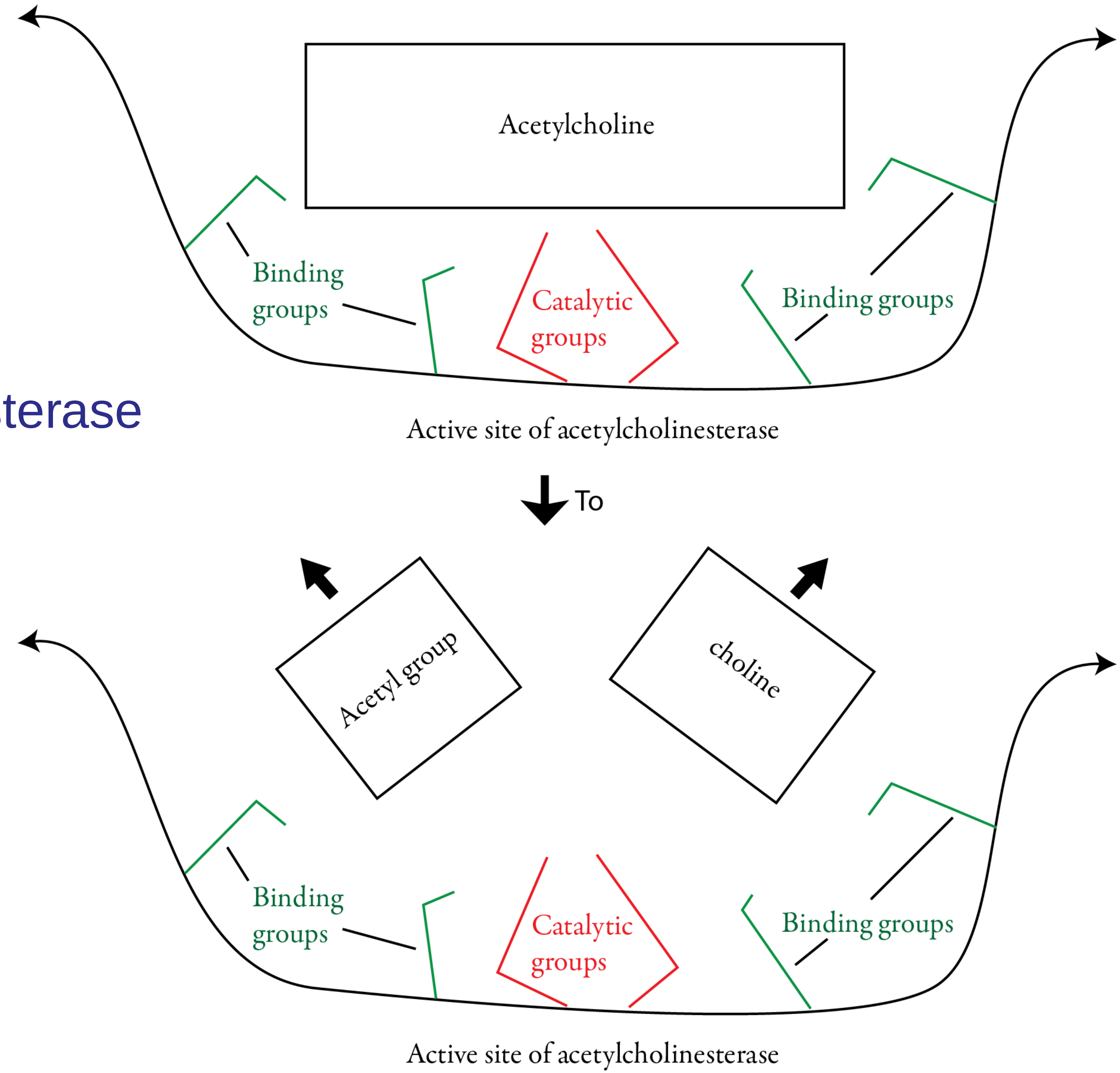
From Nature 436, 473-474 (28 July 2005)

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



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.

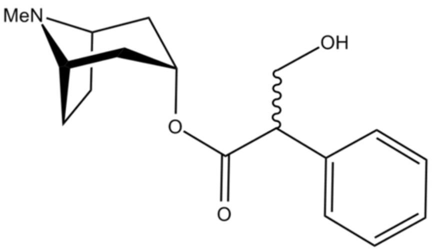
Treatment for Nerve Agent Exposure

- 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 and pralidoxime (2-PAM) 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 and CANA (Convulsive Antidote, Nerve Agent).

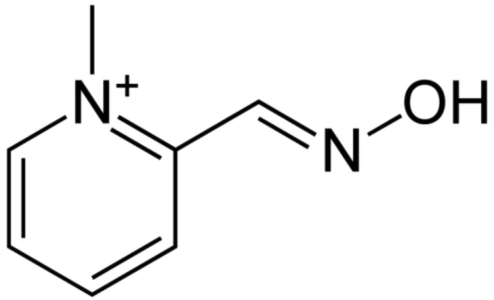
Nerve Agent Antidotes - Atropine

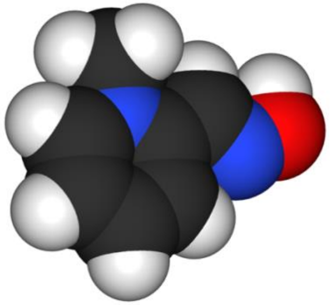


- Standard antidote for organophosphate poisoning
- Competes successfully with one type of acetylcholine receptors. This type of receptor is found in smooth muscles and glands.
- Helps relax muscles
- Stops the most serious symptoms from nerve agent poisoning, *not* the cause
- Must be administered every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

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

Nerve Agent Antidotes (2-PAM)



