Introduction to Chemical and Biological Terrorism

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YALE NEW HAVEN CENTER FOR EMERGENCY PREPAREDNESS AND DISASTER RESPONSE

What can we accomplish in 45 min?

- Solely an introduction
- History of use – this is real
- Approach/mindset
  - Useful for more routine HazMat and outbreaks
- Some places to get help
- A few examples

Objectives

- 1 . Discuss an organized approach to gathering data from a patient presenting for care after a chemical exposure (ie. discuss the signs that help one recognize toxidromes and biological agent syndromes).
- 2. List at least two of the six main classifications of chemical agents.
- 3. Compare and contrast infection versus intoxication.

Past Events

- Accidents
- Weapons - military / genocide
- Agents of Terror – instill fear

- Individuals – assassination
- Populations
  - Internal
  - External

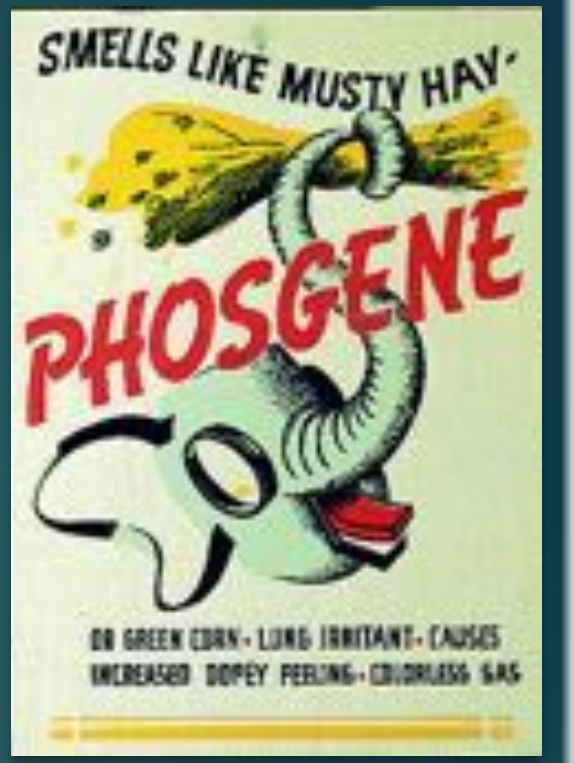
Ancient History

Ancient Greek: toxon = arrow (ancient Persian: taxa)
Cultivation of aconitum spp. banned in Rome

- ?2000 BC — Aconitine is used, perhaps as arrow poison
  - Cultivation of Aconitum is banned in ancient Rome
- 600-200 BC — Athenian, Spartan and Carthaginian forces used poison and smoke to quell enemies
- ~400 BC — Spartans killed thousands of Athenians
  Trichothecene mycotoxins? Ebola? Marburg?
- ~100 BC — 1000 of Pompeii's forces poisoned by toxic honey
- …

History – Chem

- WWI 3% of casualties caused by chemical weapons (CW). Chlorine first used in 1915, sulfur mustard in 1917
- 1925 Geneva Protocol bans use of chemical weapons
- 1935-36 Italy reportedly used chemical weapons in Ethiopia
- WWII Japan reportedly used CW in China and Germany reportedly used Cl2, $COCl_2$ and sulfur mustard; use of "Zyklon B" (cyanide) in Germany
- 1980s Iraqi Army against Iraqi Kurds, confirmed in soil samples
- 1981-88 Sulfur mustard and nerve agents mostly by Iraq against Iran
- 1992 Chemical Weapons Convention banned chemical weapons
- 1995 Aum Shinrikyo uses sarin in Tokyo subways 9 mos. after attack in Matsumoto
- 2003-04 Ricin confirmed in Dirksen Senate Office Building, in a mailed parcel in SC; London police foil ricin plot



CNN World ▸ Africa | Americas | Asia | Australia | Europe | Middle East | UK Live TV

Remaining members of Japan's doomsday cult executed

By Euan McKirdy, Yoko Wakatsuki and James Griffiths, CNN

Updated 12:21 AM ET, Thu July 26, 2018

Shoko Asahara, head of the doomsday cult Aum Shinrikyo, is transferred from Tokyo police headquarters to Tokyo District Court for questioning in July 1995.

History – Bio

- ~1300s Armies use infected/rotting bodies to transmit infection
- 1700s British troops reportedly use smallpox contaminated blankets against Native Americans
- WWI Germany reportedly infects Allied livestock with anthrax and glanders to disrupt Allied food supply
- 1925 Geneva protocol bans use of biological weapons
- 1928 USSR launches its bioweapons program
- 1932-45 Japan reportedly conducts bioweapons research and tests on human subjects
- WWII Japan reportedly attacks 11 Chinese cities with cholera, anthrax and plague; Allies trial anthrax
- 1950s US and USSR research novel bioweapons dispersal
- 1969-70 Nixon orders dismantling of US bioweapons program
- 1972 Biological Weapons Convention bans bioweapons
- 1980s Soviet Union continues bioweapons research

Mexico 1520

Spanish Conquistadors introduced smallpox to the New World via a ship landed in Hispaniola. Spread occurs to mainland in 2 years, resulting in the decimation of the Aztec population after several outbreaks over the next century.

Hernando Cortés

By 1520 Tenochtitlan was under siege by Cortés and the people were both starving and dying from smallpox. Bernal Diaz, Cortés' chronicler, described the scenes in the city:

"We could not walk without treading on the bodies and heads of dead Indians. I have read about the destruction of Jerusalem, but I do not think the mortality was greater there than here in Mexico. Indeed, the stench was so bad that no one could endure it…and even Cortés was ill from the odours which assailed his nostrils."

Aztec Emperor Moctezuma

South America 16th Century

Spanish explorer Pizarro conquest of Inca's of South America in the 16th Century was allegedly aided by presenting the natives with gifts of clothing contaminated with smallpox. In any case, infectious diseases, principally smallpox and measles caused a decline in population of ~93% between 1524 and 1591.

