NERVE AGENTS

Tabun

Sarin

Soman

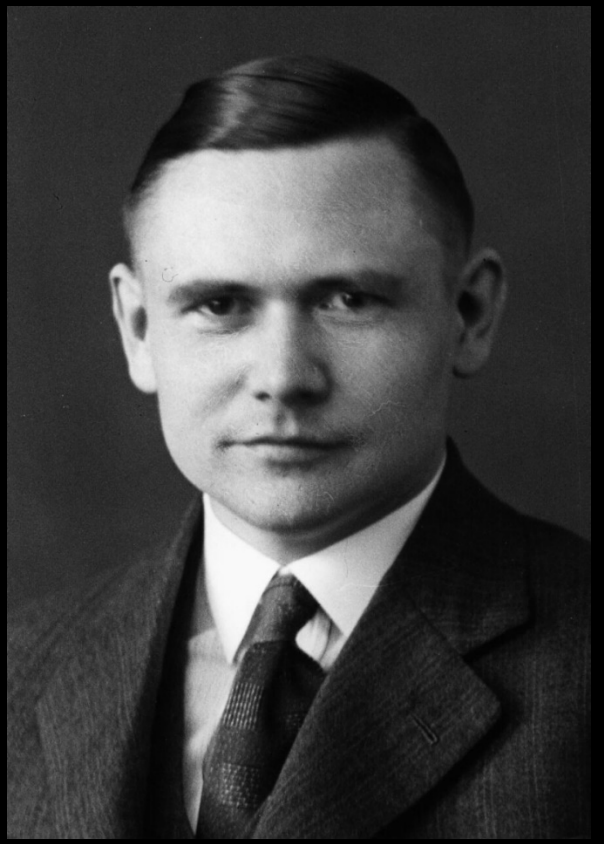
VX

NERVE AGENT HISTORY
Germany

1930's:

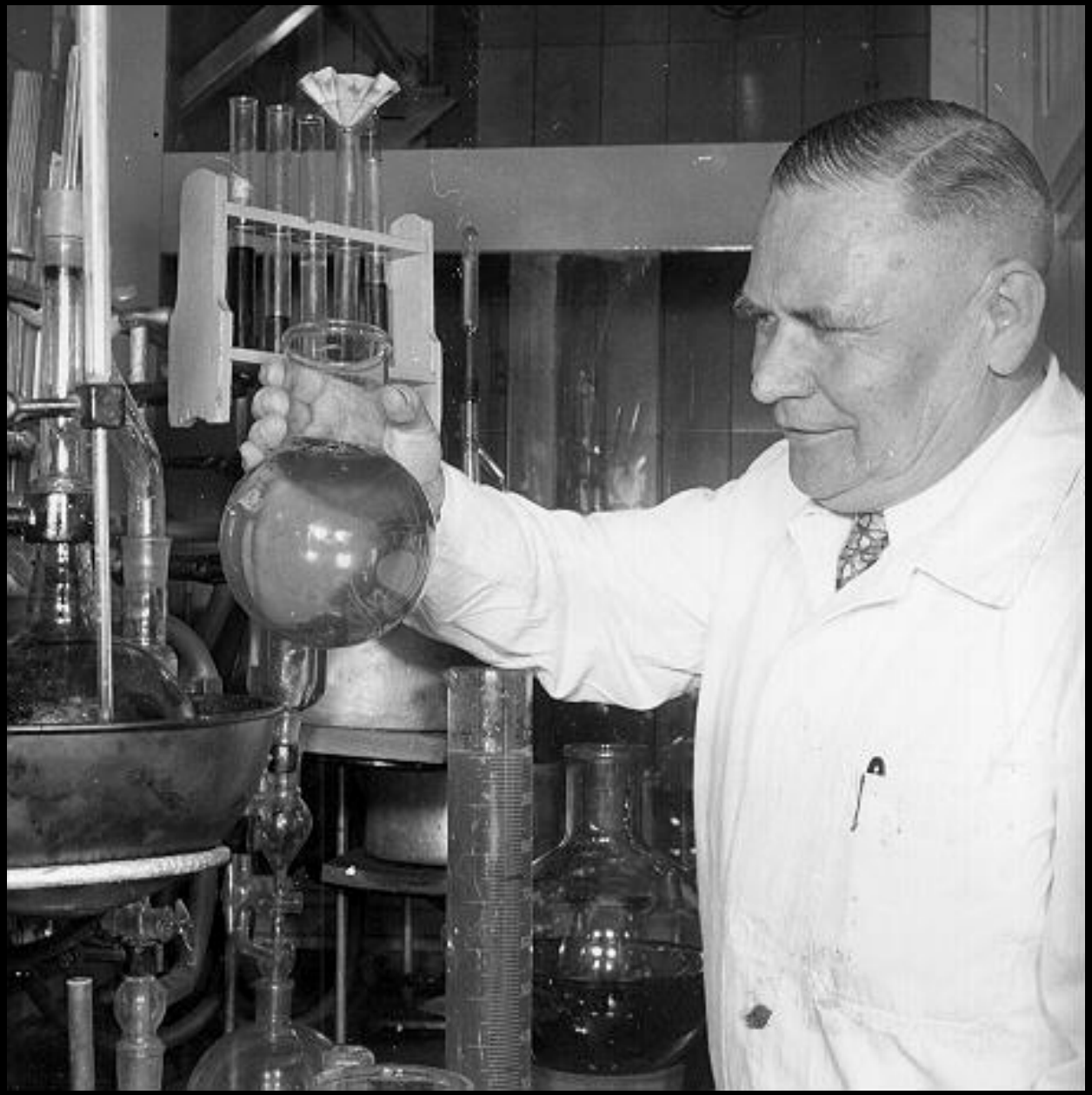
Dr. Gerhard Schrader (Ig Farben) performing research on pesticides. Spills one drop of tabun. Within minutes staff developed anticholinesterase poisoning. Discovery reported to Third Reich.

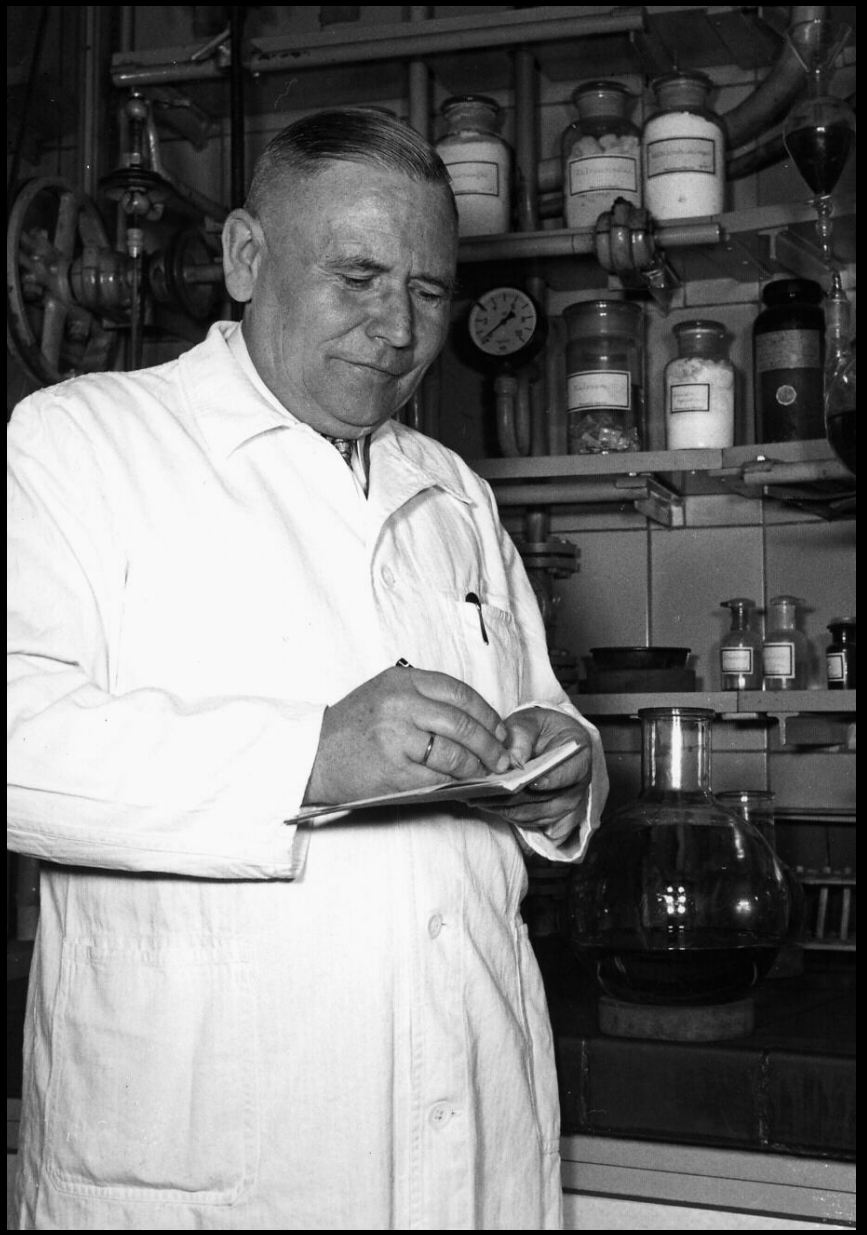
Spandau Citadel, Berlin



Gerhard Schrader
1903 - 1990


Systox





NERVE AGENT HISTORY

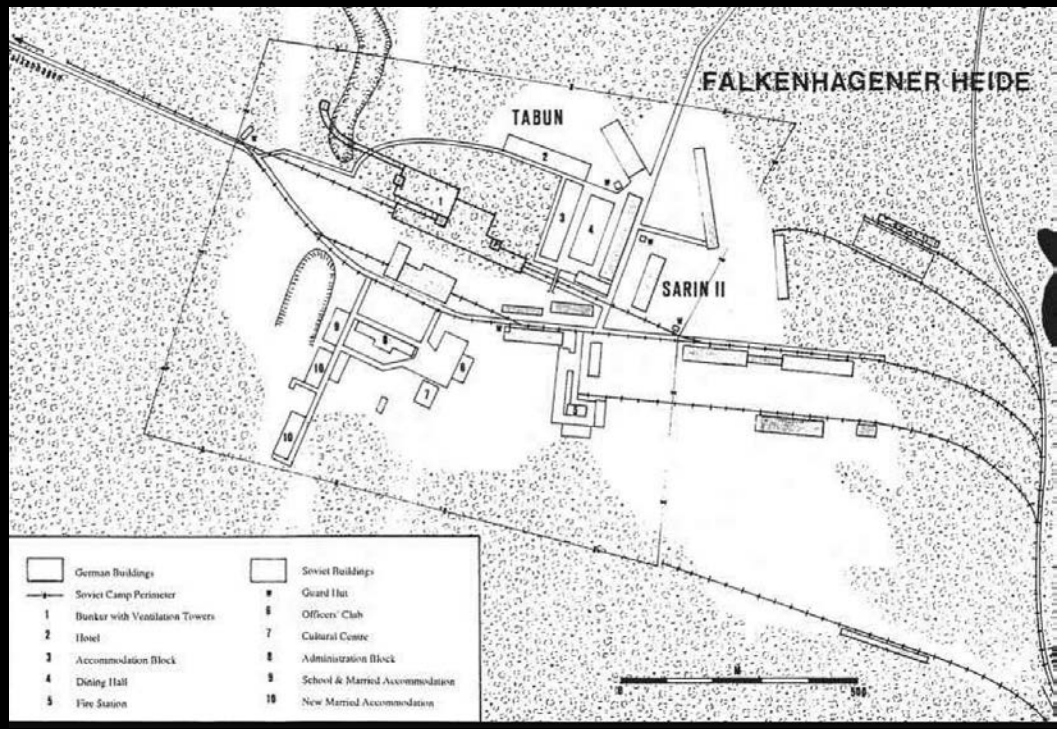
1938: Schrader synthesizes “Substance 146” which was given name of sarin (Schrader, Ambros, Ritter, vonder Linde).

Production facilities produced tabun and sarin. By 1943, Dyhernfurth was producing 350,000 Kg tabun per month and produced 12,000 Kg by end of war, loaded into artillery shells and aerial bombs.

A WWII tabun-filled bomb.

NERVE AGENT HISTORY

1943: New sarin production plant established at Falkenhagen, 70 Km from Berlin. Both sarin and tabun produced. Between 5 to 10 tons sarin produced during war.