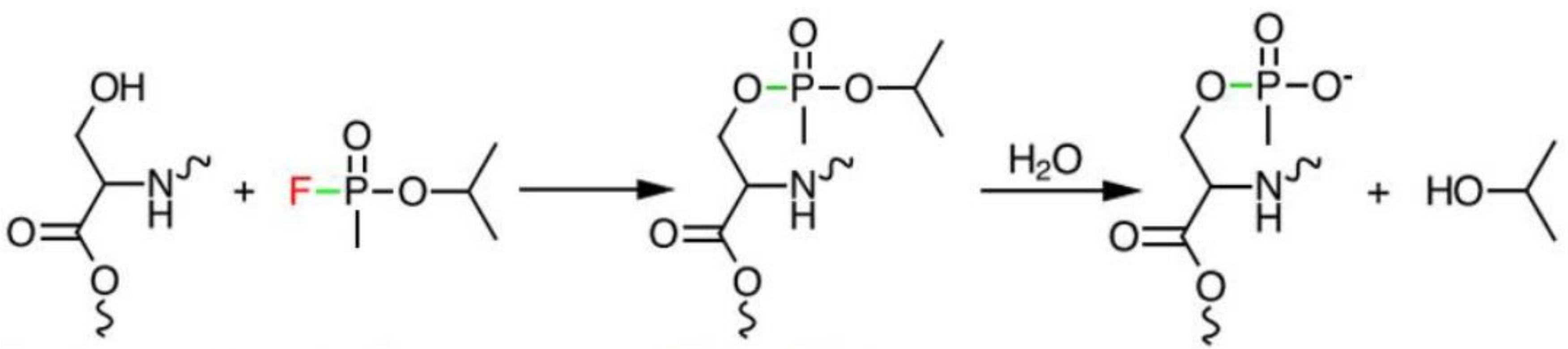


- Pralidoxime (2-pyridine aldoxime methyl chloride,) or 2-PAM
- Removes the nerve agent from the active site of acetylcholinesterase, restoring the enzyme to more normal levels
- Too slow to work well alone
- Works best when administered with atropine, which acts more quickly, giving the slower-acting 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

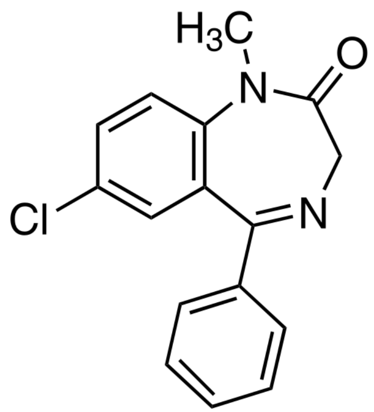
Inhibited and Aged Acetylcholinesterase

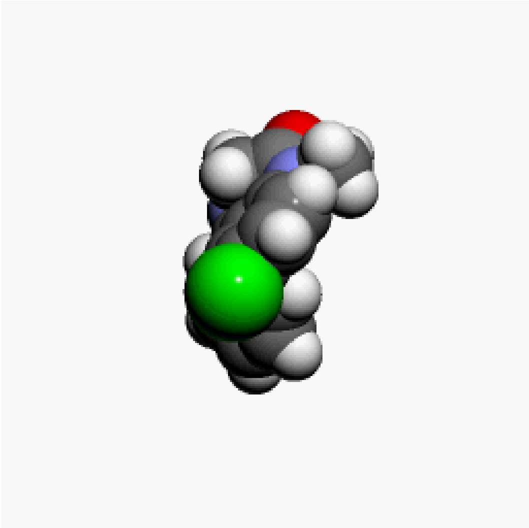
- The 2-PAM must be administered as quickly as possible because the loss of the isopropyl group from the sarin yields the *aged* form of the enzyme, and the sarin cannot be removed in this form.



Serine in protein Sarin inhibited Serine aged form Isopropanol

Diazepam (Valium)

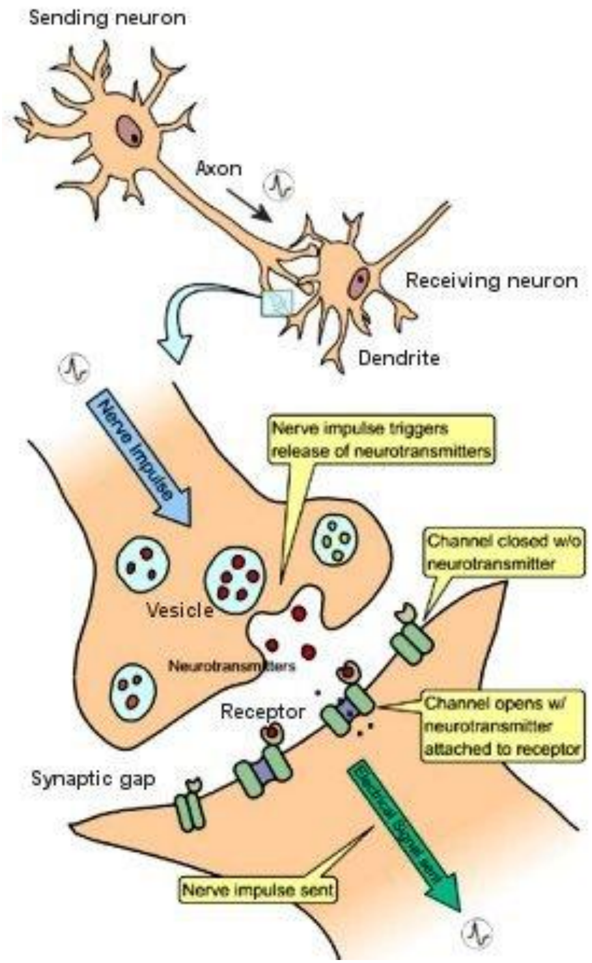




- Because 2-PAM is positive, very little of it gets through the blood-brain barrier.
- Valium (diazepam), which is an anticonvulsant, can be used to lessen the effects on the central nervous system (the brain and spinal cord).

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.