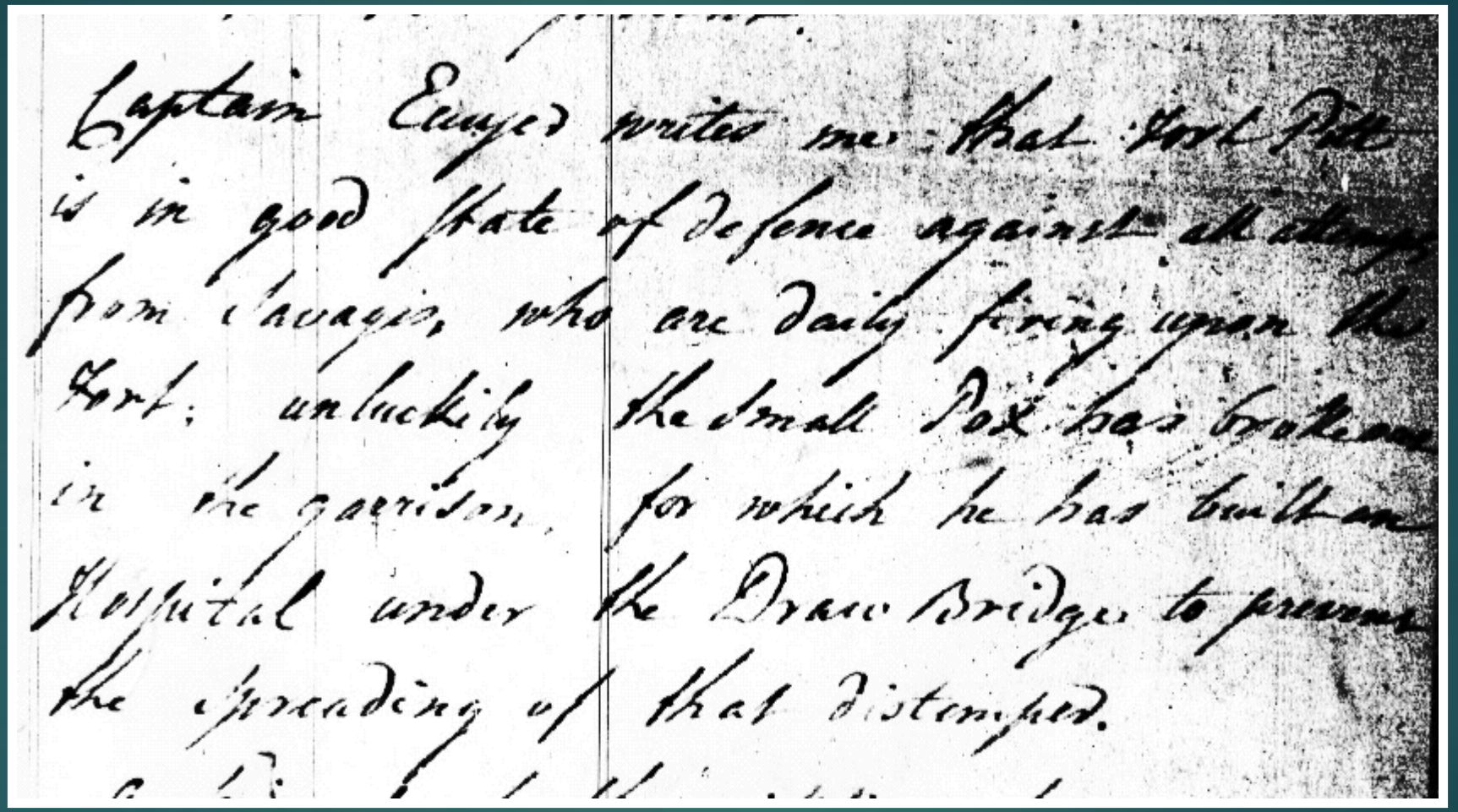
French – Indian Wars 1763

British General Sir Jeffrey Amherst

Swiss Colonel Henry Bouquet

British Army provided Delaware Native Americans, who were loyal to the French, with blankets and handkerchiefs taken from smallpox hospitals. The smallpox epidemic decimated the Indian tribes, and the British successfully attacked Fort Carillion which they rename Fort Ticonderoga.

Sir Jeffrey Amherst writes of the drawback of using smallpox:


Captain Ecuyer writes me that Fort Pitt
is in good state of defence against all attempts
from Savages, who are daily seen upon the
Fort; unluckily the small Pox has broke out
in the garrison, for which he has built an
Hospital under the Draw Bridge, to prevent
the spreading of that distemper.

"Unluckily, the small pox has broken out in the garrison…"

The American Revolution

A similar strategy of deliberately infecting adversaries with smallpox was used during the Revolutionary War by smallpox-immune colonists, whose vaccinations against smallpox had been made mandatory by General George Washington.

Eitzen Edward et al. “Historical Overview of Biological Warfare,” Chapter 18, *Medical Aspects of Chemical and Biological Warfare*, p.417.

GENERAL GEORGE WASHINGTON

Japan 1930's

JAPANESE LIEUTENANT SHIRO ISHII, MD, PHD

Champions the use of bacteriological warfare as a strategic edge for the Japanese Empire.

Surgeon General Shirō Ishii (1892 – 1959) was a Japanese Army medical officer, microbiologist and the director of Unit 731, a biological warfare unit of the Imperial Japanese Army involved in forced and frequently lethal human experimentation during the Second Sino-Japanese War (1937–1945).

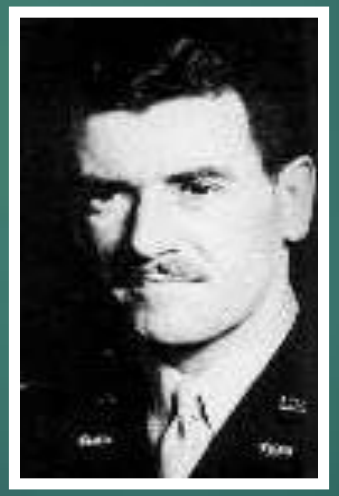
Like many other former scientists at Unit 731, he was granted immunity and recruited by the United States to conduct more research after the WW II ended.

General Ishii gives orders for his officers and staff to flee, for Pingfan to be completely destroyed, and for all prisoners to be executed immediately.

All that remained were the smokestacks of the crematoriums used to dispose of the remains of prisoners.

Top Secret Post-War Deal

General Douglas MacArthur
Supreme Commander
of Allied Powers



LTC Murray Sanders
US Army Chemical Services
Dispatched to investigate Japanese
BW allegations.

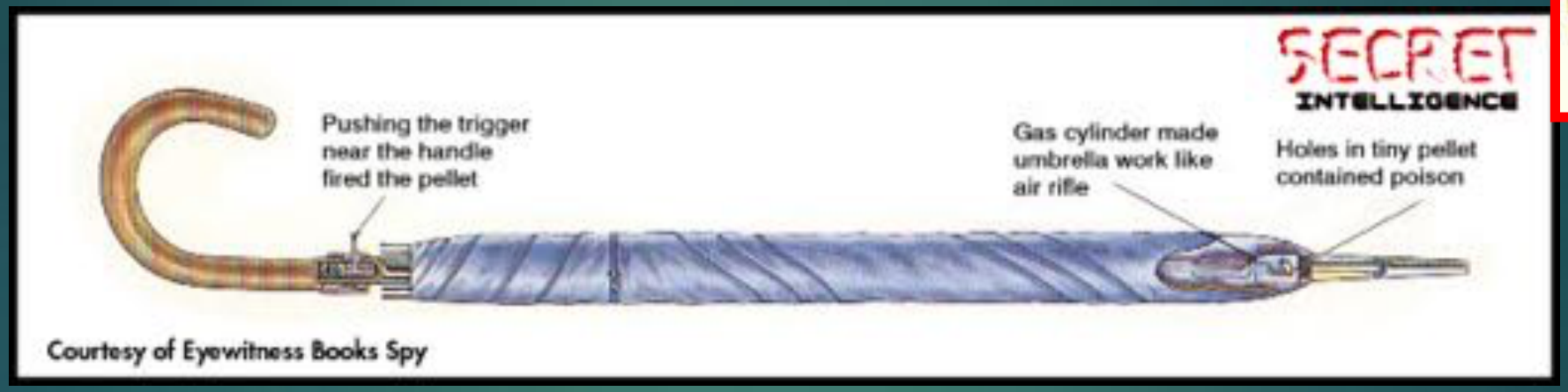
Lt. General Ishii Shiro
Commander of Unit 731

Recent History

- "The chemical warfare legacy of the Yemen war"
  - Chemical weapons use in the modern Middle East began with the Yemen War of 1962-1967. Egyptian chemical attacks against hostile Yemeni tribesmen were initiated at a modest and fairly ineffective level in 1963. They became deadlier, however, as time went on and the scope of the Egyptian military presence in Yemen (later North Yemen) expanded. Had it not been for the Egyptian military defeat in the June 1967 war with Israel, chemical attacks could have become a fundamental part of Egyptian strategy for defeating the Yemenis.