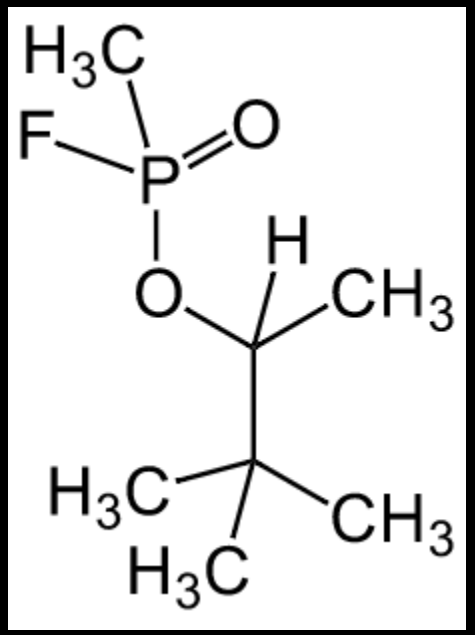
Early 1945, Germany went to extremes to hide sarin and tabun munitions. US dropped bombs on freight cars containing tabun munitions near Lossa, killing 4 town residents in minutes. Thousands of tabun bombs transported by barge on Danube and Elbe rivers.

NERVE AGENT HISTORY

1943: Dr. Richard Kuhn recruited to work on chemical weapons. Nobel prize winner in 1938 for work on vitamins and carotenoids.

1944, Kuhn synthesized soman.

No soman production facility created.



Grave, Heidelberg

Dr. Richard Kuhn
1900 - 1967

NERVE AGENT HISTORY

Russian troops attacked Dyhernfruth in 1945 and discovered sarin and tabun facilities, scientific journals, scientists and workers. Moved plant to Stalingrad.

Americans shelled a barge on Danube, which immediately waved surrender flags. Captured soldiers explained that tabun-filled bombs could kill all of them.

British discovered large numbers of files pertaining to chemical research at the Spandau Citadel at Raubkammer. Americans and British troops began rounding up scientists. Schrader found at home and informed them Russians had taken control of the Dyhernfruth plant and created facilities in Russia.

American production of nerve agents began.

NERVE AGENT HISTORY

Military names chosen for German nerve agents.

> 600,000 artillery shells →

Common name	Code name
tabun	GA
sarin	GB
soman	GD

NERVE AGENT HISTORY

1952: Ranajit Ghosh and JF Newman discovered V-series nerve agents in England.

1959: 2.12 ug/Kg VX given IV to Dr. Van M. Sim, a volunteer. Pallor, diaphoresis, delirium. Infusion halted.

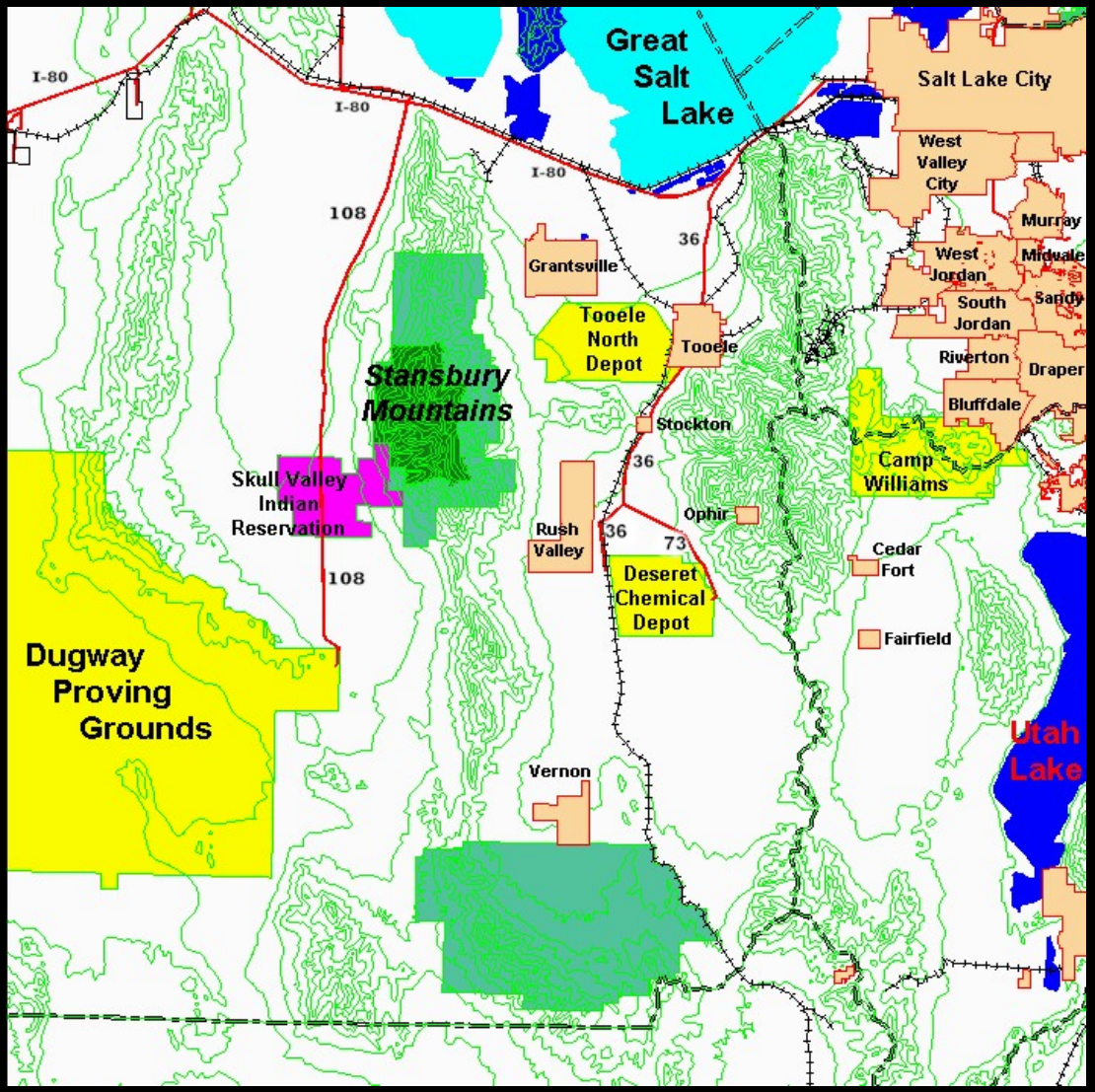
By 1961 VX production at Newport, Indiana had begun.

Other V agents developed, especially by Russia (VE, VG, VM, VR, EA-3148)

VX

NERVE AGENT HISTORY

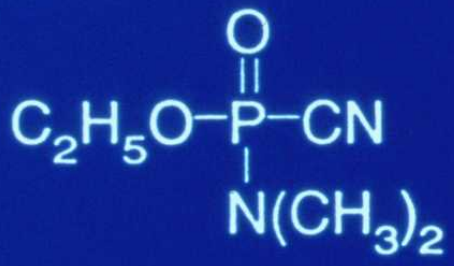
1968: VX leaked from aerial spray tanks from Dugway Proving Ground, killing about 6000 sheep in Skull and Rush Valley.



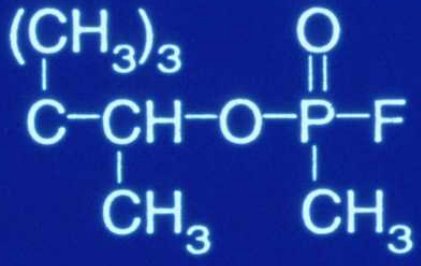
NERVE AGENTS

- Never used in WW II.
- Iraq used sarin and tabun against Kurds and against Iran in the 1980-1988 war - first documented use of nerve agents in war.