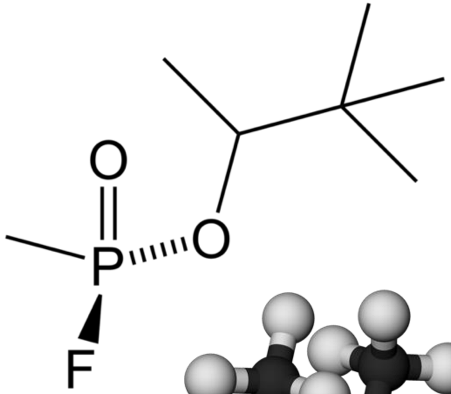


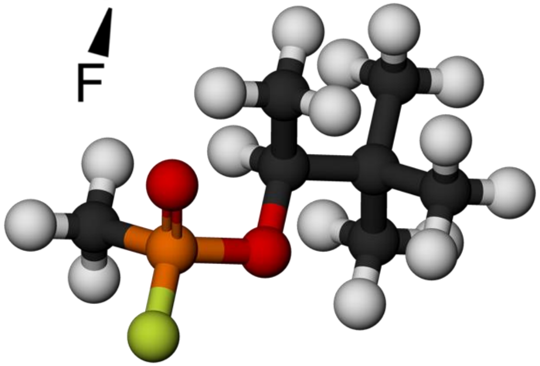
Possible New Antidotes

- 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.

Soman (GD)

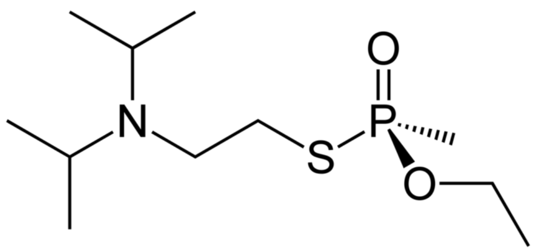
- Developed by the Germans in 1944
- Replaced isopropyl alcohol with the more difficult to make and more expensive pinacolyl alcohol
- Twice as potent as sarin
- Easily penetrates skin
- Slower to evaporate than sarin
- Lack of reliable antidote, making it more difficult treat accidental exposure

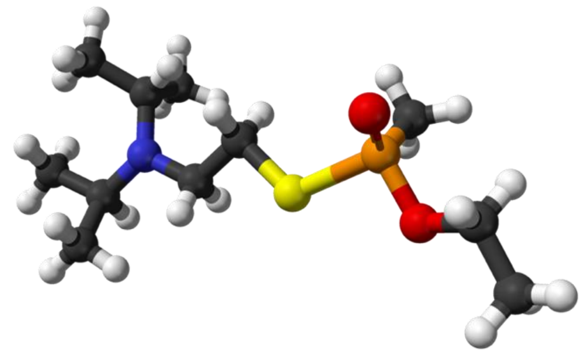


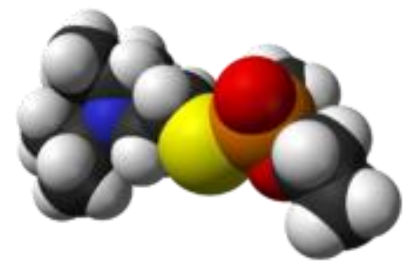


http://chemapps.stolaf.edu/jmol/jmol.php?model=FP%28%3DO%29%28OC%28C%29C%28C%29%28C%29C%29C

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.

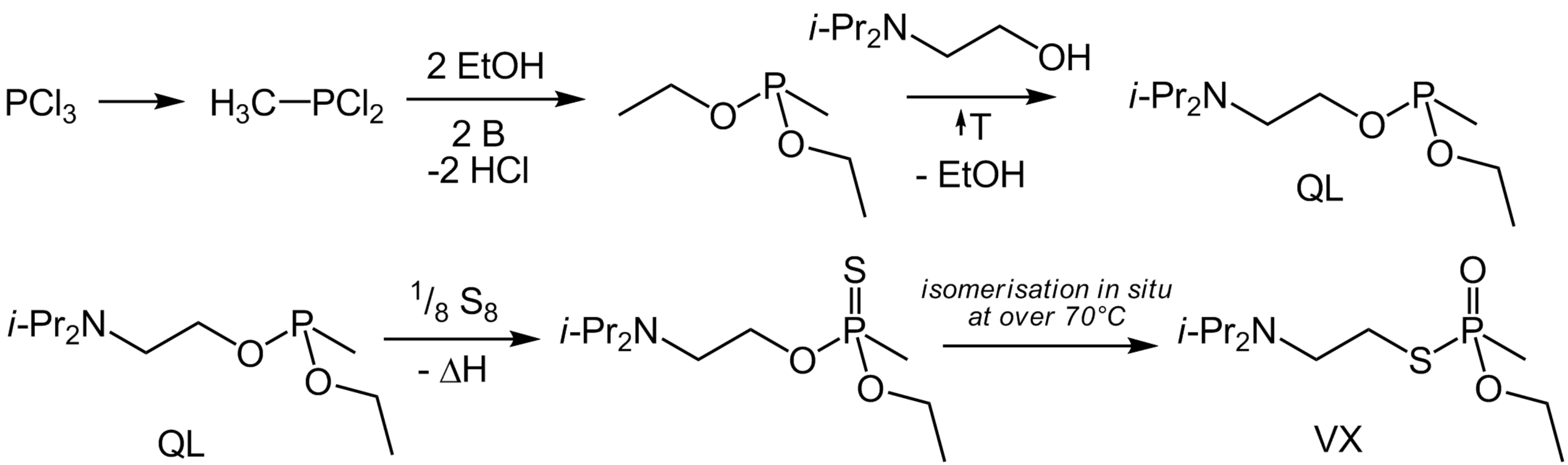
http://chemapps.stolaf.edu/jmol/jmol.php?model=CCOP%28C%29%28%3DO%29SCCN%28C%28C%29C%29C%28C%29C

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 (or vaper if the temperature is high).
- 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.