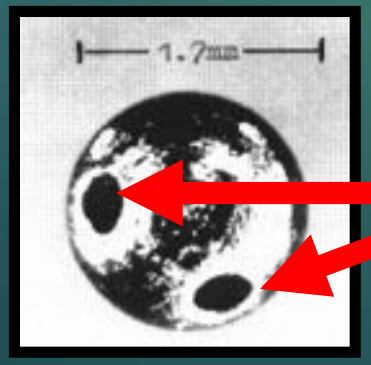
    - Comparative Strategy 10(2):109-119 · April 1991

Assassination of Georgi Markov
London, September 1978



Umbrella weapon designed by KGB Special Operations Office

5 Hr: Weak, dizzy
35 hr: Febrile, tachycardic, Lymphadenopathy
2 d: hypotension
3 d: anuric, hematemesis, heart block, death



1.7mm pellet with holes drilled to hold ricin grains

Top Secret Soviet Offensive BW Program

Биопрепарат

The All-Union Production Association Biopreparat

Biopreparat HQs Moscow

- ESTABLISHED IN 1973
- 32,000 WORKERS
- 9,000 SCIENTISTS
- 40 R&D AND PRODUCTION FACILITIES
- 6 MAJOR RESEARCH LABS
- 5 MAJOR PRODUCTION FACILITIES

Биопрепарат

Soviet Secret BW Program Biopreparat

Vladimir Pasechnik
Defected to GB in 1989

Kenatjen Alibekov
Defected to US in 1992

WESTERN INTELLIGENCE REMAINED COMPLETELY UNAWARE OF THE MASSIVE, SECRET SOVIET OFFENSIVE BW PROGRAM UNTIL THE DEFECTION OF TWO SENIOR BIOPREPARAT SCIENTISTS.

Secret Soviet BW Program, 1979

Sverdlovsk, USSR

(Ekaterinburg, Russia)

April 4, 1979

Dr. Marguerita Ilyenko
Chief Physician
City Hospital No.24
Sverdlovsk, USSR

YEKATERINBURG, Russia – On April 4, 1979, the chief physician of Hospital No. 24, Margarita Ilyenko, got a surprising phone call. A doctor at a neighboring hospital reported two unusual deaths that day and asked, "Are any of your patients dying?"

Soviets report 66 deaths due to gastrointestinal anthrax from "Tainted Meat"

Anthrax victims secretly buried in a corner of a Soviet cemetery accompanied by KGB officers and secured by military forces. Some sources report over 100 related deaths.

Dr. Faina Abromova
Sverdlovsk Pathologist

Brain on autopsy showing classic "Cardinal's Cap" of anthrax

However, pathologist Dr. Faina Abramova soon discovered that the epidemic of deaths was not due to gastrointestinal anthrax from tainted meat as the officials insisted, but *inhalation anthrax* instead.

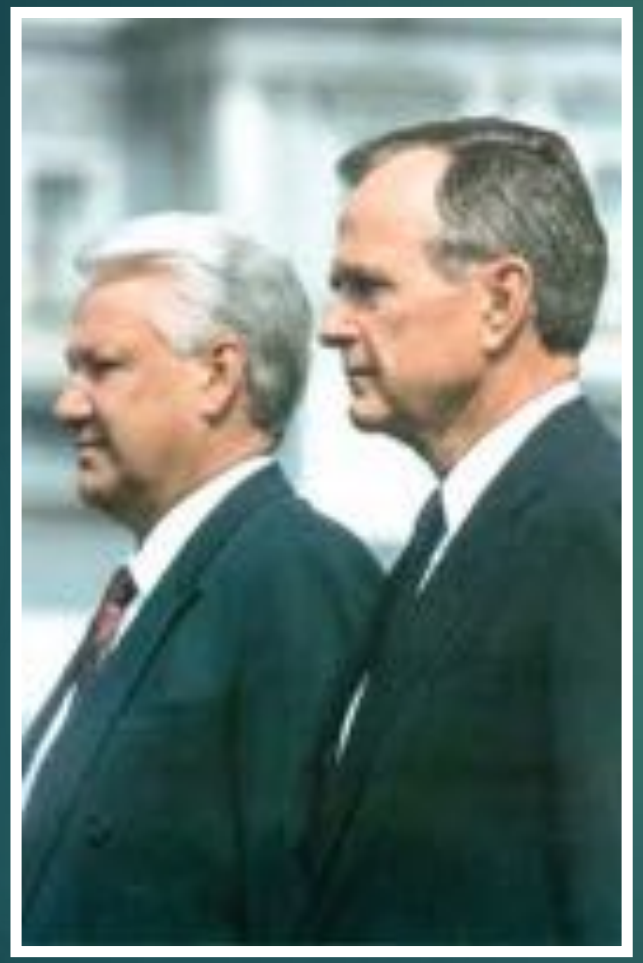
Anthrax Spores

Sverdlovsk, USSR 1979

Military Compound No.19

Plot of anthrax victims locations illustrates 50+ km plume

1992



Boris Yeltsin and George Bush at Camp David

Shortly after the 1992 Camp David visit with President Bush, Boris Yeltsin publicly announces that the outbreak of pulmonary anthrax in the city of Sverdlovsk in 1979 was due to an accidental release from a BW facility.

Saddam Hussein (1937–2006) initiated an extensive **biological weapons (BW) program in Iraq** in the early 1980s, in violation of the Biological Weapons Convention (BWC) of 1972. Details of the BW program—along with a chemical weapons program—surfaced only in the wake of the Gulf War (1990–91) following investigations conducted by the United Nations Special Commission (UNSCOM) which had been charged with the post-war disarmament of Saddam's Iraq. By the end of the war, program scientists had investigated the BW potential of five bacterial strains, one fungal strain, five types of virus, and four toxins.[1] Of these, three—anthrax, botulinum and aflatoxin—had proceeded to weaponization for deployment.[2]

https://en.wikipedia.org/wiki/Iraqi_biological_weapons_program

Saddam Hussein reportedly “gases” Kurds, 1989

Iraq July, 1995

FOLLOWING THE DEFECTION OF IRAQI GENERAL HUSSEIN KAMAL HASSAN, HEAD OF IRAQ'S MILITARY INDUSTRIAL PROGRAM, IRAQI AUTHORITIES ADMIT TO HAVING EXTENSIVE BW WEAPONS, TONS OF STORED AGENTS AND SIGNIFICANT R&D CAPABILITIES.

Inspections

Because of the UN disarmament program that followed the war, more is known today about the once-secret bioweapons program in Iraq than that of any other nation.

UNSCOM INSPECTORS, UNDER THE DIRECTION OF HANS BLIX, CONTINUED TO INSPECT IRAQ FOR EVIDENCE OF WMD AND COMPLIANCE WITH UN SECURITY COUNCIL RESOLUTION 687.

George Mason University Unveils Center for Biodefense; Scientists Kenneth Alibek, Charles Bailey to Direct

Feb. 14, 2002

MANASSAS, Va.---George Mason University announced today the creation of a Center for Biodefense to address issues related to the broad array of challenges to national and international security posed by the threats of biological terrorism and the proliferation of biological weapons. Kenneth Alibek, former first deputy chief of the civilian branch of the Soviet Union's Offensive Biological Weapons Program, and Charles Bailey, former commander for Research at the U.S. Army Medical Research Institute of Infectious Diseases, serve as executive administrators of the center.

In the late 1970s and 1980s, Alibekov oversaw projects that included weaponizing glanders and Marburg hemorrhagic fever, and created Russia's first tularemia bomb. Perhaps his signal accomplishment was the creation of a new "battle strain" of anthrax, known as "Strain 836", later hailed by the *Los Angeles Times* as "the most virulent and vicious strain of anthrax known to man".