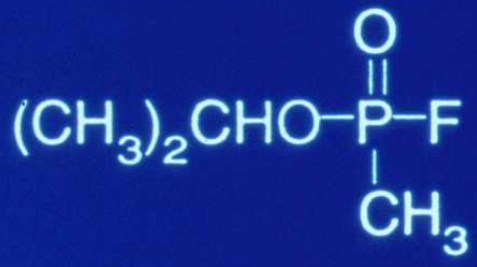
Tabun



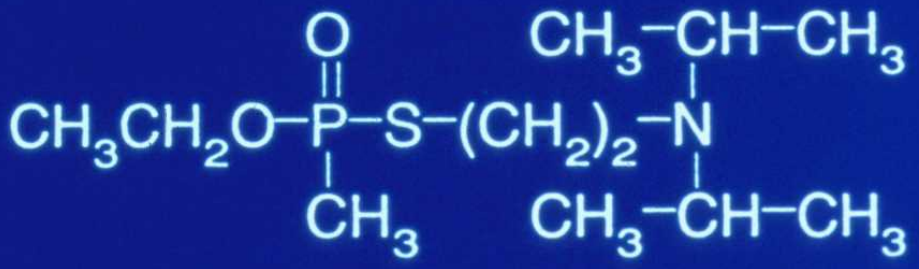
Soman



Sarin

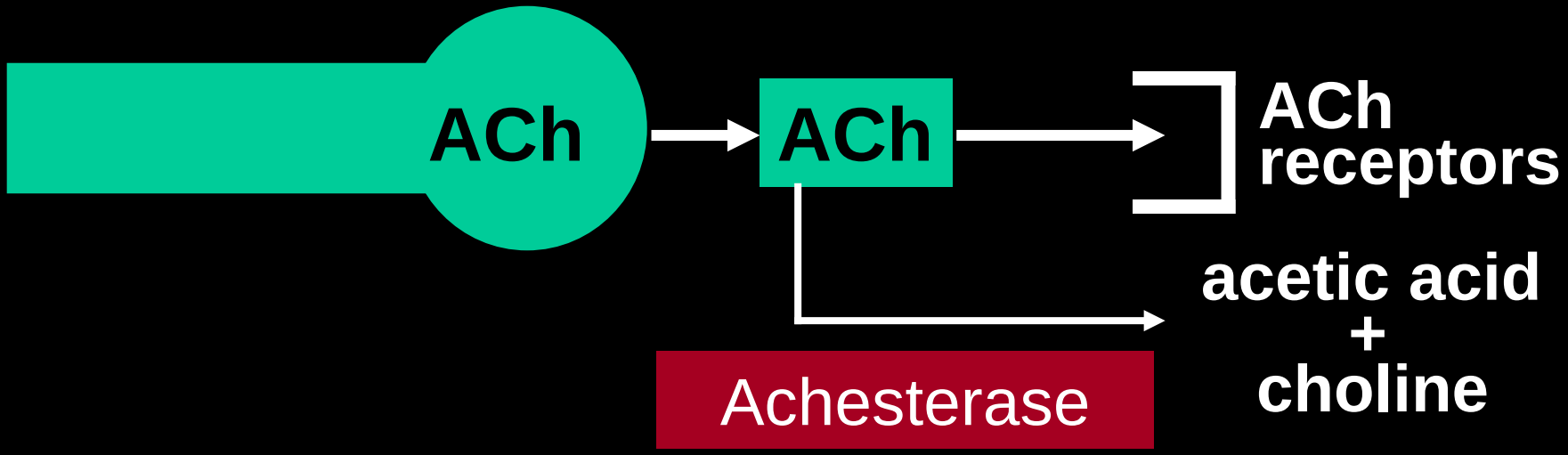


VX



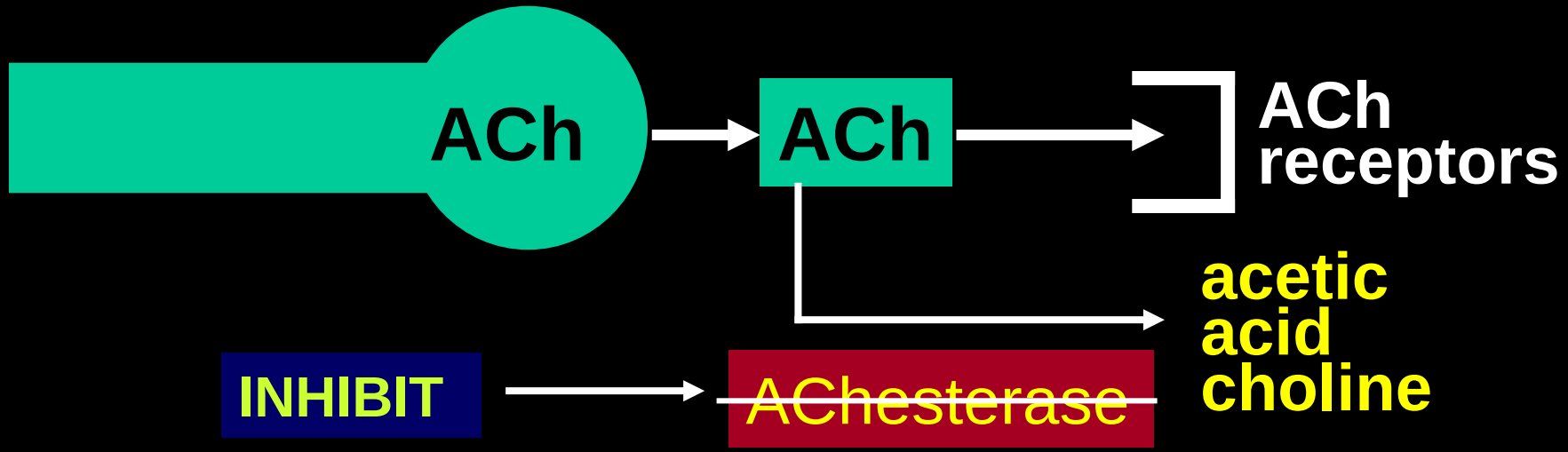
ORGANOPHOSPHATES

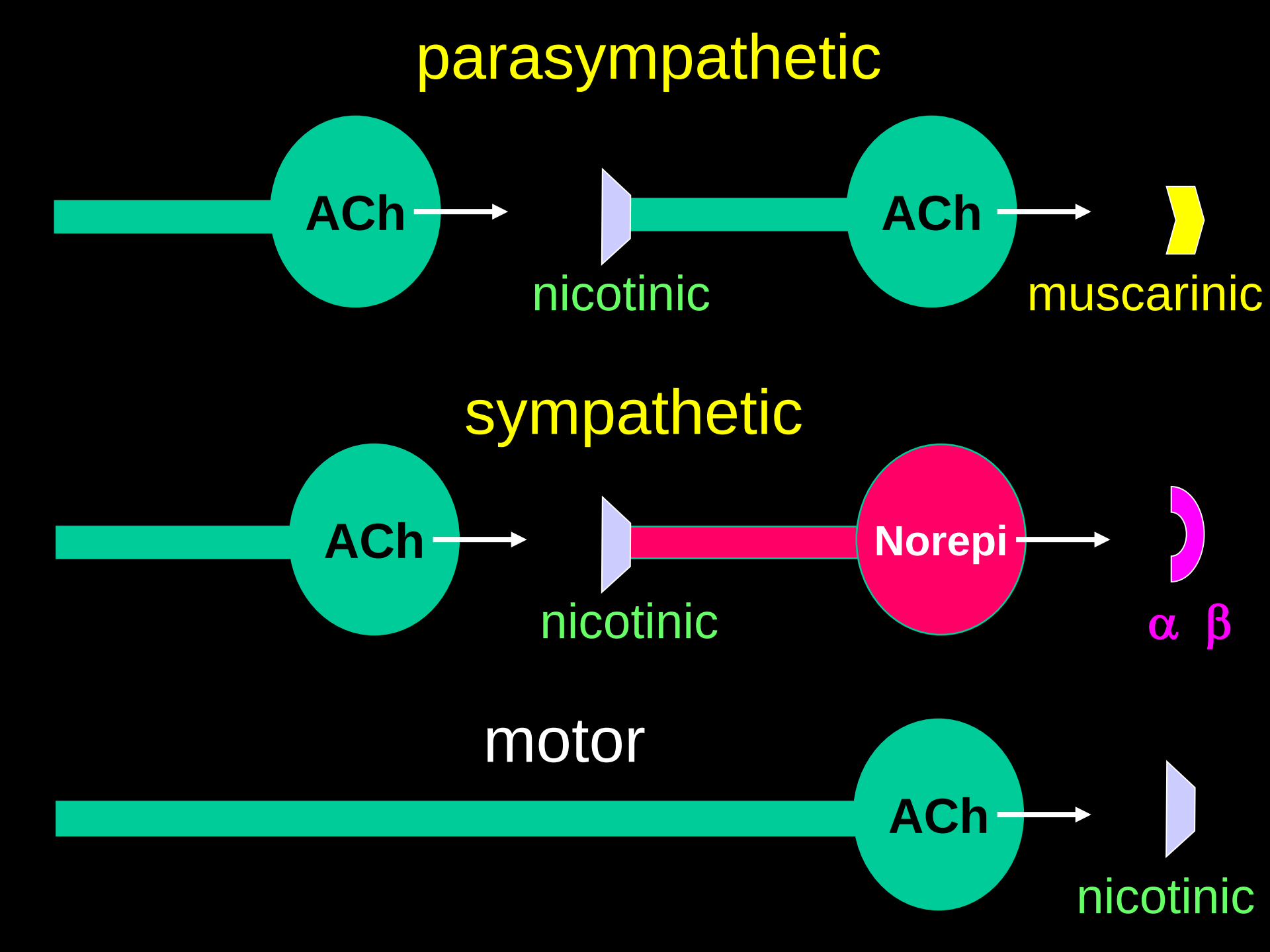
1. Well-absorbed by all routes
2. Onset of symptoms minutes to hours
3. Mechanism of action



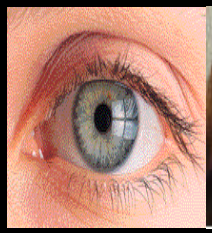
NERVE AGENTS
Mechanism of Action

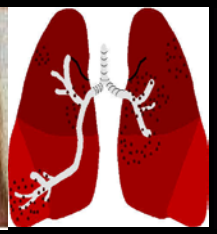
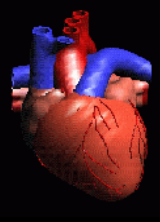
- All nerve agents are organophosphates
- All inhibit acetylcholinesterase in a manner similar to organophosphate insecticides

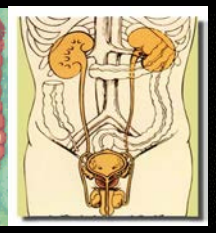
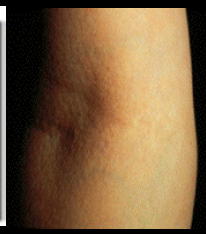



parasympathetic
ACh
nicotinic
ACh
muscarinic
sympathetic
ACh
nicotinic
Norepi
α β
motor
ACh
nicotinic

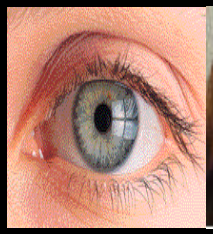
OP TOXICITY

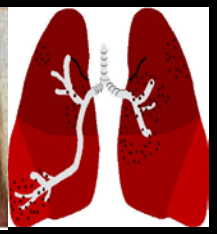
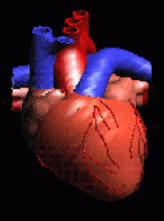


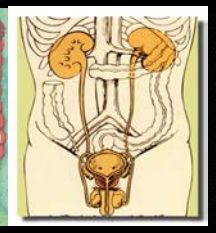
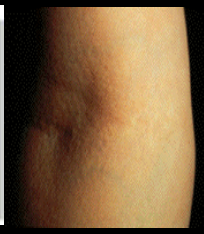



OP TOXICITY



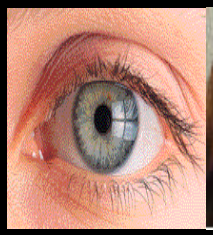



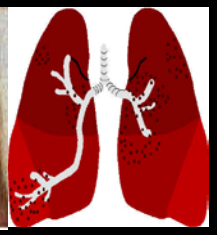
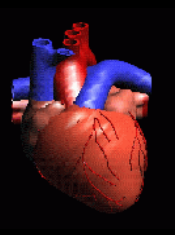
miosis
lacrimation

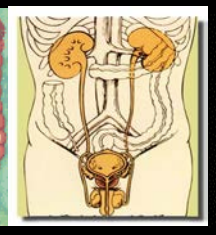
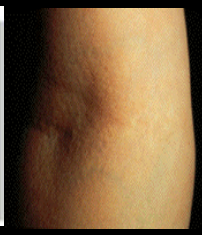
Miosis

Syrian child, 2013

OP TOXICITY



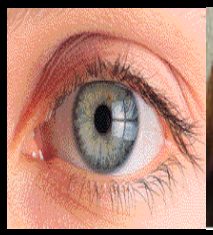



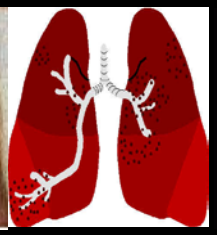
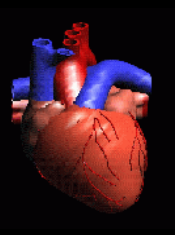



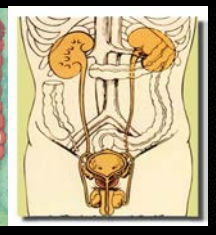
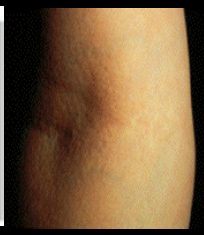
salivation

miosis
lacrimation

OP TOXICITY



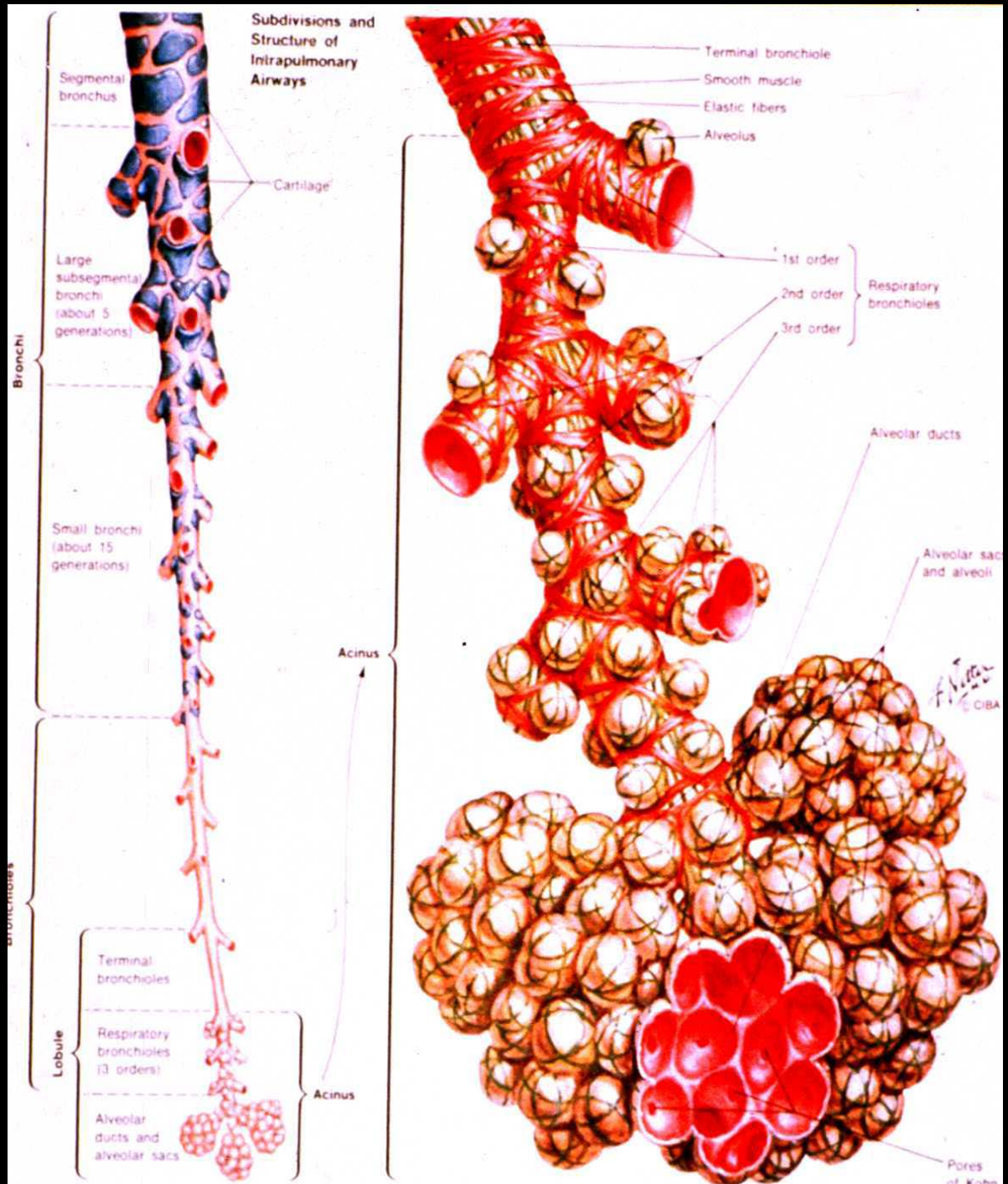



bronchospasm
bronchorrhea

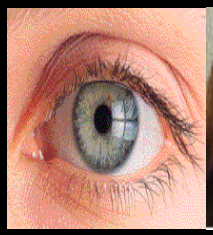
salivation

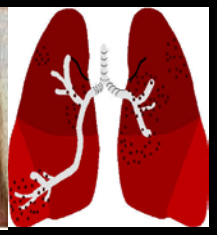
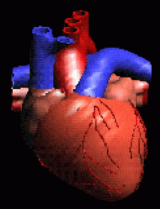
miosis
lacrimation

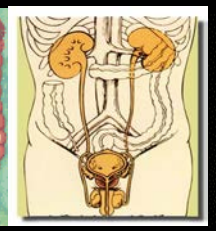
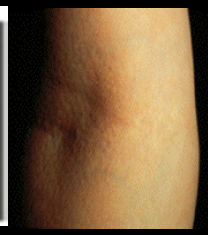