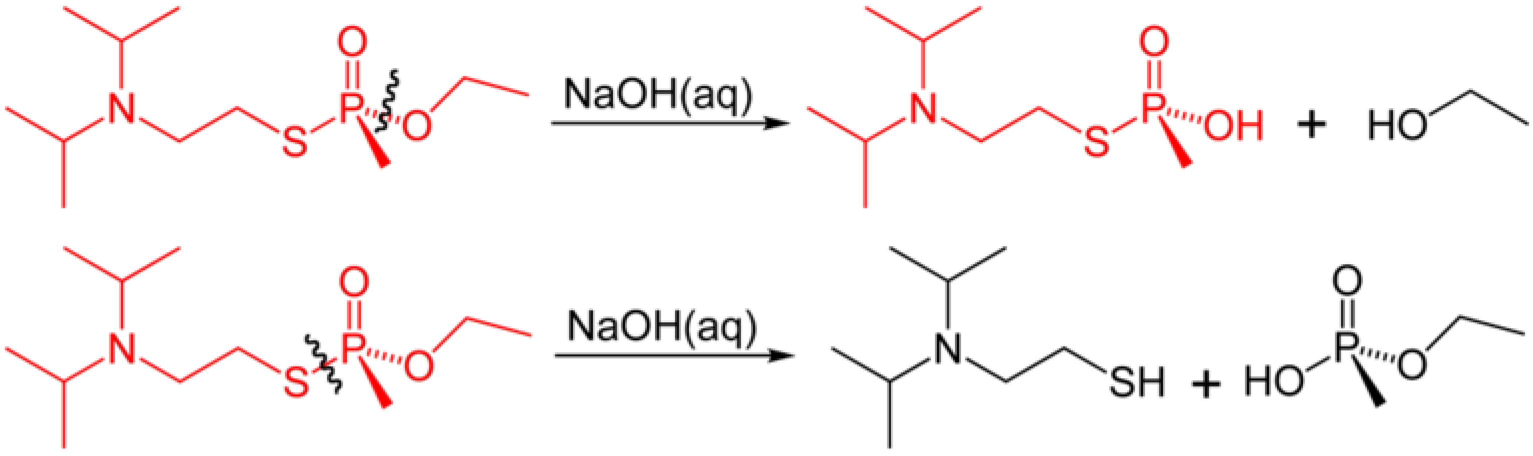
Production of VX

- Phosphorus trichloride (schedule 3, part b) is methylated, forming methyl phosphonous dichloride, which reacts with ethanol to form a diester. This reacts with N,N-diisopropylaminoethanol (Schedule 2, part b) to produce QL (Schedule 1, part b), which reacts with sulfur to form VX.
- Has difficult alkylation step but not corrosive HF gas.



Destruction of VX

- VX can be converted into safer substances by combining it with a concentrated solution of sodium hydroxide, NaOH.
- The reaction is called **hydrolysis**, in which water, H_2O, divides into H, which combines with one part of a molecule, and OH, which combines with another part of the molecule, splitting the molecule into two parts.

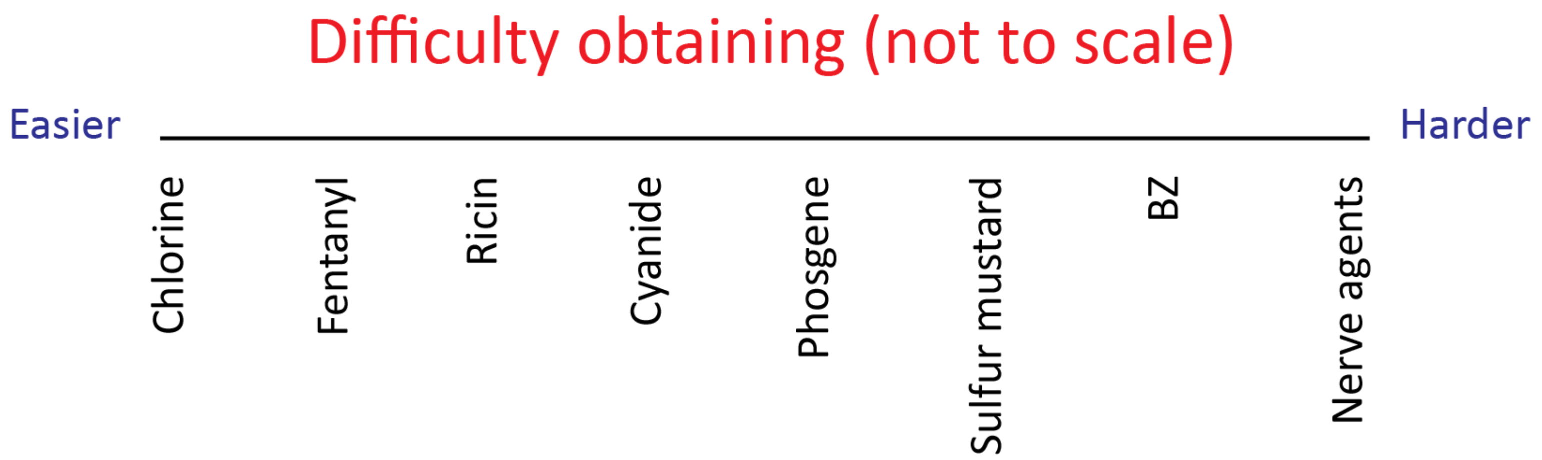


Sarin or VX?

- 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 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 = $mg{\bullet}min/m^3$
- 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.