Alibek resigned as executive director of GMU's National Center for Biodefense and Infectious Diseases in September 2006, despite his position as a tenured Distinguished Professor. According to a 2007 *Los Angeles Times* article, "Alibek said the college administration had grown displeased with his company's role in sharing grant-funded research. The university, he said, requested that he dismantle or leave AFG Biosolutions. He chose to resign from George Mason."

In 2010, by invitation he began working in Kazakhstan at Nazarbayev University in Kazakhstan. He published a number of articles in research journals and taught various courses in biology and medicine. He focuses on a possible role of chronic infections, metabolic disorders and immunosuppression on cancer development. He continues his work as a physician and research and educational professor. He keeps his American citizenship and residence and his family lives in the United States.

Authority control

Soviet biological weapons program

Weaponized agents	Smallpox · Anthrax · Plague · Botulism · Brucellosis · Glanders · Q fever · Staphylococcal Enterotoxin B · Tularemia · VEE · Marburg · Wheat stem rust · Rice blast
Researched agents	AHF · BHF · Bird flu · CHIKV · Dengue fever · EEE · Hantavirus · Lassa fever · Melioidosis · Newcastle disease · Plague · Potato blight · Psittacosis · Rinderpest · Typhus · WEE · Yellow fever
Operations and projects	Project Bonfire · Project Factor
Facilities and test sites	Biopreparat · State agricultural Scientific and Technical Institute · Institute of Ultra Pure Biochemical Preparations · VECTOR · Institute of Applied Biochemistry · Kirov bioweapons production facility · Zagorsk smallpox production facility · Berdsk bioweapons production facility · Obolensk bioweapons research facility · Military Compound 19 · Aralsk-7 (Vozrozhdeniya Island) · Institute of Virus Preparations · Protein laboratory of the Soviet secret services
Bioweaponeers	**Kanatjan Alibekov** (Ken Alibek) · Vladimir Pasechnik · Sergei Popov · Yuri Ovchinnikov · Igor Domaradskij · Nikolai Ustinov · Pyotr Burgasov
Accidents	Sverdlovsk anthrax leak · Aral smallpox incident
Related topics	Biological agent · Biological warfare (BW) · Entomological warfare · U.S. biological weapons program · History of biological warfare · Sanitary-epidemiological reconnaissance

Categories: American people of Kazakhstani descent | Kazakhstani emigrants to the United States | Kazakhstani scientists | Living people | People from Almaty Region | Siberian State Medical University alumni | Soviet biological weapons program | Soviet military doctors | Soviet microbiologists | The Heritage Foundation | 1950 births | 2001 anthrax attacks | 20th-century biologists

Current Events

- 2011: At the outbreak of the Syrian Civil War concerns were raised about the security of Syria's chemical weapon sites and about the potential use of chemical weapons. In July 2012, Syrian Foreign Ministry spokesman Jihad Makdissi stated: "No chemical or biological weapons will ever be used... “
- Aug. 20,2012: Obama "We have been very clear to the Assad regime… that a red line for us is we start seeing a whole bunch of chemical weapons moving around or being utilized.” In Sept. Syrian military moves chemical weapons from Damascus to Tartus, a port city.
- Sept. 2013: Congress authorizes use of military force, alternative is complete chem weapons surrender, Syria agrees. Destruction of declared weapons declared complete in June 2014.
- Aug. 17, 2017 *Reuters* publishes a report detailing the extent of Syria’s failure to abandon chemical weapons, citing information from investigators, inspectors and diplomatic sources.

https://en.wikipedia.org/wiki/Use_of_chemical_weapons_in_the_Syrian_Civil_War

Sarin, Cl_2, Mustard, ?

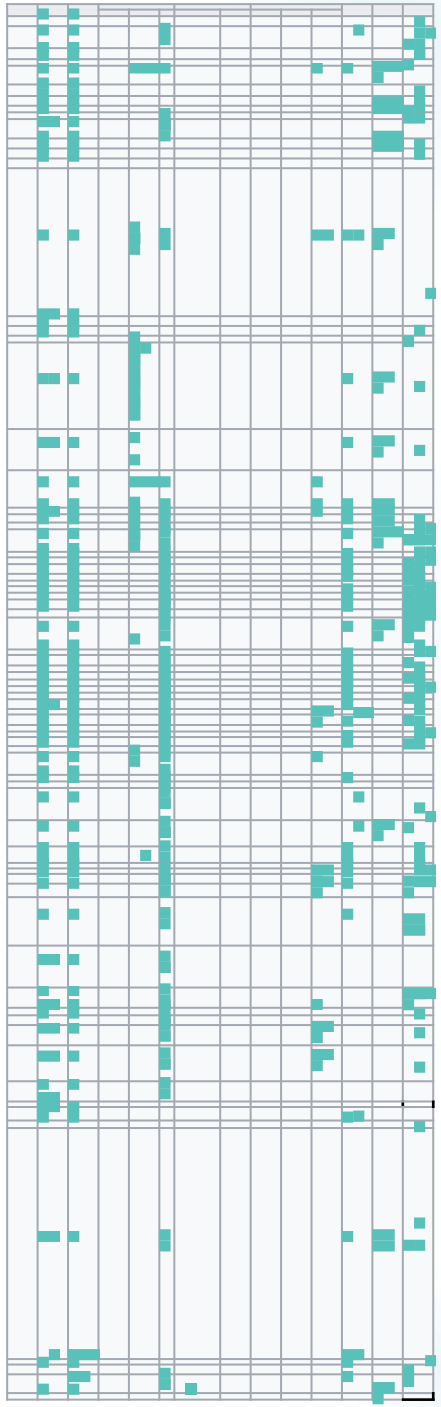
17 October 2012 – 7 April, 2018

Reported chemical weapons attacks, **Syria.**
The table below lists the reported attacks and the main points. See the main articles for details.

"Timeline of Syrian Chemical Weapons Activity, 2012-2018 | Arms Control Association"

"Third report of the Organization for the Prohibition of Chemical Weapons United Nations Joint Investigative Mechanism"

https://en.wikipedia.org/wiki/Use_of_chemical_weapons_in_the_Syrian_Civil_War



Biological Warfare vs. Bioterrorism

- Desirable BW agents
  - Massive casualties
  - Induce prolonged illness
  - Resource intensive
  - Specialized care needed
  - Inadequate detection
  - Communicable
  - Incubation period
  - Non-specific symptoms
  - Mimic endemic infectious disease

- Desirable BT agents
  - Induce terror

Intoxication vs. Infection

- Intoxication – manmade & natural
  - Immediacy of onset
  - Point source
  - Forward deployment of countermeasures
    - Force protection
    - Patient care
  - PPE
  - Decontamination
  - Person to person transmission unlikely
    - Especially unlikely by inhalation
- Infection – natural & bioengineered
  - Period of incubation
  - Person to person transmission
  - Contact tracing
  - Broad dissemination
    - Contact
    - Airborne
    - Droplet
  - Vaccination
  - Antibiotics