Subdivisions and Structure of Intrapulmonary Airways
Segmental bronchus
Cartilage
Large subsegmental bronchi (about 5 generations)
Small bronchi (about 15 generations)
Bronchi
Terminal bronchioles
Respiratory bronchioles (3 orders)
Alveolar ducts and alveolar sacs
Lobule
Acinus
Acinus
Terminal bronchiole
Smooth muscle
Elastic fibers
Alveolus
1st order
2nd order
3rd order
Respiratory bronchioles
Alveolar ducts
Alveolar sac and alveoli
Pores
CIBA


AP

OP TOXICITY



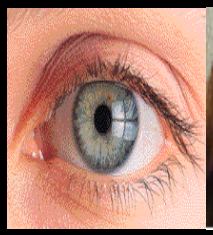
tachycardia
bradycardia

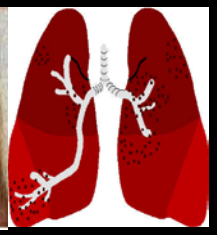
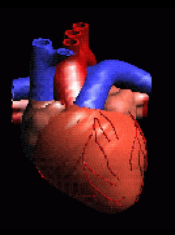
bronchospasm
bronchorrhea

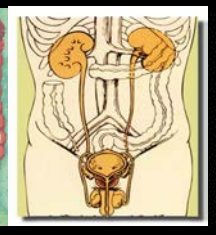
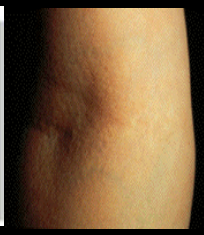
salivation

miosis
lacrimation

OP TOXICITY



vomiting
diarrhea

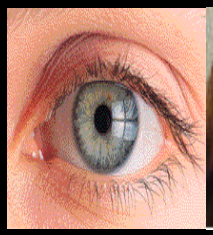
tachycardia
bradycardia

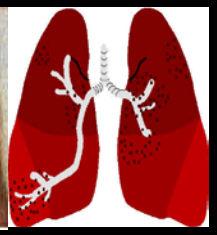
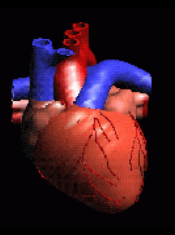
bronchospasm
bronchorrhea

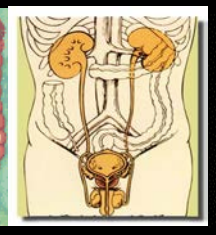
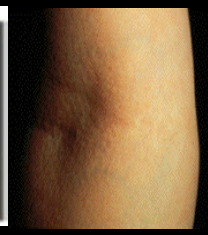
salivation

miosis
lacrimation

OP TOXICITY



vomiting
diarrhea

urination

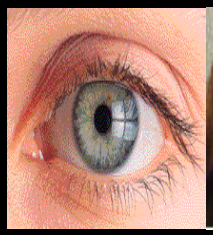
tachycardia
bradycardia

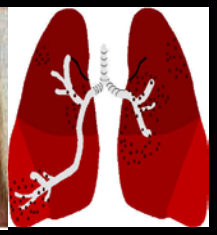
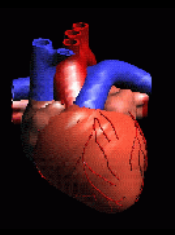
bronchospasm
bronchorrhea

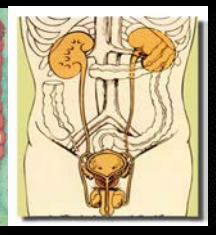
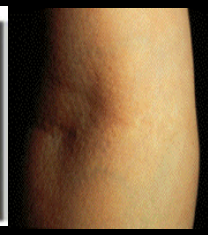
salivation

miosis
lacrimation

OP TOXICITY



vomiting
diarrhea

urination

tachycardia
bradycardia

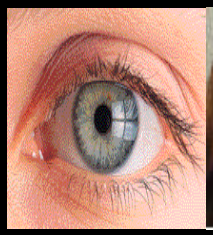
diaphoresis

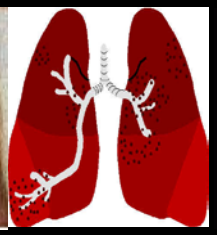
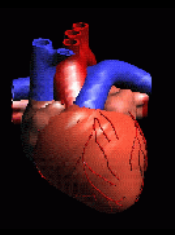
bronchospasm
bronchorrhea

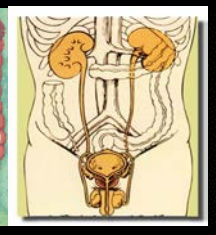
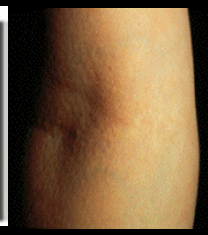
salivation

miosis
lacrimation

OP TOXICITY



vomiting
diarrhea

urination

tachycardia
bradycardia

diaphoresis

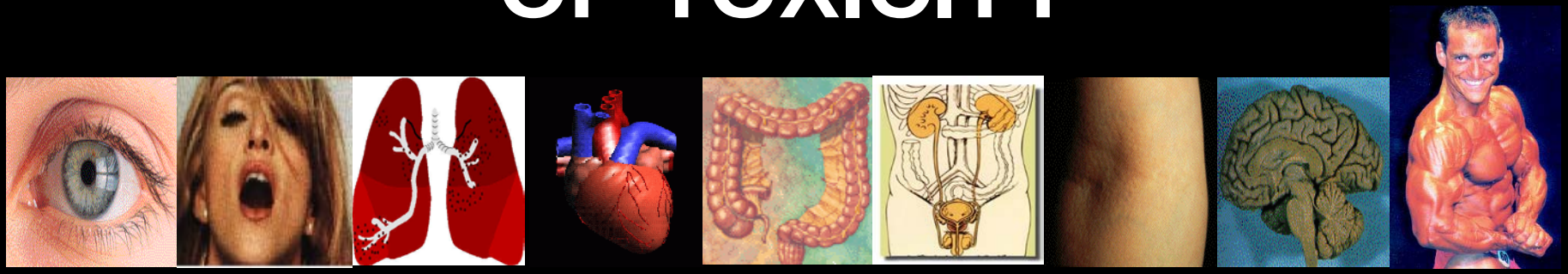
bronchospasm
bronchorrhea

seizures
lethargy
coma

salivation

miosis
lacrimation

OP TOXICITY



miosis
lacrimation

salivation

bronchospasm
bronchorrhea

tachycardia
bradycardia

vomiting
diarrhea

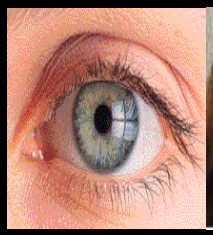
urination

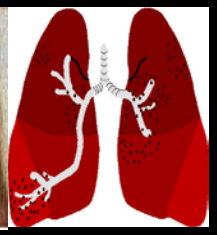
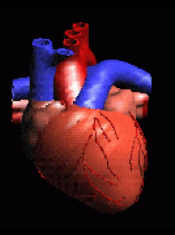
diaphoresis

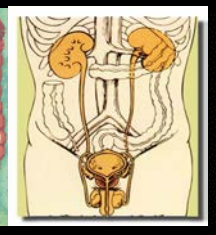
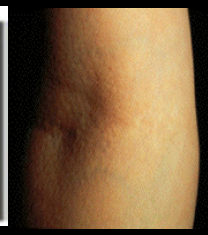
seizures
lethargy
coma

weakness
fasciculations
paralysis

NERVE AGENT TOXICITY



miosis
lacrimation

salivation

bronchospasm
bronchorrhea

tachycardia
bradycardia

vomiting
diarrhea

urination

diaphoresis

seizures
lethargy
coma

weakness
fasciculations
paralysis

Vapor Exposure

- Only seconds or minutes of exposure can be serious
- Local first
  - miosis, rhinorrhea, dyspnea

- Systemic follows
  - vomiting, diarrhea, coma, seizures, paralysis, apnea

- In general, once removed from exposure, symptoms do not progress

Skin Exposure

- Delayed presentation possible following small exposures and no contamination
- Local
  - sweating, fasciculations first
- Systemic follows
  - nausea, vomiting, coma, miosis, convulsions paralysis, apnea
- Experts concede:
  - anyone making it to the hospital alive is unlikely to suffer significant residual skin exposure (or they would be dead)

Death from Nerve Agents

- Mainly from respiratory failure
  - –secretions
  - –bronchospasm
  - –paralysis
  - –coma

NERVE AGENT PROPERTIES

Agent	LCT50 $mg(min)m^3$	Volatility mg/m^3	Vapor Density (air=1)	Topical LD_{50} mg
tabun	400	610	5.63	1000
sarin	100	22,000	4.86	1700
soman	50	3,900	6.33	100
VX	10	10.5	9.20	10
[HCN]	[5000]			

NERVE AGENTS

- Sarin
  - very volatile - evaporates about the same as water at low humidity
  - easily dispersed as gas
- VX
  - oily liquid
  - persists in environment for long periods of time

WEAPONIZED NERVE AGENTS

- Artillery shells
- Missiles
- Mortars
- Land mines
- Bombs
- Aerial spray tanks

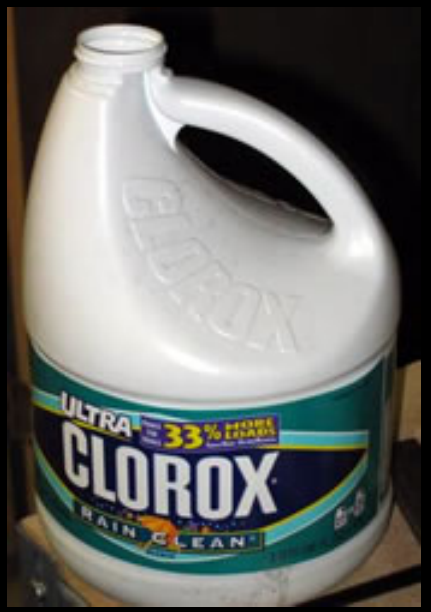
NERVE AGENT TREATMENT

- Protect Personnel!!!!
  - at least butyl rubber apron
  - at least butyl rubber gloves
    - nerve agents quickly penetrate double layer latex gloves
  - at least boots

NERVE AGENT TREATMENT
Inhalation

- Patients suffering inhalation exposure who are not severely ill will not worsen
- Simply remove outer layers of clothing and begin medical care

NERVE AGENT TREATMENT
Skin Contact



- Decontamination
  - water, soap, water
  - 1:10 dilution of household bleach
- major contamination threat is from dead victims
- contamination from condensed nerve agent on victims' clothing possible