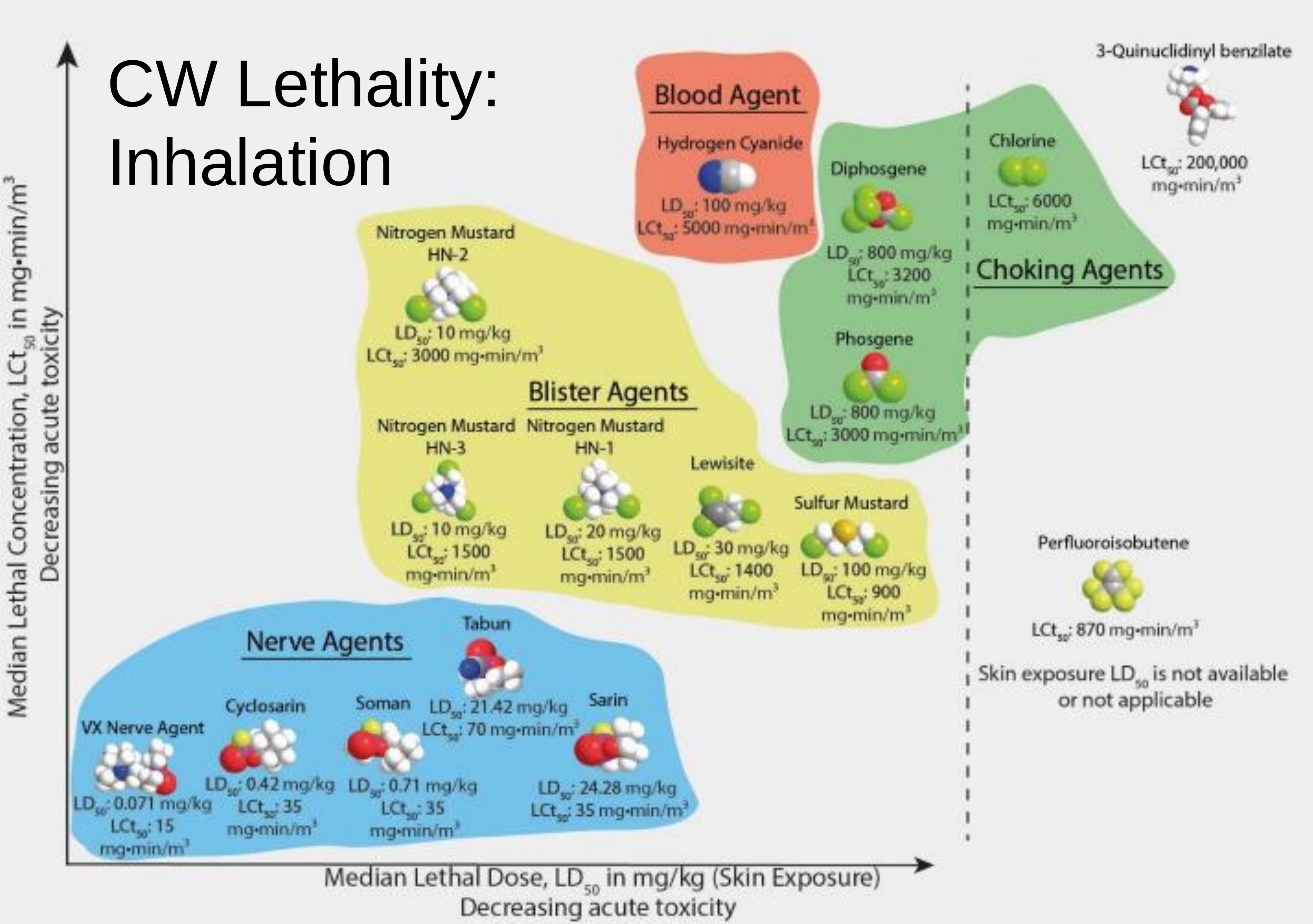
Dosage Units

- 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 = $mg \cdot min/m^3$

Dosage Units

- TD_{LO} = Lowest toxic dose; the lowest dose of a chemical reported to cause an observable toxic effect in test animals

CW Lethality: Inhalation

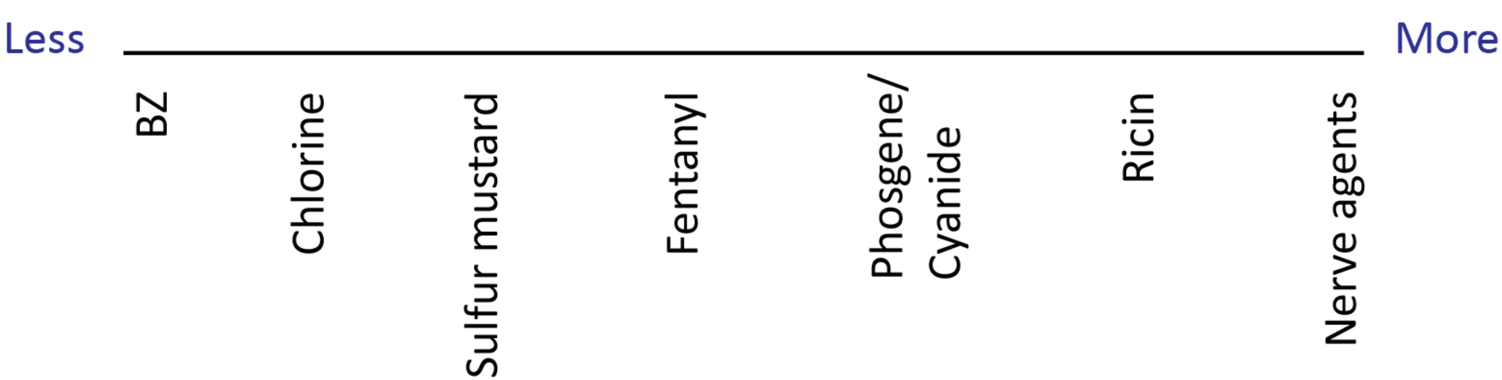


Source: Organisation for the Prohibition of Chemical Weapons (OPCW)

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.

Lethality (not to scale)



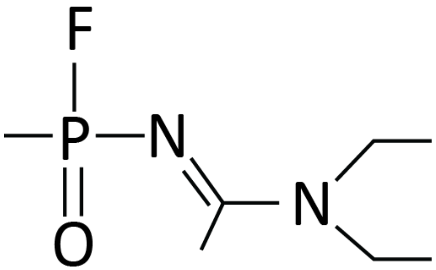
Amiton

- VG
- V-series nerve agent chemically similar to VX
- Used as an insecticide in the 1950s.
- Toxicity similar to that of sarin
- Now considered too dangerous for use in agriculture
- North Korea may have stockpiles it.
- Schedule 2, Part A