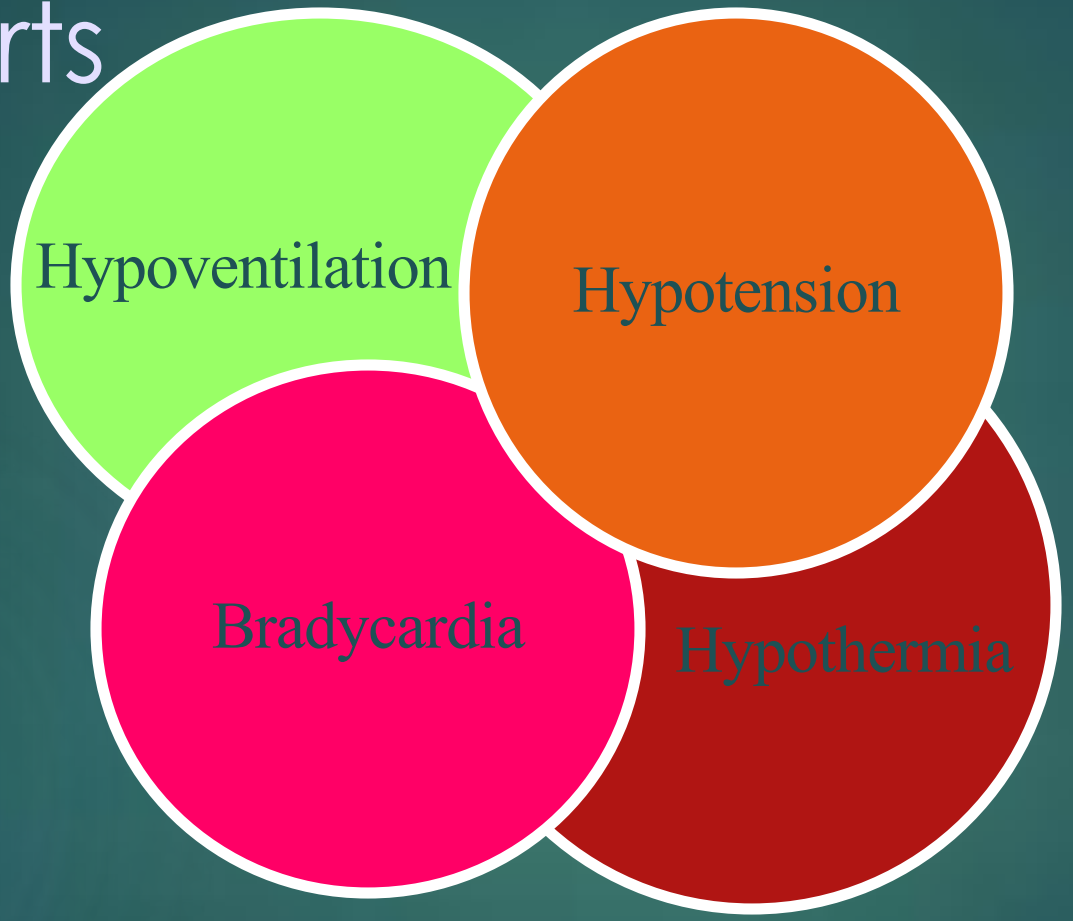
Identification, Testing & Response

- Resources:
  - Hospital lab: "send out"
  - Local HazMat teams
  - NG CSTs
  - State labs and epidemiologists
  - Poison Centers
  - CDC
  - Homeland Security
  - Selected Tools
    - M8, M9 paper
    - Draeger tubes
    - PID and other meters/monitors
    - Scintillation counters

Toxidrome

- A constellation of clinical clues to the identity of a poison.
  - Concept by Mofenson & Greensher, 1970.
- Present in whole or in part
- Vital signs, Mental Status, Symptoms, Signs, Labs

Toxidromes: In Whole or In Parts



Opioids: Add Altered Mental Status

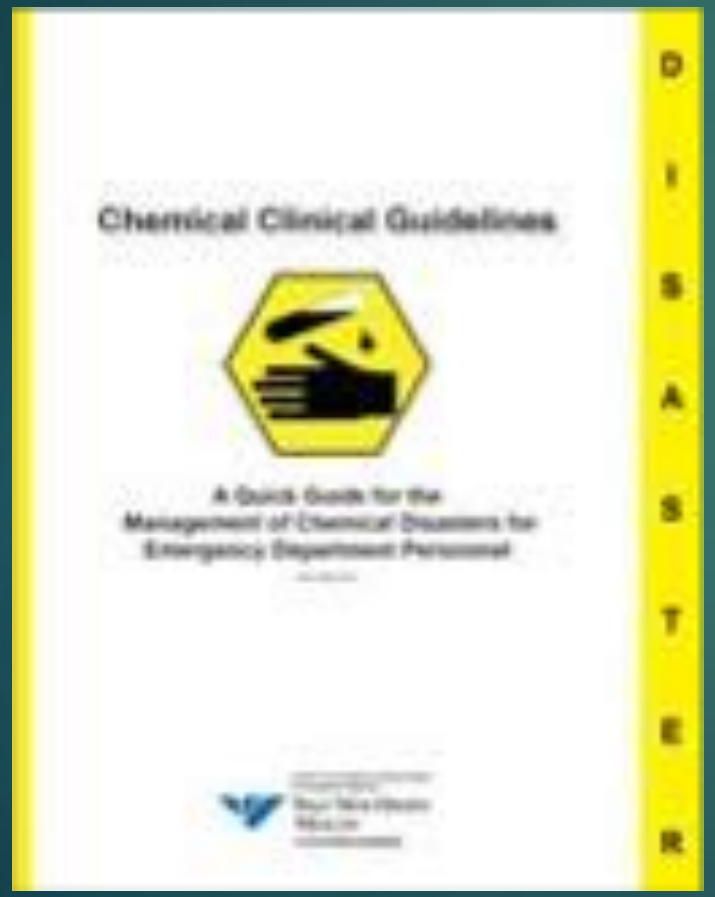
What's the poison? Putting the toxidrome together:

- Vital signs
  - T
  - P
  - R
  - BP
- What's the fifth vital sign?
- Other autonomic indicators:
  - Pupils, bowel sounds, secretions…

Chemical Agents

- Irritant gases / choking/ / lung agents (chlorine, phosgene, diphosgene)
- Chemical asphyxiants /blood agents (cyanide)
- Nerve agents (sarin, soman, cyclohexylsarin, tabun, VX)
- Incapacitating agents (anticholinergics and opioids)
- Lacrimating / riot control agents (tear gas, pepper spray)
- Vesicants / blistering agents (mustard, lewisite)
- Vomiting agents (adamsite)

Syndromic Recognition: the YNHH guidelines

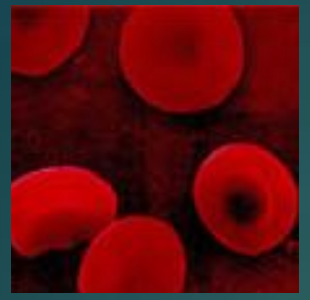


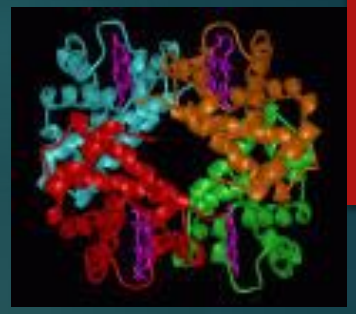
HAZMAT TOXIDROMES

TOXIDROME	TYPICAL TOXICANTS
Asphyxiant: Simple asphyxiant	Carbon dioxide (CO_2) Methane (CH_4) Propane (CH_3CH2CH_3) 
PREDOMINANT ROUTE OF EXPOSURE	PREDOMINANT TOXICODYNAMICS
Inhalation	Displacement of oxygen

HAZMAT TOXIDROMES

TOXIDROME	TYPICAL TOXICANTS
Asphyxiant: Systemic (chemical)	Isobutyl nitrite $[(CH3)_2CHCH_2NO_2]$ Carbon monoxide (CO) Hydrogen cyanide (HCN) Hydrogen sulfide (H_2S) Hydrogen azide (HN_3)
PREDOMINANT ROUTE OF EXPOSURE	PREDOMINANT TOXICODYNAMICS
Inhalation	Impaired O_2 transport or utilization