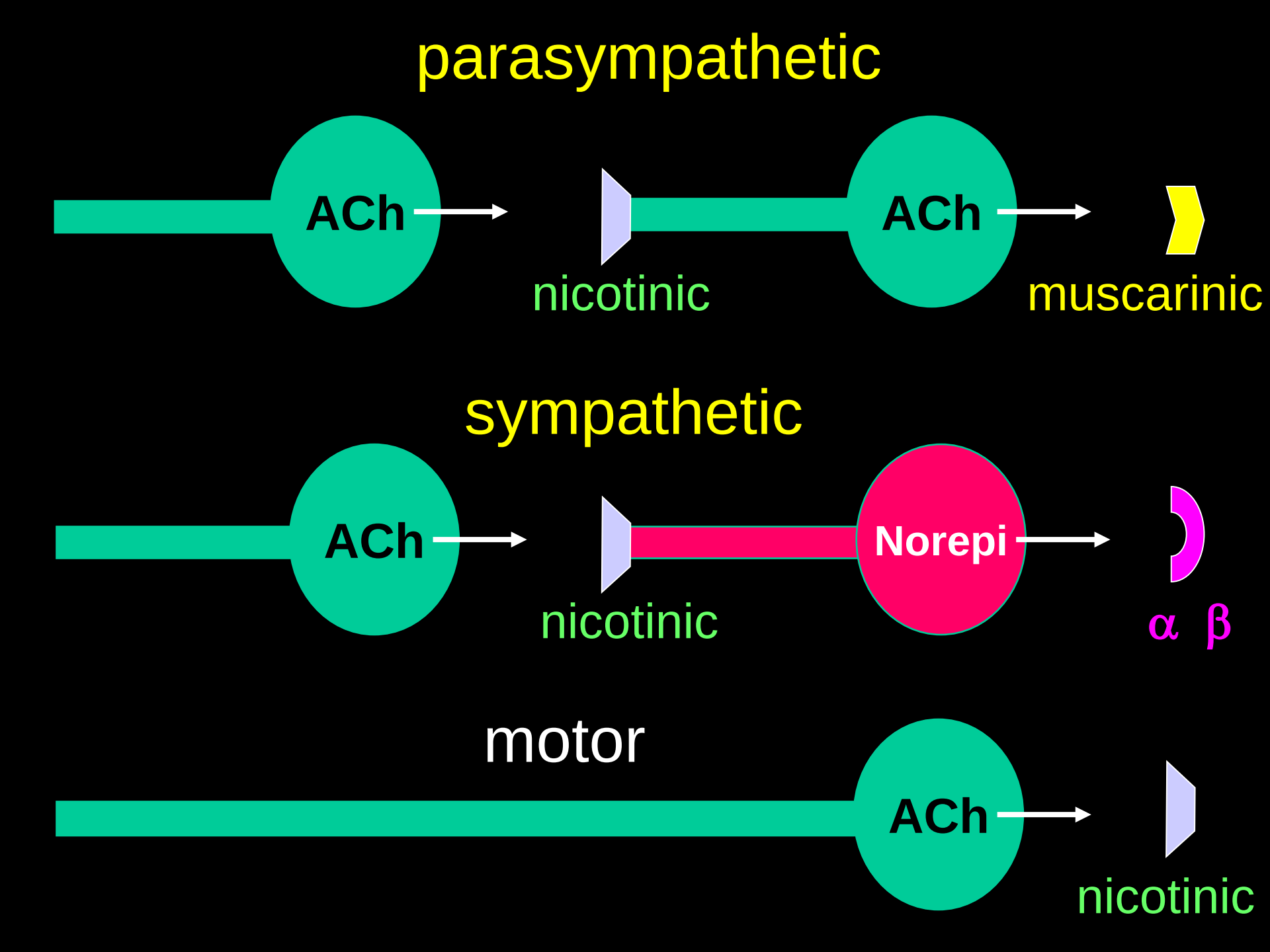
NERVE AGENT TREATMENT

- Treat similar to organophosphate insecticide poisonings

Atropinization

Pralidoxime hydrochloride

Diazepam or lorazepam for seizures


parasympathetic
ACh
nicotinic
ACh
muscarinic
sympathetic
ACh
nicotinic
Norepi
α β
motor
ACh
nicotinic

OP TREATMENT

1. ABCs and DECONTAMINATION
2. Atropine sulfate

   adults: 2-5 mg IV q 2-5 min prn

   kids: .05 mg/kg IV q 2-5 min prn

GIVE UNTIL ATROPINIZED!!!

GIVE ATROPINE UNTIL:

1. No wheezing
2. No bronchorrhea
3. No bradycardia
4. No diarrhea
5. No diaphoresis
6. Pupils may or may not dilate


No. 246-01
1 ml.
ATROPINE
SULFATE
INJ.,
U.S.P.
1 mg. per ml
For I.M., I.V.
or S.C. Use.
See Insert
INVENEX
Div. of The
Dexter Corp.
Chagrin Falls,
Ohio 44022

NERVE AGENT TREATMENT

2. Atropine sulfate

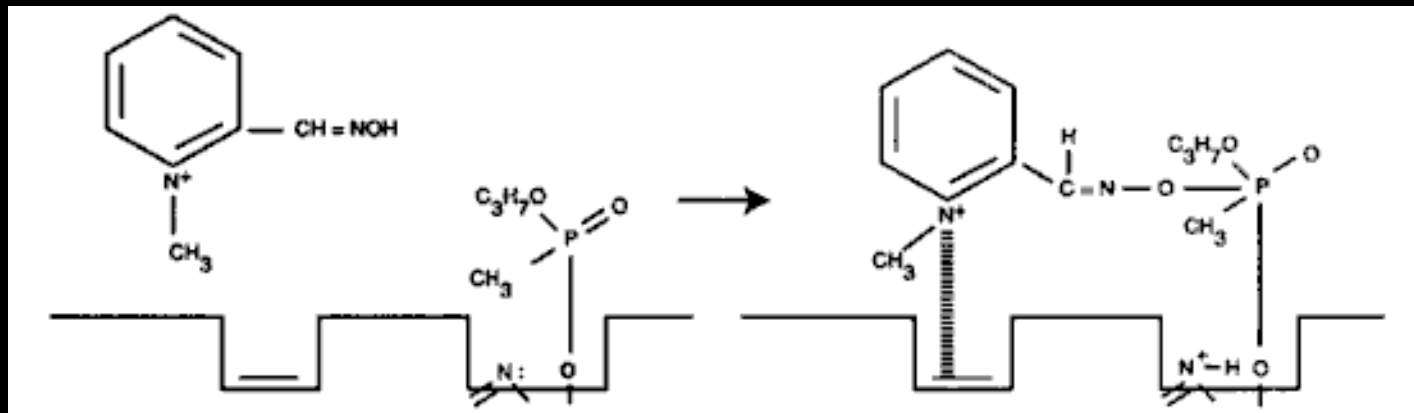
3. Pralidoxime hydrochloride

OP TREATMENT

3. Pralidoxime chloride (2-PAM)

adults: 1-2 grams IV over 10-15 min

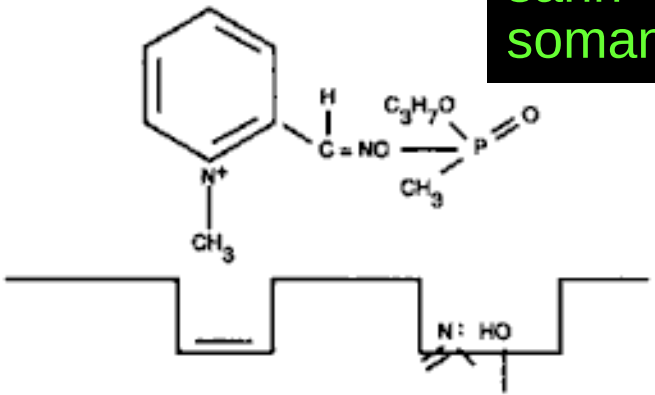
kids: 30-50 mg/kg IV over 10-15 min



Pralidoxime removes the OP from acetylcholinesterase, “reactivating” or “rejuvenating” the enzyme

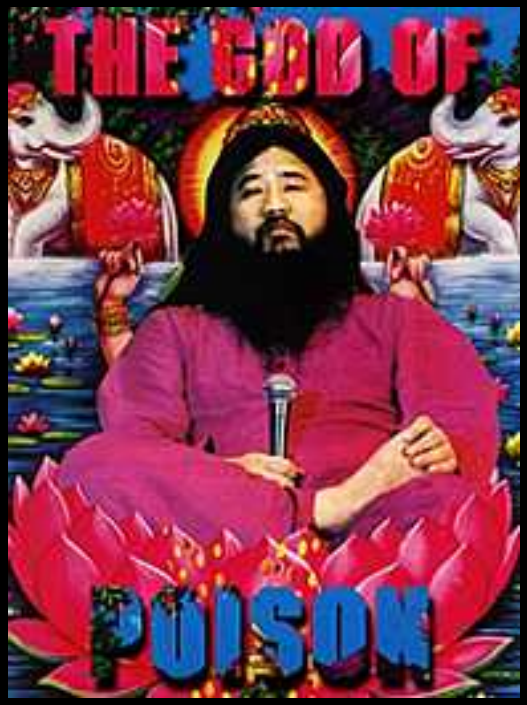
Aging half-lives	
VX	48 hr
tabun	14 hr
sarin	3-5 hr
soman	2-6 min

3



Mark I Kit


2
1
PRALIDOXIME CHLORIDE INJECTION, AUTOMATIC
TRAINING DEVICE
CONTAINS NO DRUG PRODUCT OR NEEDLE
Atropine Injection, Automatic
Training Device
CONTAINS NO DRUG PRODUCT OR NEEDLE



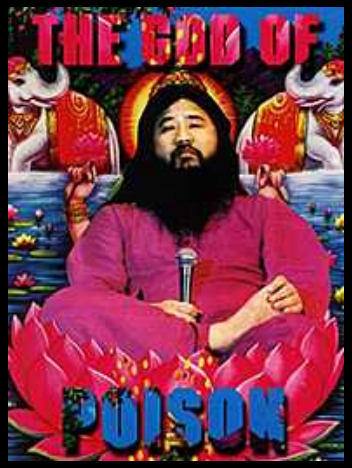
1984 - Aum Shinrikyo founded by Shoko Asahra in his apartment.

1980s – cult development, lost lawsuit, extortion.

1990 – failed candidates in elections. War declared on Japan.

1993 – began manufacturing sarin and VX. Sarin tested on sheep (29 killed).

1994 – 1995 – several assassinations and attempts. VX used to attack 3 persons, one (28-years-old) who died after VX sprinkled on his neck.



Matsumoto, Nagano, Japan
27 June 1994

City of 200,000. Hot and humid.

~10:40 PM: Residents near center of city began sneezing and complaining of rhinorrhea. Fog seen with pungent and irritating odor.

11:30 PM: Urgent requests for ambulances.

By 0200, 3 found dead; 4 died on way to hospital; 56 admitted.

Next day, dead fish, crayfish found in pond. Carcasses of dogs, sparrows caterpillars found under trees. Trees and grass at scene withering.

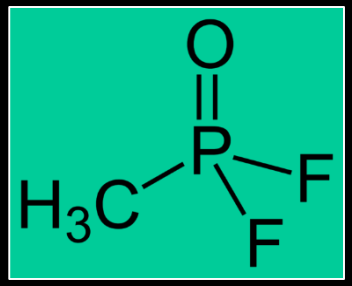
Nearly all casualties within 150 meters of near pond. Autopsies showed miosis, pulmonary edema, bronchial secretions.

Analysis of pond water, wipes, nasal swab, and other material revealed “sarin”.