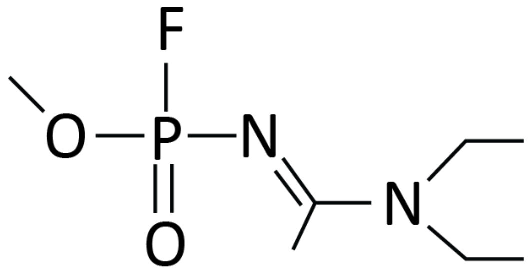
Russia's Novichoks

- A lot of uncertainty associated with Novichoks
- A category of similar solid and liquid compounds
- Alleged Soviet secret program called Foliant
- Novichok (new guy or newcomer) – a category of nerve agents developed in the 1970s and 1980s
- 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.
- Allegedly more lethal than VX
- Resistant to treatment

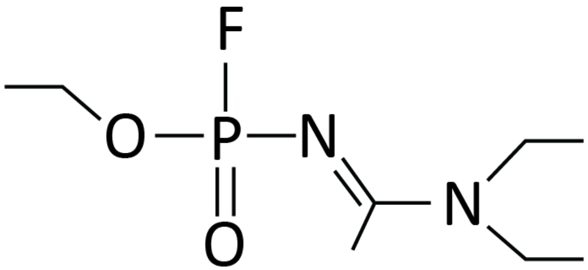
Russia’s Novichoks (Mirzayanov)



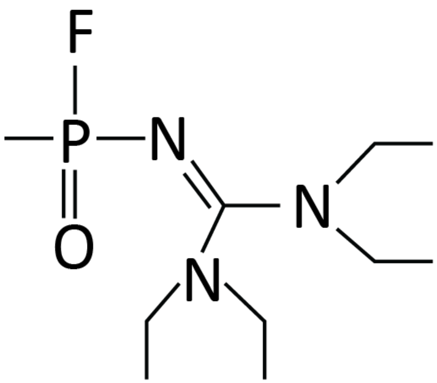
A-230



A-232



A-234



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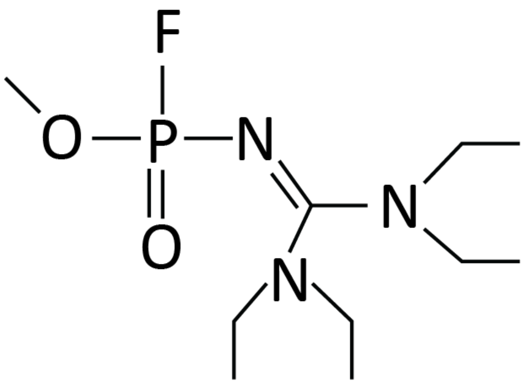


A-262

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

Russia's Novichok

- In March of 2018, A-234 was used in the Salisbury, UK attack on the former Russian military intelligence (GRU) officer Sergei Skripal and his daughter Yulia. Confirmed by four independent laboratories.
- In 2016, Iranian scientists produced seven Novichok agents and generated mass spectral data that was added to the OPCW database, which makes identifying Novichoks easier.
- Czech Republic admitted to making a small quantity of A-230.

Novichok to Schedule 1

- October 2018 - the U.S., Canada, and the Netherlands proposed adding two groups of novichok chemicals, including A-234, to Schedule 1.
- January 14, 2019 - OPCW Executive Council recommended adoption.
- April 2019 - Russia submitted its formal objection to the joint proposal, thus preventing the Executive Council's recommendation from becoming final.

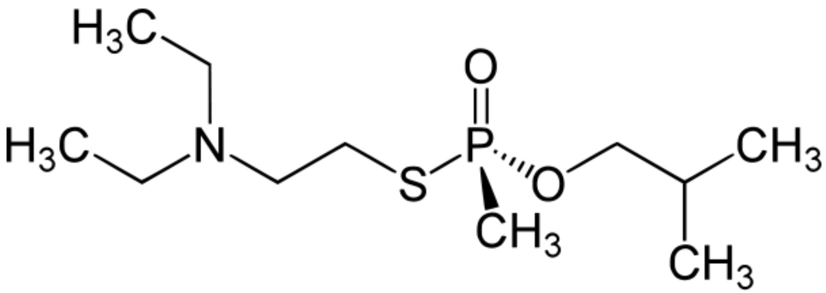
Novichok to Schedule 1

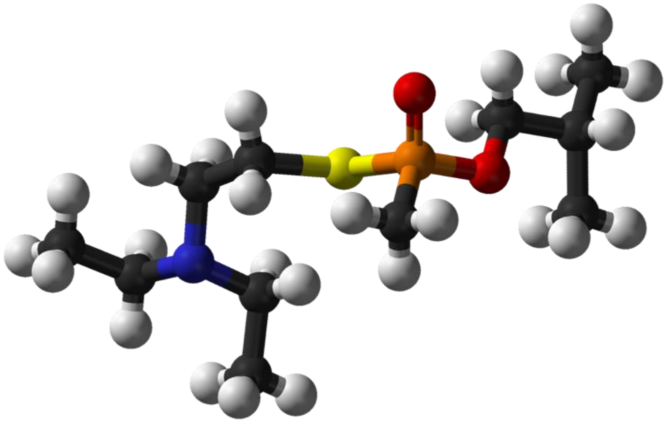
- November 27, 2019 - Twenty-Fourth Session of the Conference of the States Parties to the CWC adopted two decisions to amend for the first time the Annex on Chemicals to the Convention by adding novichoks to Schedule 1
- Went into effect 180 days after Director-General notifies all States Parties and the United Nations Secretary-General of the decisions adopted by the Conference

https://www.opcw.org/media-centre/news/2019/11/conference-states-parties-adopts-decisions-amend-chemical-weapons

Russia's VR or Substance-33

- Nerve agent similar to VX.
- Developed in Foliant program as prototype for Novichoks
- Reportedly used to poison banker Ivan Kivelidi and his secretary Zara Ismailova in 1995.