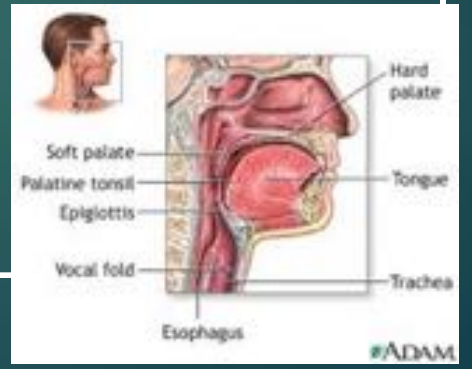


Hydrogen cyanide (HCN): affects heme & cytochrome oxidase

antidotes:

1) amyl nitrite, sodium nitrite + sodium thiosulfate
2) hydroxocobalamin, a form of vitamin B12

TOXIDROME	TYPICAL TOXICANTS
Irritant Gas: Highly water-soluble	Ammonia (NH_3) Formaldehyde (HCHO) Hydrogen chloride (HCl) Sulfur dioxide (SO_2)
PREDOMINANT ROUTE OF EXPOSURE Inhalation	PREDOMINANT TOXICODYNAMICS Irritant & corrosive Upper airway



HAZMAT TOXIDROMES

TOXIDROME	TYPICAL TOXICANTS
Irritant Gas: Moderately water-soluble	Chlorine (Cl_2)
PREDOMINANT ROUTE OF EXPOSURE	PREDOMINANT TOXICODYNAMICS
Inhalation	Irritant & corrosive Upper & lower airways

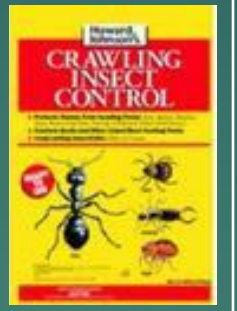
HAZMAT TOXIDROMES

TOXIDROME	TYPICAL TOXICANTS
Irritant Gas: Slightly water-soluble	Phosgene ($COCl_2$) Nitrogen dioxide (NO_2)
PREDOMINANT ROUTE OF EXPOSURE	PREDOMINANT TOXICODYNAMICS
Inhalation	Irritant & corrosive Delayed noncardiogenic pulmonary edema

Irritant Gases: Slightly water soluble

Anteroposterior portable chest radiograph in a male patient who developed phosgene-induced adult respiratory distress syndrome. Notice the bilateral infiltrates and ground-glass appearance. Image courtesy of Fred P. Hirschmann, MD, and Ferdinando L. Miranti, DO.

HAZMAT TOXIDROMES

TOXIDROME	TYPICAL TOXICANTS
Cholinergic 	Organophosphate Pesticides (Phosphorothioic acid, O,O-diethyl O-[6-methyl-2-(1-methylethyl)-4-pyrimidinyl] ester - Diazinon®) Carbamate insecticides & meds (carbaryl - Sevin®) Sevin® Brand Carbaryl Insecticide
PREDOMINANT ROUTE OF EXPOSURE	PREDOMINANT TOXICODYNAMICS
Skin & mucous membranes	Excess Acetylcholine due to inhibition of acetyl cholinesterase

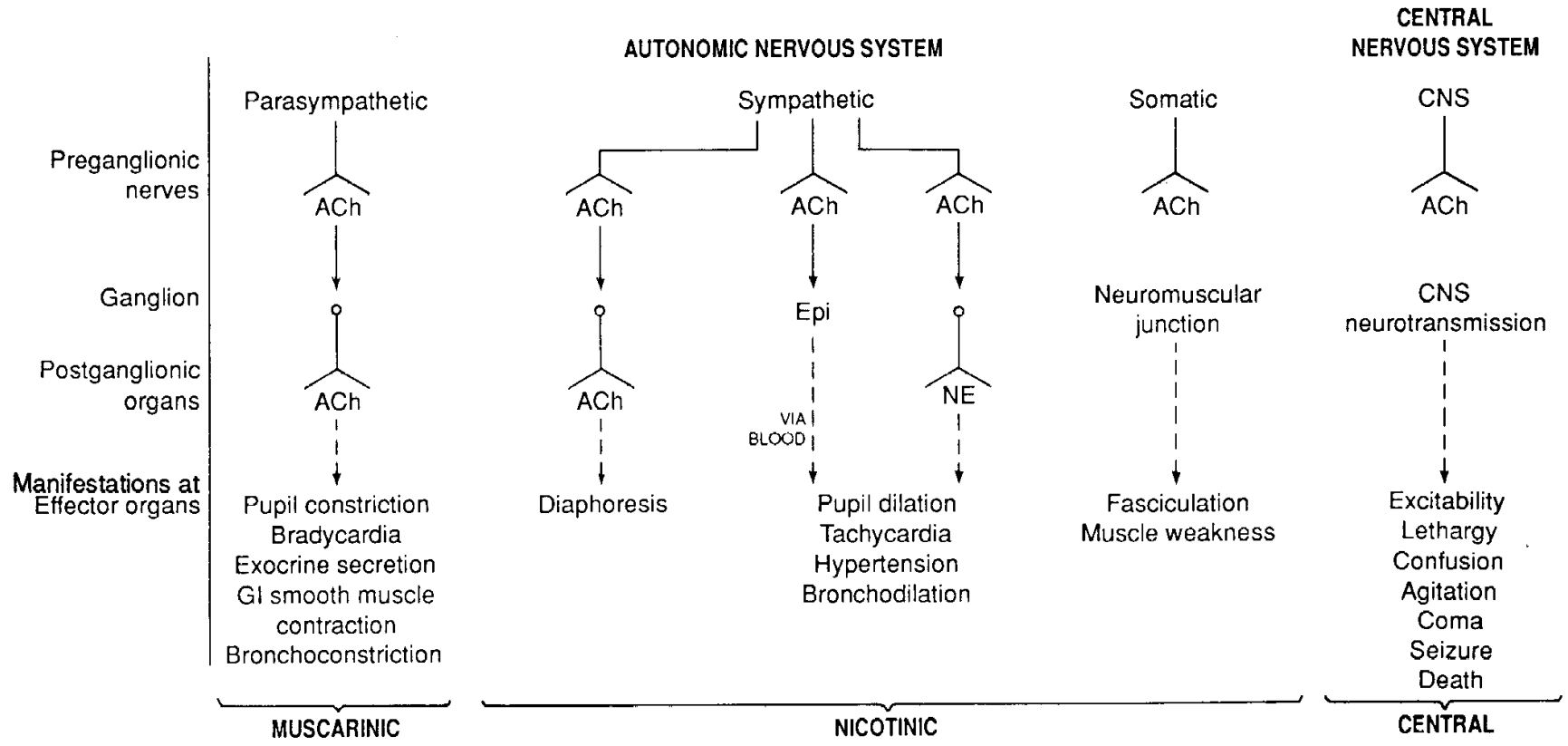


Figure 78–1. Human peripheral nervous system and anticholinesterase. *(Adapted from Tafuri J, Roberts J: Organophosphate poisoning. Ann Emerg Med 16:196, 1987. As modified from Rymer WZ: Organization of the Autonomic Nervous System, Northwestern University Medical School, 1981.)*

'Sweating profusely' and clutching his head: Kim Jong Nam's last moments

TOXIDROME	TYPICAL TOXICANTS
Cholinergic	Organophosphate nerve agents 
PREDOMINANT ROUTE OF EXPOSURE Inhalation &/or skin & mucous membranes	PREDOMINANT TOXICODYNAMICS Excess acetylcholine due to inhibition of acetyl cholinesterase 