Examining foliage around pond

Apartment building

Matsumoto

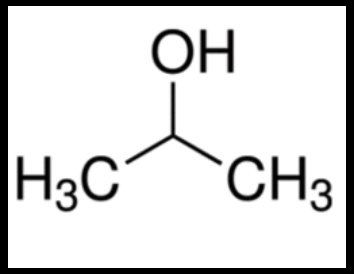


methylphosphonyl difluoride

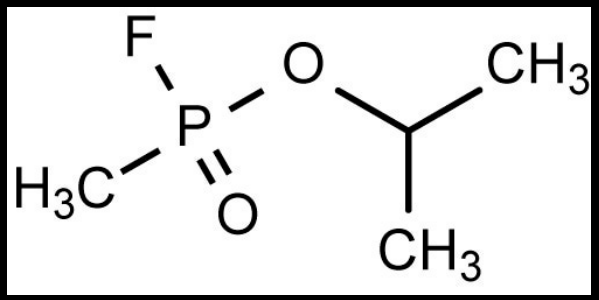
NaF

mixture

+



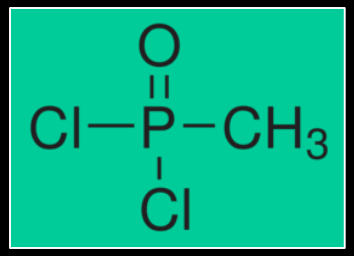
isopropanol



sarin

+

contaminants

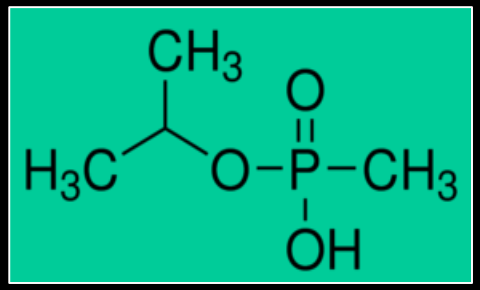


methylphosphonyl dichloride

hydrolysis

HOH

HF



isopropanol methylphosphonate

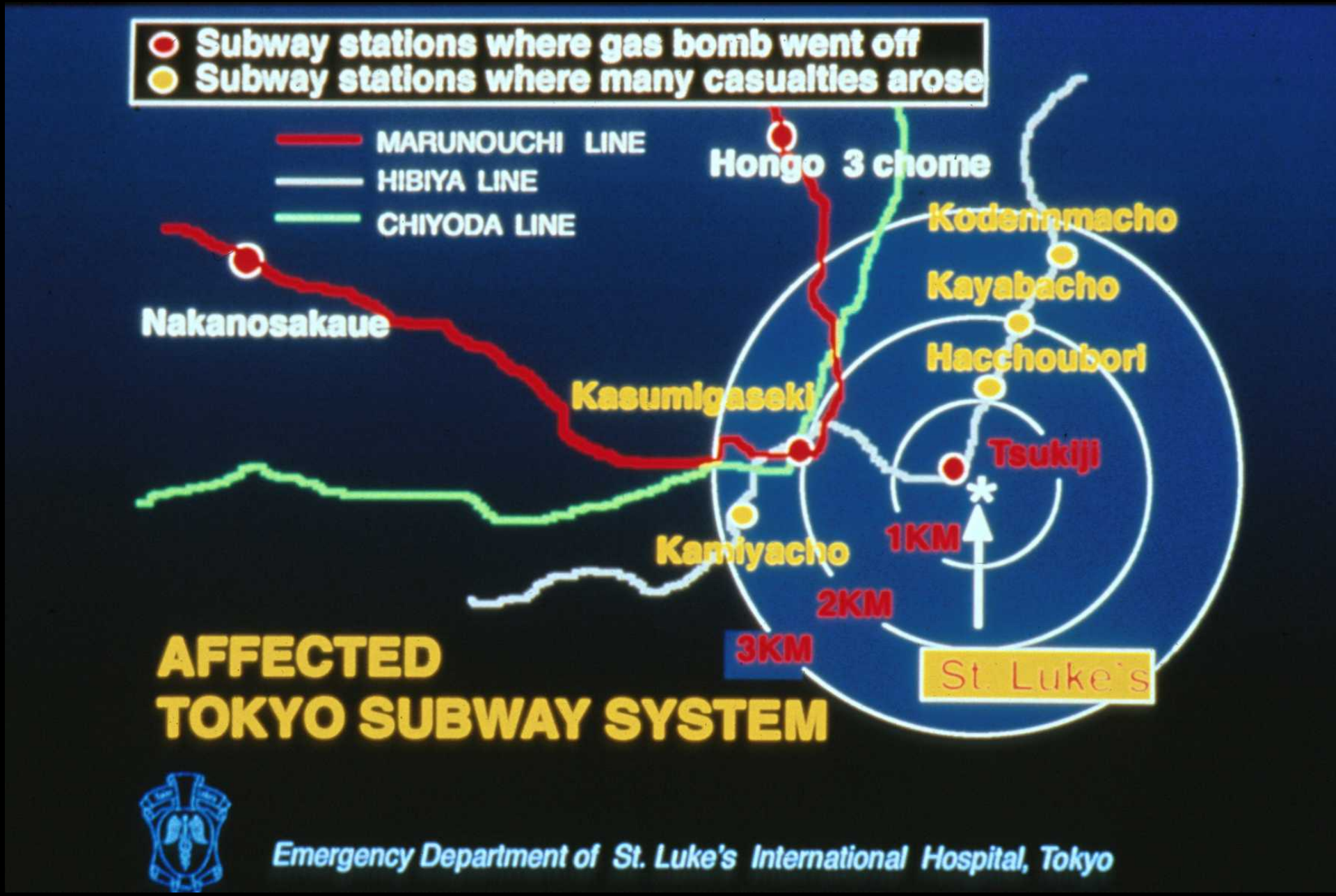
most easily detected in water and other samples

Tokyo, Japan; 20 March 1995

5 sarin releases within subway lines. 5 men released sarin; 5 get-away drivers. Release during rush hour peak.

Sarin in ~ 1 liter plastic bags wrapped in news-paper. Bags dropped at various stations and punctured with tip of umbrella. Sarin spread on floor and volatized into air.

8 deaths, 275 seriously injured, about 700 transported by ambulance, > 5,000 seen at hospitals.


Subway stations where gas bomb went off
Subway stations where many casualties arose
MARUNOUCHI LINE
HIBIYA LINE
CHIYODA LINE
Hongo 3 chome
Kodemmacho
Kayabacho
Hacchoubori
Nakanosakaue
Kasumigaseki
Tsukiji
Kamiyacho
1KM
2KM
3KM
St. Luke's
AFFECTED
TOKYO SUBWAY SYSTEM
Emergency Department of St. Luke's International Hospital, Tokyo


20
外來小手術室


神谷町駅
Kamiyacho Sta.

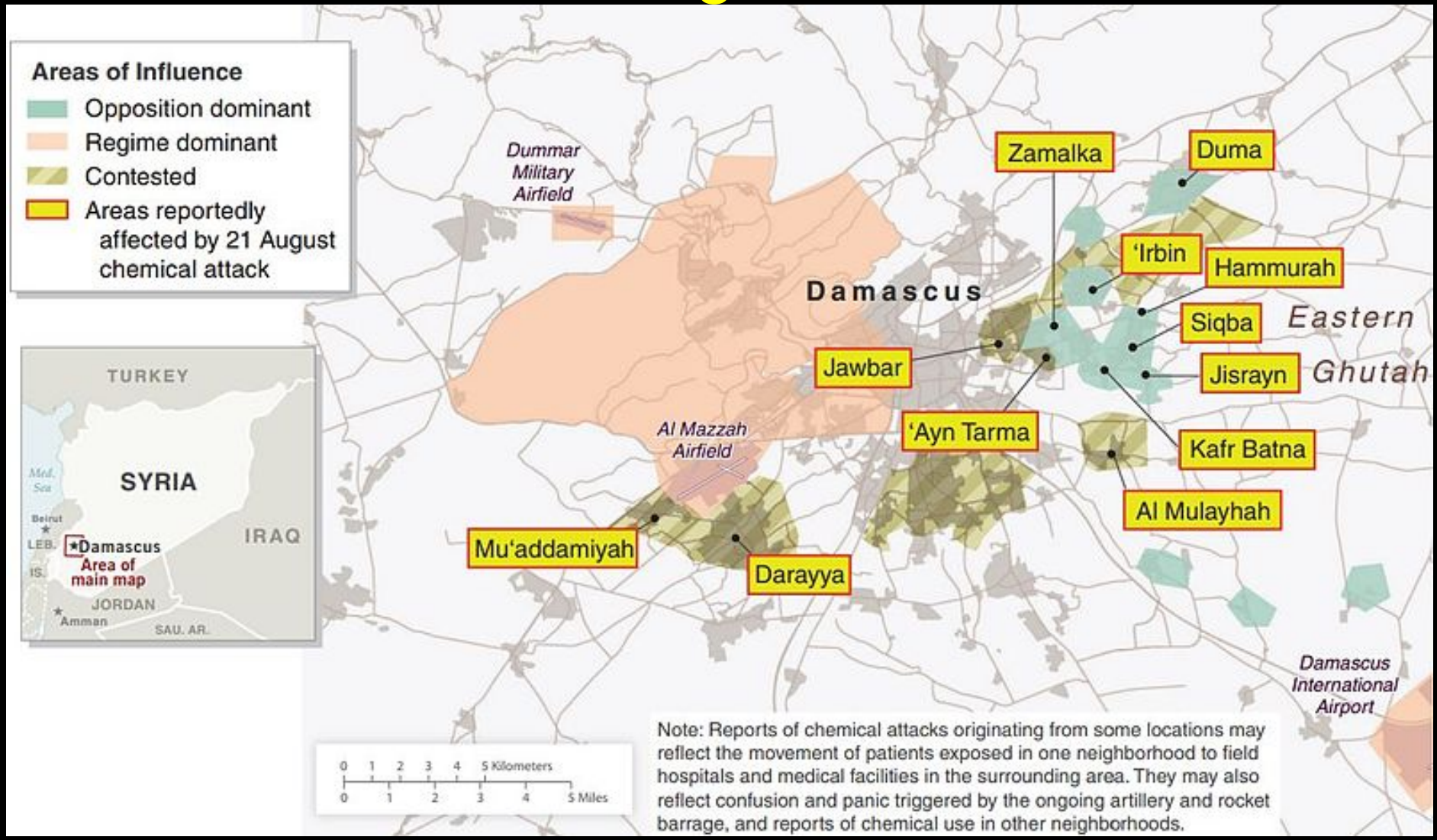
theguardian

UK and France claim Syrian attack victims have tested positive for sarin

British and French governments say they have shown evidence of chemical weapon use to UN investigation

Ian Sample, science correspondent, and Julian Borger
The Guardian, Tuesday 4 June 2013

Ghouta, Syria
21 Aug 2013



Wikipedia


الفوطة
الشرقية

United Nations Mission to Investigate Allegations of the Use of Chemical Weapons in the Syrian Arab Republic

Report on the Alleged Use of Chemical Weapons in the Ghouta Area of Damascus on 21 August 2013

SN	Sampling date	Sample code		Result laboratory 1			Result laboratory 2			Description of the sampling
				CW Agent	Degradation or and by-Products	Other interesting chemical	CW Agent	Degradation Products	Other interesting chemical	
14	28/08/2013	OISDS	DCM ex	None	IPMPA DIMP		GB	DIMP	Ethyl isopropyl methylphosphonate Hexamethylentetramine	A metal fragment found on the roof of the building.
			MeOH ex	None	IPMPA DIMP		None	IPMPA DIMP	Hexafluoro phosphate	
15	28/08/2013	06WPS		None	IPMPA DIMP		GB	DIMP	Hexamethylentetramine	A methanol wipe sample taken from a metal fragment found on the roof of the building.
16	28/08/2013	03WPS		None	IPMPA DIMP		GB	DIMP	Hexamethylentetramine Isopropyl methyl methylphosphonate	A dichloromethane wipe sample taken from a metal fragment found on the roof of the building.
17	28/08/2013	02SLS		None	IPMPA DIMP		GB	DIMP	Ethyl isopropyl methylphosphonate Isopropyl methyl methylphosphonate Isopropyl propyl methylphosphonate Trinitrotoluene Hexamethylentetramine	Rubble taken from the impact point on the roof of the building.

Of the 34 blood samples tested, 91% tested positive for Sarin exposure in Laboratory 4 and 85% tested positive in Laboratory 3 (Table 2). There was discordance of results for two samples only. A slightly higher percentage of samples from Moadamiyah were positive (Laboratory 4 100% and Laboratory 3 93%) than from Zamalka (Laboratory 4 91% and Laboratory 3 85%).

Table 2: Results of biomedical testing

	Laboratory 3				Laboratory 4			
	Plasma		Urine		Plasma		Urine	
	Number	%	Number	%	Number	%	Number	%
Moadamiyah								
Positive	14	93%	N/A	N/A	15	100%	4	100%
Negative	1	7%	N/A	N/A	0	0%	0	0%
Total	15	100%			15	100%	4	100%
Zamalka								
Positive	15	79%	N/A	N/A	16	84%	10	91%
Negative	4	21%	N/A	N/A	3	16%	1	9%
Total	19	100%			19	100%	11	100%
Combined totals								
Positive	29	85%	N/A	N/A	31	91%	14	93%
Negative	5	15%	N/A	N/A	3	9%	1	7%
Total	34	100%			34	100%	15	100%

Feb 2017

North Korea used VX agent to kill Kim Jong un's brother: US

Kim Jong Nam

Kuala Lumpur International Airport, Sepang, Malaysia, 26 Feb 2017

Witnesses testify VX killed brother of North Korean leader

DR. NIK MOHAMAD ADZRUL ARIFF RAJA AZLAN, airport clinic physician

Nik continued his testimony from Monday, in which he described how Kim arrived at the airport clinic conscious but in pain, with very high blood pressure and pulse. He said Kim then had seizure-like symptoms and his blood pressure, blood oxygen level and pulse plunged. Nik said he injected Kim with atropine, a standard procedure to boost slow heart rates, and said he did not know at the time that it is also a treatment for counteracting VX and other nerve agents.

Nik said he also inserted a tube into Kim's trachea to improve his oxygen level, and that stabilized Kim's blood pressure and oxygen level so he could be transported to the hospital.

DR. NUR ASHIKIN OTHMAN, chemical pathologist at Kuala Lumpur Hospital

Nur Ashikin said Kim's blood had a very low level of 344 units per liter of cholinesterase, an enzyme used to break down neurotransmitters in the body that send signals to the brain and control the muscles. The normal level is above 5,300 units per liter, she said.

THE WALL STREET JOURNAL

Ex-Russian spy was poisoned by nerve agent, British police say

Published: Mar 8, 2018 2:45 a.m. ET

LONDON — A former Russian spy and his daughter were poisoned by a nerve agent, police said Wednesday, in an attack on British soil that has strained relations between London and the Kremlin.

Sergei Skripal, a 66-year-old former colonel in Russian military intelligence, and his 33-year-old daughter, Yulia, were in critical condition being found unconscious on a bench outside a shopping mall in southwestern England on Sunday afternoon.

A police officer responded to the collapsed pair also visited Skripal's home became critically ill and was hospitalized. It is believed he was contaminated at the home. Doctor at scene (benches) was unaffected.

Reported to be neither VX nor sarin.

Sergei Skripal

Russian spy attack: focus falls on Salisbury cemetery

Hundreds of troops arrive on streets and experts in hazmat suits work near grave of Sergei Skripal's wife

▲ A tent used by police investigators covers the memorial for Alexander Skripal. Photograph: Peter Nicholls/Reuters

Almost 200 members of the armed forces arrived on the streets of Salisbury on Friday to support police investigating the nerve agent attack on a Russian former spy and his daughter, as attention focused on the cemetery where the remains of Sergei Skripal's wife and son lie.

In extraordinary scenes at the city's London Road cemetery that indicated the investigation was gathering pace, experts in full hazmat suits helped set up tents over the grave of Liudmila Skripal and the memorial of Alexander Skripal, who both died in recent years.

Across the city, soldiers, bomb disposal specialists, marines and RAF personnel were called in to help secure vehicles and scenes that may have been contaminated and to take the pressure off the police. The new deployment included experts in chemical warfare.