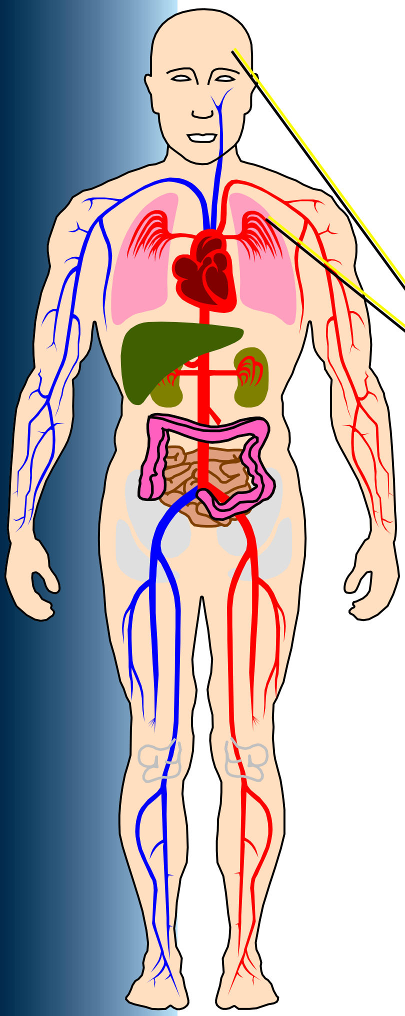




Incapacitants Classification

- **Irritants** Riot-control agents (CS, CN, etc.); pepper spray
  - The OPCW recognizes 17 riot control agents.
- **Central nervous system stimulants** (Amphetamines, cocaine, caffeine, nicotine, strychnine, metrazole)
- **Central nervous system depressants** (Barbiturates, opioids, antipsychotics, benzodiazepines)
- **Psychedelics** (LSD-25, psilocybin, ibogaine, harmine, MDMA…“ecstasy”, PCP)
- **Deliriants** (Many, especially anticholinergics, such as BZ)

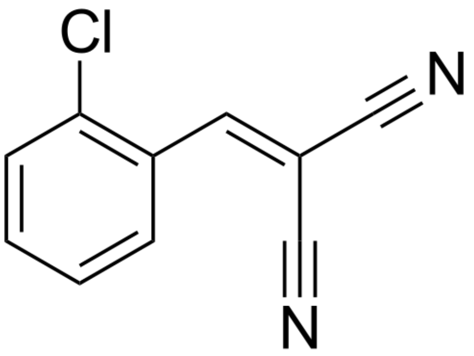
Physiological Incapacitants

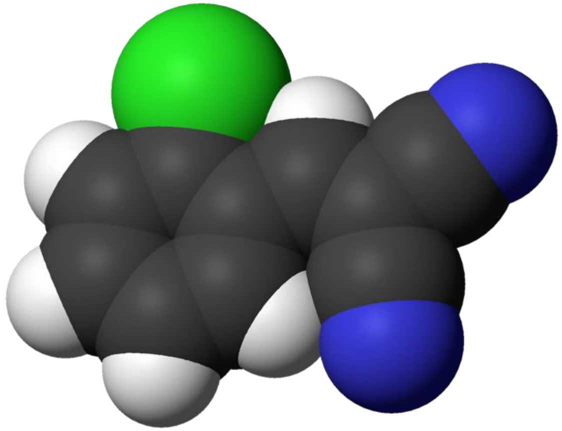


- CN (mace), CS, pepper spray, fentanyl
- Modes of action: mucous membrane irritation, vomiting inducing, sleep inducing
- Physiological effects - variable
  - Can cause uncontrolled tearing, itching, vomiting, unconsciousness
  - Acts immediately
- Form when disseminated: powder, aerosol
- Required defensive gear: protective mask & clothing

CS

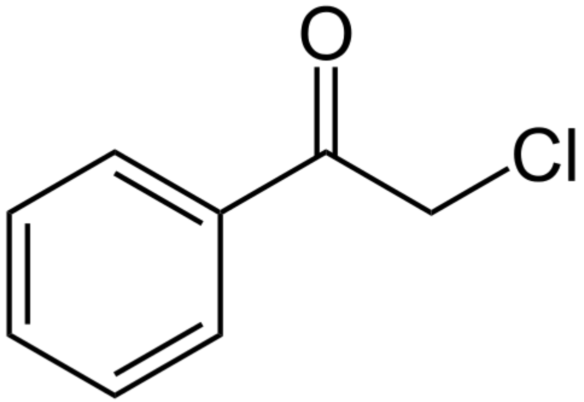
- **2-chlorobenzalmalononitrile**, $C_{10}H_5ClN_2$,
- Tear gas - riot control agent.
- Causes a burning sensation and tearing of the eyes and irritation of the nose, mouth, and throat
- Causes eyes to close, coughing, nasal discharge, disorientation, and difficulty breathing, partially incapacitating the subject.
- Dispersed as an aerosol of a volatile solvent and CS, which is a solid at room temperature.
- Discovered in 1928 by Ben Corson and Roger Stoughton at Middlebury College.





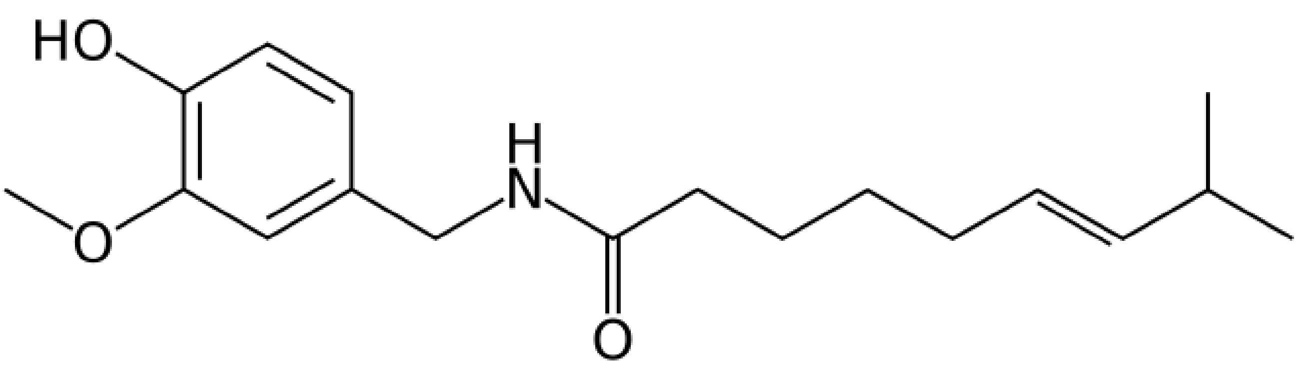
CN

- **Phenacyl chloride,** C_8H_7OCl
- Historically used as a riot control agent, where it is designated **CN**.
- More toxic than CS, so not widely used now.
- Mostly supplanted by pepper spray, which works more quickly than CN.