Organophosphate-Cholinesterase Complex Aging

- Organophosphates bind irreversibly to cholinesterase, unless pralidoxime is given prior to "aging."
  - Time is tissue.
- **"Aging" is the average time for irreversible binding between organophosphates & cholinesterase.**

Organophosphate Inhibition of Acetylcholinesterase

Acetylcholine

Irreversible Covalent Bond

Nerve Agent Aging Half-Times

Name	Synonym	"Aging" Half-Time
Sarin	GB	~ 5 hours
Soman	GD	~ 2 minutes
Tabun	GA	> 14 hours
VX	None	~ 48 hours

Cholinergic Toxidrome: Nerve Agent Signs & Symptoms

Peripheral Nervous System		Central Nervous System (CNS)
Muscarinic	**Nicotinic**	
Diarrhea **U**rination **M**iosis **B**ronchorrhea, **B**ronchospasm, **B**radycardia **E**mesis **L**acrimation, **L**aryngospasm **S**alivation, **S**ecretion, **S**weating	**M**ydriasis **T**achycardia **W**eakness **H**ypertension, **H**yperglycemia **F**asciculations	Confusion Convulsions Coma

Chemical effects witnessed may vary by route of exposure and dose

- Dermal
- Ocular
- Inhalation
- Ingestion

Nerve Agents

- S/Sx
  - Cholinergic excess: WET!
  - Severe difficulty breathing
  - Seizures
  - DUMBBBELSS
  - Fasciculations, weakness, paralysis, coma, arrest
- Tx
  - Pretreatment with pyridostigmine
  - Airway protection, suction, O_2
  - Atropine blocks ACh receptors
  - Oximes reactivate AChase
  - Diazepam minimizes brain damage
  - Decon
  - Supportive care

Division of Strategic National Stockpile

Centers for Disease Control and Prevention

CHEMPACK Equipment

CHEMPACK STORAGE CONTAINER

- 60.5” long X 32.5” wide X 60.5” high
- Approx 800 lbs when filled with pharmaceuticals
- constructed of wire-lexan mesh
- approved by the Drug Enforcement Agency (DEA) for storage of schedule IV controlled drugs when external security enhancements are in place

ChemPack: Antidotes to Organophosphates

- Atropine
  - test dose 2-4 mg IV in adults
  - 0.05 mg/kg in kids
  - double q 5-10 min until dry
- Pralidoxime – for irreversible inhibitors
  - 1 g IV in 200 cc NS over 30 min.- may repeat x 1
  - do not underdose (“pure” nicotinic syndrome)
- Diazepam
  - Treat/limit seizures; reduces morphologic brain damage in animals
- Non-ChemPack agents: Scopolamine, other oximes

Triage

- How would you effectively separate “frightened” from “exposed and frightened” people in a rushing crowd after a mass organophosphate exposure?

The power of the toxidrome…
Sympathomimetic vs. Cholinergic Muscarinic

Ability to dilate in a dark room returns over weeks following nerve agent exposure.

https://ccc.apgea.army.mil/sarea/products/textbook/Web_Version/images/P146_Fig5-4.JPG

HAZMAT TOXIDROMES

TOXIDROME	TYPICAL TOXICANTS
Incapacitating Agent Anticholinergic Toxidrome	BZ (3-Quinuclidinyl benzilate) DMHP (Dimethylheptylpyran – abandoned - a synthetic cannabinoid)
PREDOMINANT ROUTE OF EXPOSURE	PREDOMINANT TOXICODYNAMICS
Inhalation &/or skin & mucous membranes	Competitively occupies acetylcholine receptors Hallucinations

Anticholinergic Toxidrome

- Red as a beet.
- Dry as a bone.
- Mad as a hatter.
- Hot as a stone.
- Blind as a bat. (Pupillary dilatation and loss of accommodation)
- Bladder & bowel lose their tone,
- and the heart runs alone.
- (also tremor, myoclonus, altered speech & coma)

BZ Treatment

- Decon
- Airway support
- Restraints
- Intravenous hydration; maintain adequate urinary output; Foley catheter for urinary retention
- Agitation, consider benzodiazepine administration (a longer-acting safe alternative to physostigmine)
- Hyperthermia, temp monitoring, cooling as indicated
- Cardiac monitoring

Sometimes diagnostic…

…potentially harmful!

Incapacitating Agents: Opioid

TOXIDROME	TYPICAL TOXICANTS
Incapacitating Agent Opioid Toxidrome	Fentanyl
PREDOMINANT ROUTE OF EXPOSURE	PREDOMINANT TOXICODYNAMICS
Inhalation	Occupies opioid receptors Narcosis

Classification	Specific Names	Main Clinical Effects	Antidotes
Nerve Agents: Cholinergic Agents	Tabun; Sarin; Soman; VX	Cholinergic crisis; Respiratory distress; Seizures; Coma; Paralysis; Ventilatory failure	Pralidoxime; Atropine; Benzodiazepine
Vesicants	Lewisite; Sulfur mustard; Phosgene oxime	Vesiculation; Chemical burns of skin & mucous membranes	BAL (British-Anti-Lewisite) or DMPS (Unithiol) for Lewisite only
Cyanides: Systemic asphyxiants	Hydrogen cyanide; Cyanogen chloride	Cellular asphyxia; Anaerobic metabolism; Lactic acidosis; Cardiovascular collapse; Shock; CNS dysfunction; Seizures; Coma	Amyl nitrite; Sodium nitrite; Sodium thiosulfate; Hydroxocobalamin
Pulmonary Agent: Irritant Gas	Phosgene	ARDS; Hypoxemia; Respiratory failure	None
Riot Control Agents: Irritant Aerosols	CN; CS ;OC	Mucous membrane & skin irritation; Lacrimation	None
Incapacitating Agents	BZ; Carfentanil	Inability to perform military or occupational activities	Physostigmine for BZ; Naloxone for carfentanil

Biological Agents: a brief illustration

- The AHLS program has an excellent unit on chemical and biological terrorism.
- Perhaps we might offer AHLS or the toxic Terrorism course in the future?

- Used by permission.

Comparison of Chemoterrorism Agents & Bioterrorism Toxins

Chemoterrorism Agents		**Toxins**
Man-made	vs.	Natural origin
Many volatile	vs.	None volatile
Vapor or Aerosol delivery	vs.	Aerosol Delivery
Dermally active	vs.	Not dermally active*
Poor immunogens	vs.	Many are effective immunogens **

*Exception: trichothecene (T-2) mycotoxins

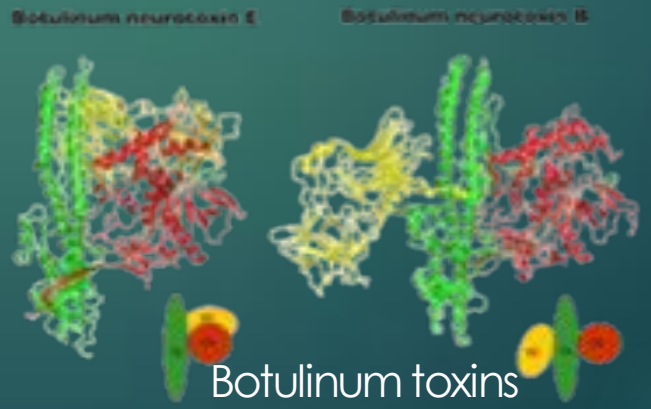
** The body recognizes them as foreign proteins & makes protective antibodies against them.