новичок agents

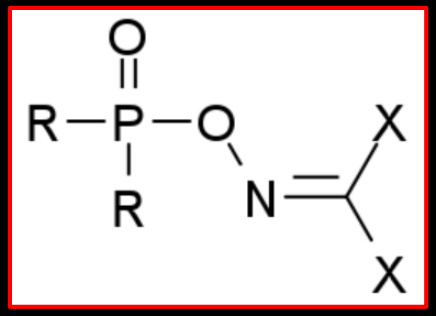
More than 200 organophosphate nerve agents designed in 1970s - 1990s in Russia.

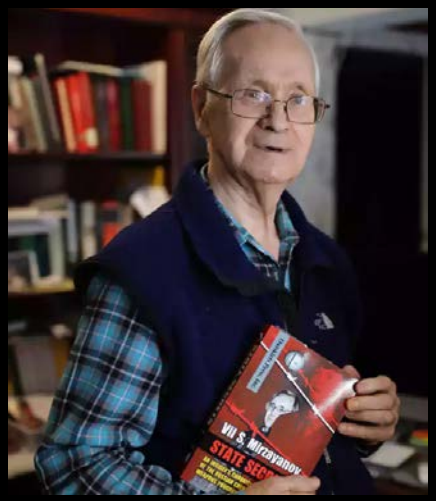
Can be delivered in powder form.

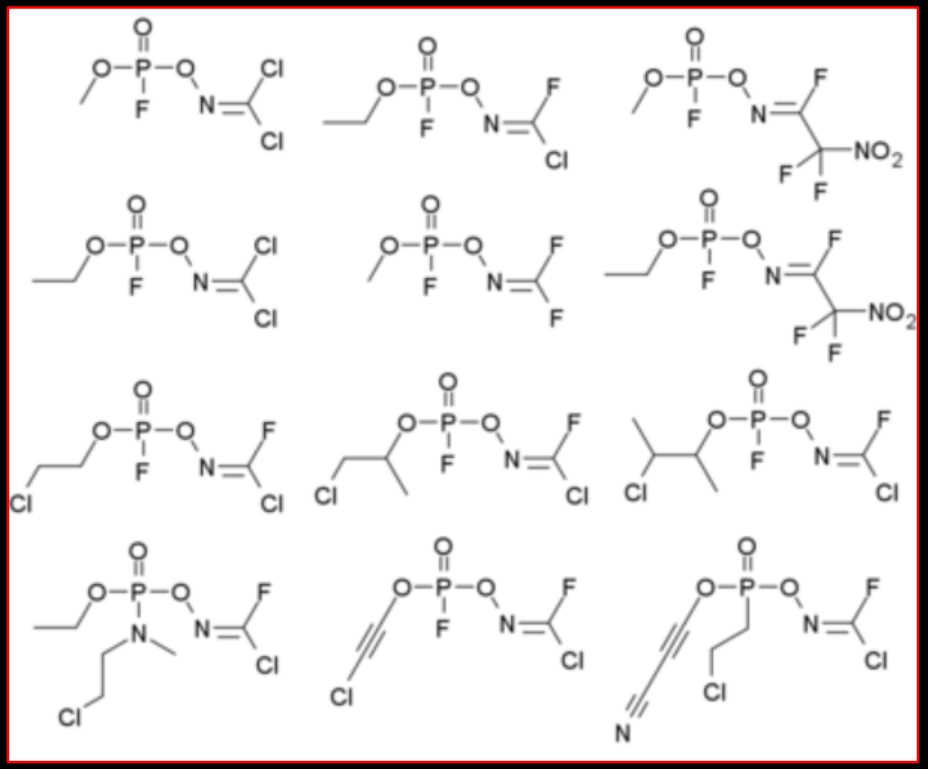
At least some can be binary weapons with precursors that are not banned by the chemical weapon treaty.

Developed in facility in present-day Uzbekistan.

Mainly described by Vil Mirzayanov, a Russian chemist.



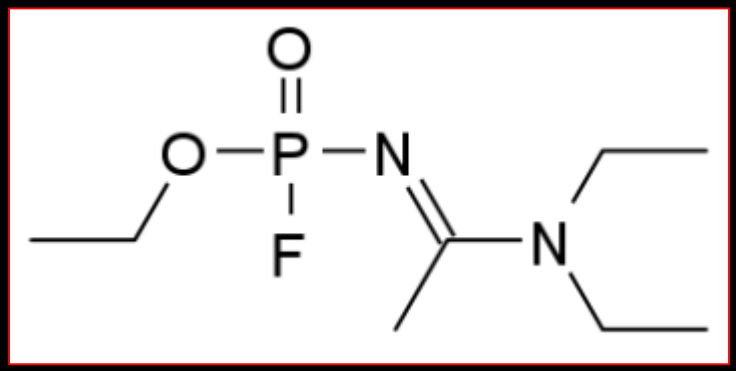




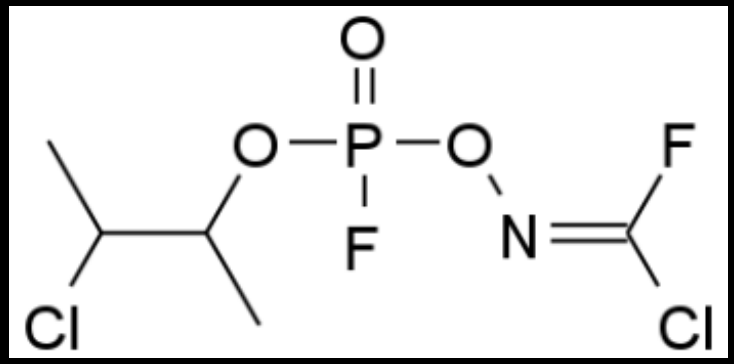
Suitcase spy poisoning plot: nerve agent 'was planted in luggage of Sergei Skripal's daughter'

The Telegraph

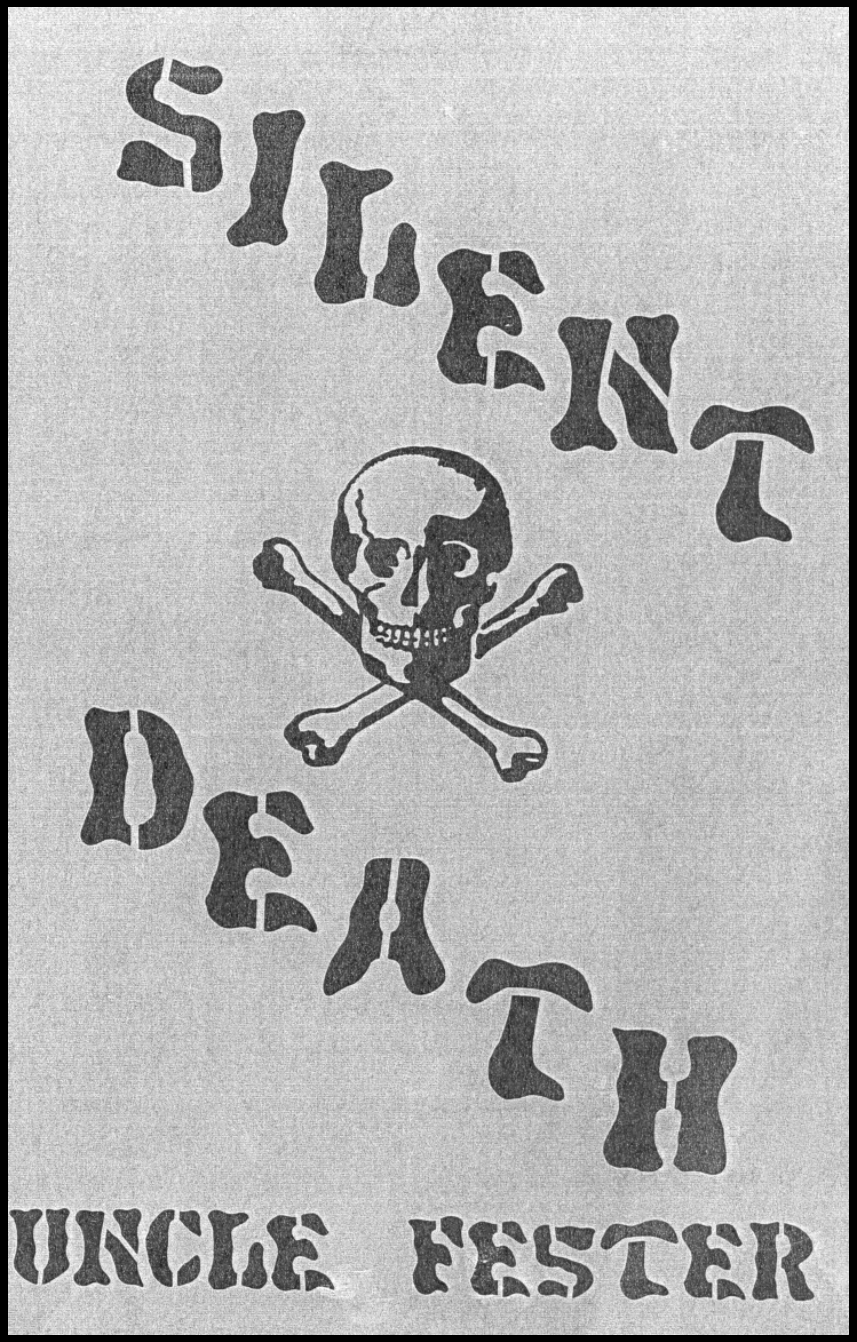
March 15, 2018



Mirzyanov: A-234



Hoenig & Ellison: A-234



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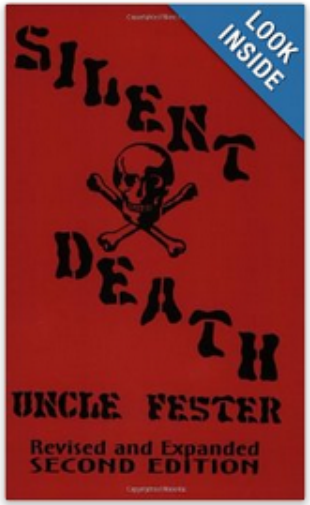

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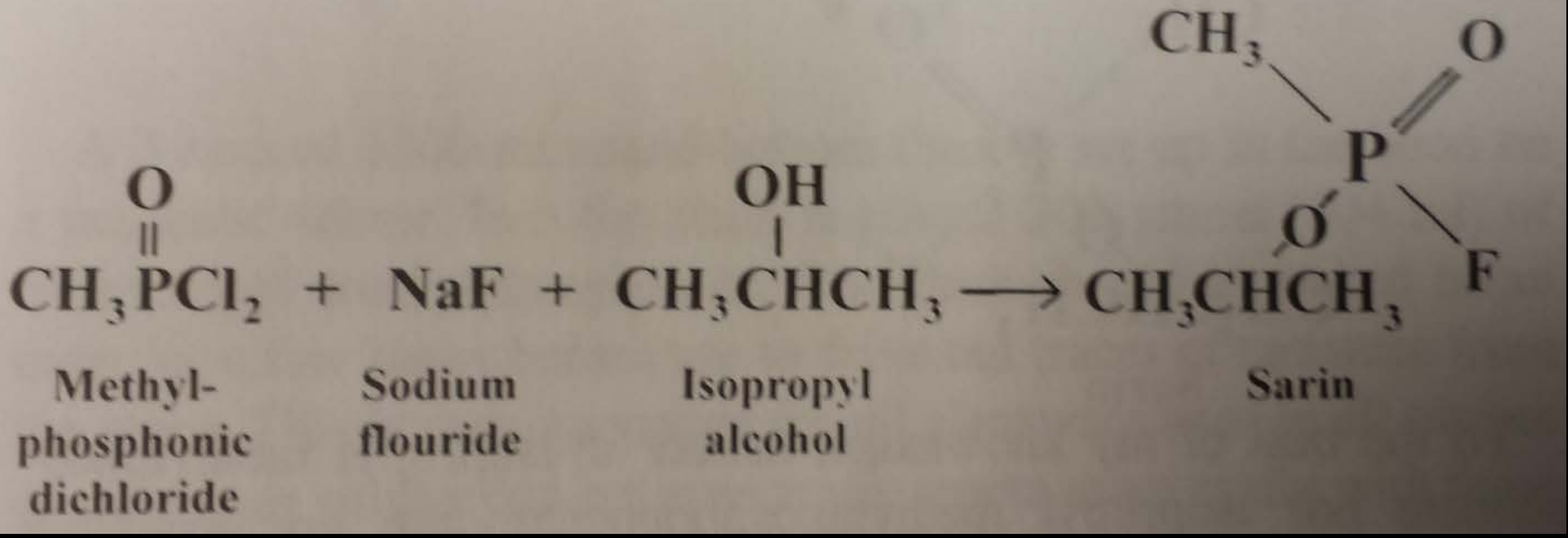
Chapter Four
NERVE GAS: THE POOR MAN'S ATOM BOMB

Ever since the detonation of the first atomic weapon in 1945, the top priority of each nation that came to possess these weapons has been to keep other "less responsible" nations from gaining access to these weapons, and above all to prevent their falling into the hands of private "terrorists." The very idea of some group putting together a "basement nuke" and dangling this weapon of decision over their heads is the ultimate nightmare for these "responsible" nuclear criminals.