Pepper Spray

- Capsaicin – active ingredient of chili peppers and pepper spray.
- Causes burning and tearing of eyes
- Dispersed as aerosol, with capsaicin mixed with solvent such as ethylene glycol
- Can be fatal
- May be carcinogenic



Opiate-like Agents

- Clinical data for opiate-like compounds, comparing the effective dose (ED_{50}) and the lethal dose (LD_{50})
- This varies with the health of the subject.

Opiate	Lowest effective dose, ED_{50}, mg/kg	LD_{50}, mg/kg	Relative safety index
Meperidine	6.0	29.0	4.8
Alfentanil	0.044	47.5	1,080
Fentanyl	0.011	3.1	277
Sufentanil	0.007	17.9	25,211
Lofentanil	0.0059	0.066	112
Carfentanil	0.0034	3.4	10,000

Moscow Theater Hostage Crisis

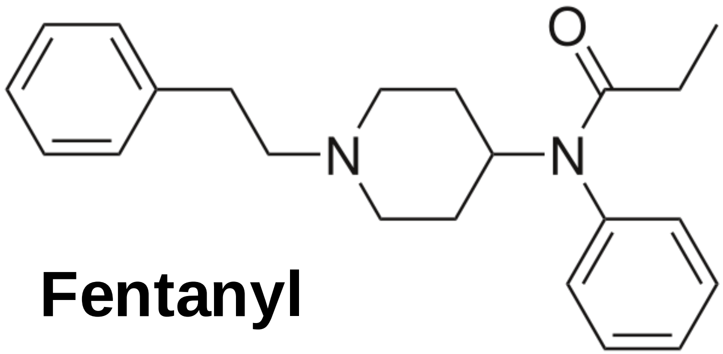
- 23 October 2002 – 40-50 armed Chechens seized a crowded Moscow theater and took 850 hostages
- Claimed allegiance to the Islamist militant separatist movement in Chechnya
- Russian forces pumped a substance thought to be carfentanyl into the building's ventilation system and raided it.
- 39 attackers and at least 129 of the hostages were killed.
- Most of the hostages who died were killed by the toxic substance pumped into the theater to subdue the militants.
- Fatalities are attributed to the weakened condition of the hostages and to lack of adequate medical attention after the attack.

Fentanyl

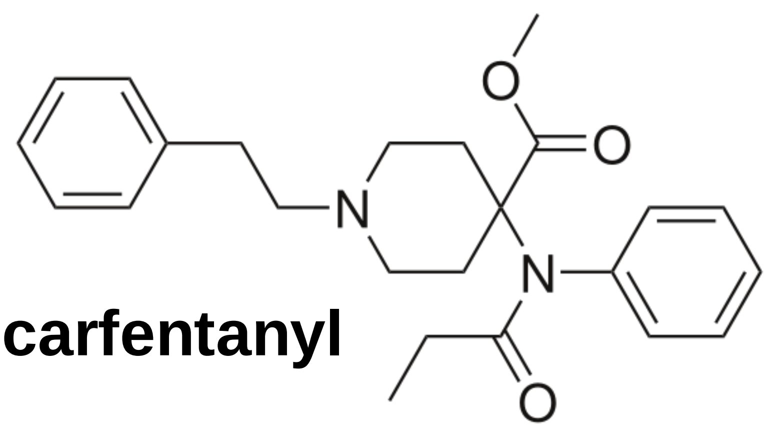
- Odorless, crystalline solid
- Can be absorbed into the body by inhalation, ingestion, or skin contact
- Inhalation results in rapid absorption. Oral exposure will occur within in a few minutes. Skin exposure results in absorption over hours to days.
- Can be released into the air as fine particles 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



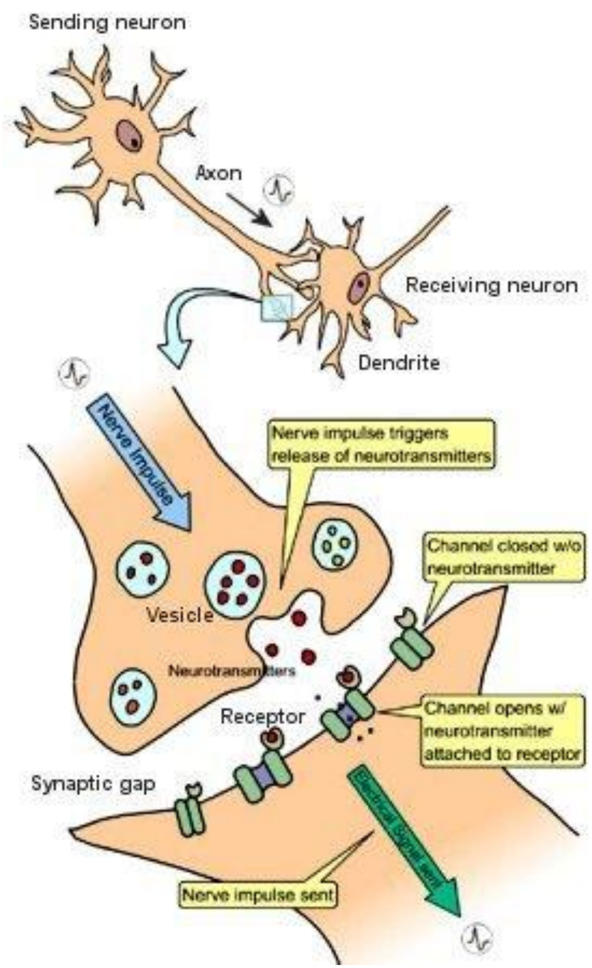
carfentanyl

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 cause 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.
- 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 inhibit 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.