Bioterrorism: Chapter 29

- Microbes
  - Replicating agents
    - Infect
    - Viruses
    - Bacteria
      - Anthrax
- Toxins
  - Intoxicate
  - Botulism

Bacillus anthracis
CDC

Ebola Virus



Botulinum toxins
Brookhaven Nat.

Biological Clinical Guidelines

A Quick Guide for the
Management of Biological Disasters for
Emergency Department Personnel

DISASTER

Bioterrorism Viruses

Category A Infectious Illnesses	Main Clinical Effects	Antiviral Agent for Treatment	Immunization for Prevention
Smallpox	Fever; Cough; Pox rash; Hemorrhagic pox rash; Viremic shock	None	Active: Vaccinia virus smallpox vaccine Passive: Vaccinia-immune globulin (VIG)
Viral Hemorrhagic Fevers (VHF)	Fever; Bleeding from mucous membranes, skin, lungs, etc.; Viremic shock; Multiorgan failure	None	Active: Yellow fever vaccine only Passive: None

Bioterrorism Bacteria

Category A Infectious Illnesses	Main Clinical Effects	Preferred Antibiotics for Treatment
Anthrax	Mediastinitis; Hemorrhagic meningitis; Respiratory failure; Septic shock;	Meningitis excluded: Ciprofloxacin + Clindamycin or Linezolid + Antitoxin (obiltoxaximab)
		Meningitis suspected or confirmed: Ciprofloxacin + Meropenem + Linezolid + Antitoxin (obiltoxaximab)
Bubonic Plague	Swollen lymph nodes; Rash; Septic shock	Doxycycline Gentamycin Streptomycin Chloramphenicol
Pneumonic Plague	Pneumonia; Respiratory failure; Septic shock	
Tularemia	Pneumonia; Skin ulcers; Swollen lymph nodes; Septic shock	

Bioterrorism Toxins

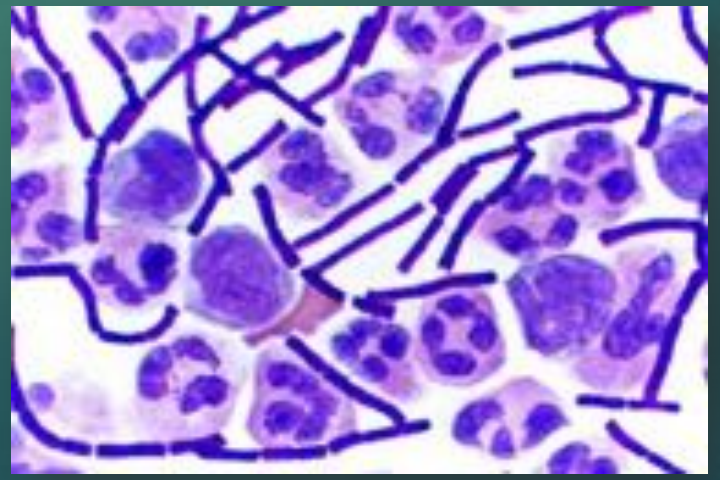
Intoxication	Main Clinical Effects	Antitoxins for Treatment
Botulism (Category A)	Weakness; Descending, flaccid paralysis; Ventilatory failure	BAT® (Botulism Antitoxin Heptavalent) from U.S. Centers for Disease Control & Prevention (CDC) for non-infant botulism or BabyBIG® antitoxin for infant botulism
Ricin (Category B)	Fever; Cough; ARDS; Respiratory failure	None
Trichothecene (T2) mycotoxins	Skin irritation & sloughing; Respiratory tract irritation & mucosal sloughing; Gastrointestinal tract irritation & mucosal sloughing; Respiratory failure; Hypovolemic shock	None

Anthrax Overview

- Disease
  - Anthrax
    - 4 Syndromes
      - 3 natural
        - Cutaneous ~ 95%
        - Inhalational ~ 5%
        - Gastrointestinal < 1%
          - Oropharyngeal
            - Subsyndrome
      - 1 acquired
        - Injection

vs.

- Bacterium
  - *Bacillus anthracis*
  - Gram-positive
  - Aerobic
  - Spore-forming
  - Rod



Cutaneous Anthrax Signs & Symptoms

Necrotic Ulcer

CDC, public domain

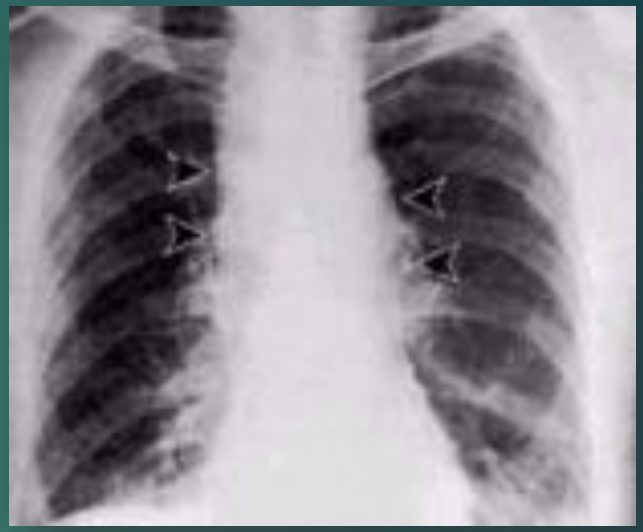
Cutaneous Anthrax Signs & Symptoms

Coal-Black Scab

CDC, public domain

Inhalational Anthrax Signs & Symptoms

- Incubation period
  - Usually 1 to 6 days
    - As long as
      - 43 days in Sverdlovsk epidemic
      - 58 days in experimental monkeys
        - Basis for 60 day antibiotic prophylaxis
- Initial symptoms nonspecific
  - Initially, URI **without rhinorrhea**
    - Fever
    - Malaise
    - Fatigue
    - Nonproductive cough
    - Mild chest discomfort
- Then, transient improvement for hours, up to 3 days
- Finally
  - Hemorrhagic mediastinitis
  - Sepsis
  - Abrupt onset
    - Dyspnea
    - Respiratory distress
    - Diaphoresis
    - Cyanosis
    - Death within 24 to 36 hours
    - Ventilatory failure
    - Septic shock



Questions for me?

Questions for you:

- **True or False**

- 1. In an organized approach to toxidrome recognition for a patient exposed to a chemical agent one should gather vital signs, assess the patient's mental status and other autonomic signs like pupillary size and skin color/moisture/temperature.

True or False

- 2. An important difference between intoxication and infection is that lack of volatility of many toxins makes person to person inhalational transmission unlikely.

Choose all correct answers

- 3. Which of the following antidotes are contained in the CDC's CHEMPACK program for the treatment of organophosphate poisoning?

- a. atropine
- b. hydroxocobalamin
- c. pralidoxime (2-PAM)
- d. sodium thiosulfate

Delivered: Nov 29 08:45-9:30 NECOEM, Newton, MA
Credits: Advanced HazMat Life Support, University of Arizona

For more reading:

Advanced Hazmat Life Support - Frank G. Walter, Ed.

Introduction to chemical, biological and radiological terrorism - Anthony J. Tomassoni
Bioterrorism - Anthony J. Tomassoni
Chemoterrorism: nerve agents - William T. Hurley
Radiation Emergencies – Jeffrey B. Nemhauser

Toxic industrial chemicals and chemical weapons: exposure, identification, and management by syndrome.
Tomassoni AJ, French RN, Walter FG.
Emerg Med Clin North Am. 2015 Feb;33(1):13-36.
doi: 10.1016/j.emc.2014.09.004. Epub 2014 Nov 15.