All this concern is quite understandable, since nuclear weapons are extraordinarily spectacular and very macho. However, there is another weapon of mass destruction that is just as devastating to human life. A well-placed nerve gas bomb of sufficient size could inflict a death toll on a city comparable to that of a medium-sized nuke.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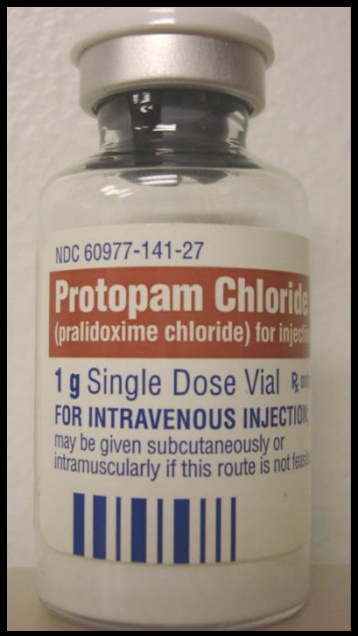

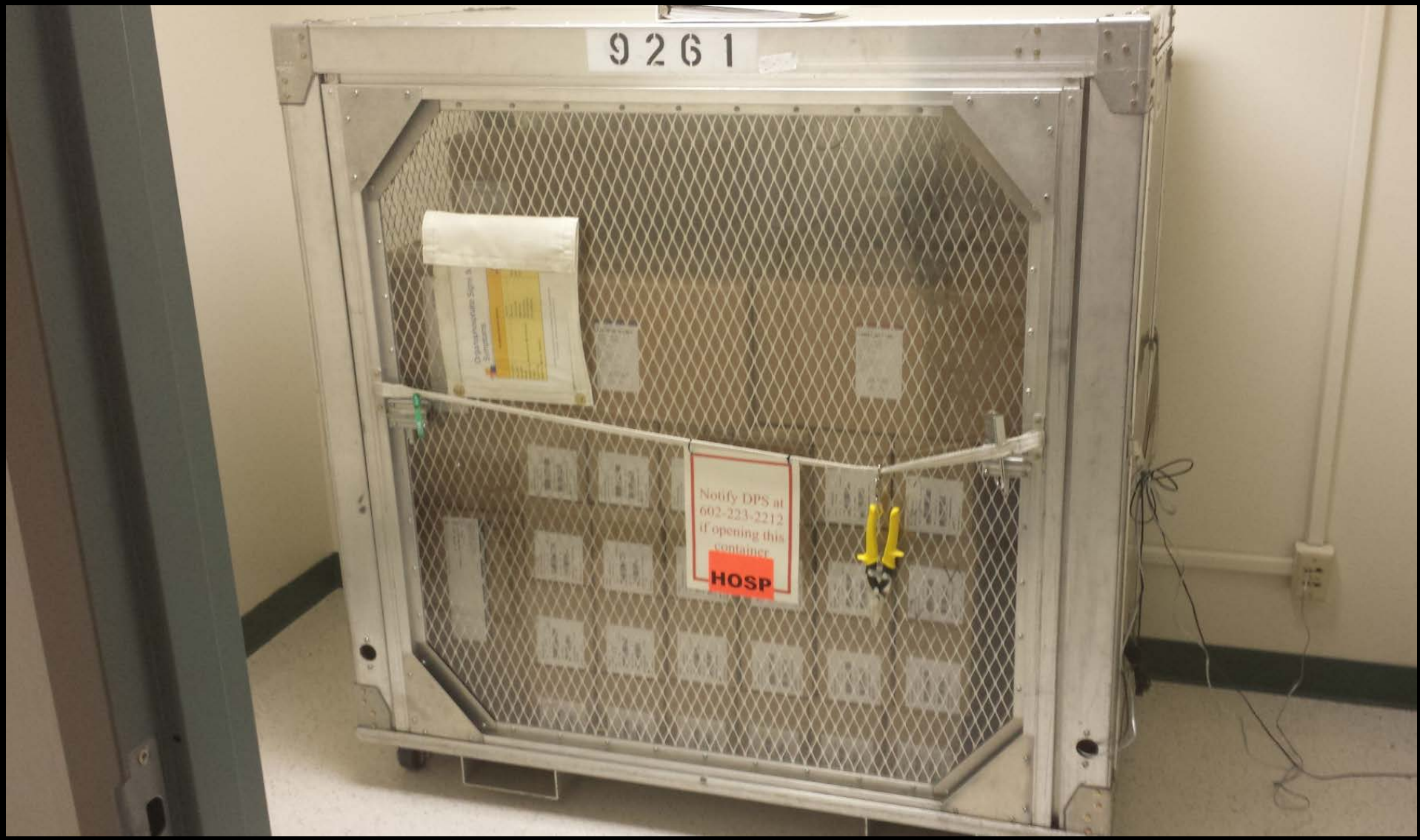
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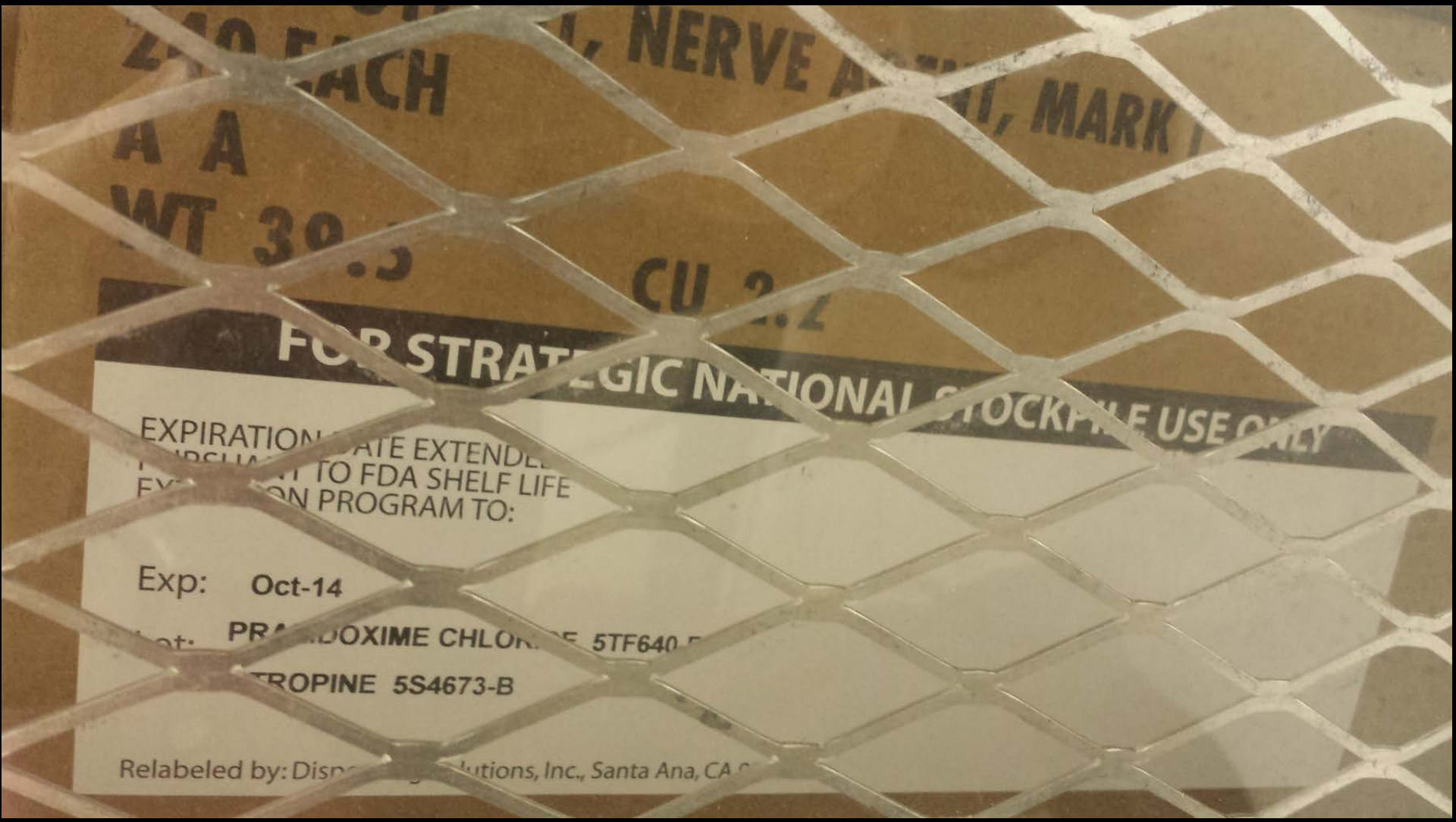
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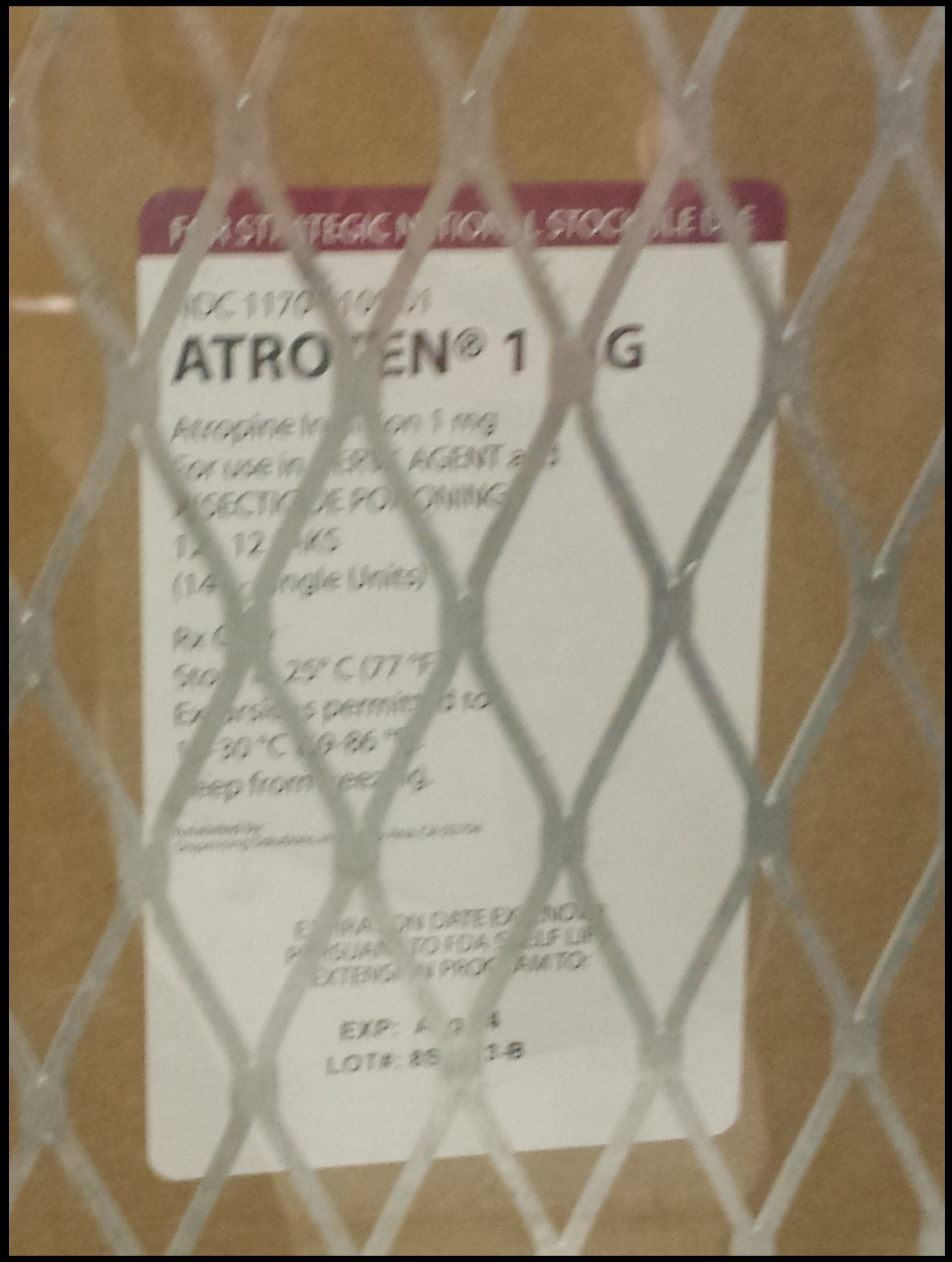
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