



Toxic Terrors: Nerve Agent Poisoning

On March 20, 1995, St. Luke's Hospital treated 640 patients in the largest documented exposure of a civilian population to a warfare nerve agent. The lecturer will discuss the most common agents to expect in a mass chemical exposure from a terrorist attack. In addition, the participant will learn early recognition and treatment of such exposures.

- Describe the most common signs and symptoms of patient exposure to warfare nerve agents.
- Review other chemical agents that might be used by terrorist groups.
- Learn the most useful antidotal and supportive therapies required in such exposures.
- Recognize the need for emergency department disaster planning to handle mass casualties from hazardous substance exposures.

TH-217
Thursday, October 14, 1999
10:00 AM - 10:55 AM
Room # N236
Las Vegas Convention Center

FACULTY

Mark A Kirk, MD

Associate Clinical Professor, Indiana University School of Medicine, Medical Toxicology Fellowship Director; Faculty, Emergency Medicine Residency, Methodist Hospital; Associate Medical Director, Indiana Poison Center, Indianapolis, Indiana

Toxic Terror

Nerve Agent Poisoning

The 1999 ACEP Scientific Assembly, Las Vegas

Mark A Kirk, MD
Indiana Poison Center
Methodist Hospital, Clarian Partners
Indiana University School of Medicine
Indianapolis, Indiana

Course Description

On March 20, 1995, St. Luke's Hospital treated 640 patients in the largest documented exposure of a civilian population to a warfare nerve agent. The lecturer will discuss the most common agents to expect in a mass chemical exposure from a terrorist attack. In addition, the participant will learn early recognition and treatment of such exposures.

Objectives

- Learn to recognize high risk situations and clinical syndromes likely to be from terrorist attacks
- Learn how to protect yourself from exposure
- Review the resources available to assist in response to a terrorist attack
- Describe the most common signs and symptoms of patient exposure to warfare nerve agents
- Review other chemical agents that might be used by terrorist groups.
- Learn the most useful antidotal and supportive therapies required in such exposures.
- Recognize the need for emergency department disaster planning to handle mass casualties from hazardous substance exposures.
- Review the lessons learned from the events of Tokyo's sarin subway attack.

Toxic Terrorism: Nerve Agent Poisoning

Summary Fact Sheet

Mark A Kirk, MD
Indiana Poison Center
October 14, 1999

Recognition

Reports from the scene of an *explosion* with dispersion of mists, liquids or gas or *paraphernalia* such as spray devices, leaking packages

Mass casualties at *potential targets* (government buildings, mass gatherings, mass transportation)

Mass casualties *without* obvious *trauma*

Mass casualties with *toxic syndromes*

The key to identifying nerve agent poisoning is recognizing its distinct Clinical Presentation

Pinpoint pupils, SLUDGE, Seizures, Cardiac arrest

The Diagnostic Challenge:

Large number of victims with varying *symptoms and signs*

Eye pain, blurred vision, Pinpoint pupils, lacrimation

Cough, chest tightness, dyspnea, wheezing, apnea, cyanosis

Diaphoretic skin

Drooling, nausea, vomiting, abdominal cramps, diarrhea

Urinary incontinence

Muscle weakness, muscle cramps, fasciculations, tremor

Anxiety, confusion, seizures, coma

Self-Protection

Do not Touch the Stuff or Breathe the Bad Air (Secondary contamination from skin contact with droplets or inhalation of vapor)

Early recognition will protect you by cautious handling and proper decontamination of victims

First Actions

Guard the door (control entry into hospital)

Decon Procedure: **Clothing and jewelry removal**, Soap and Water shower, household bleach diluted 1:10 (sodium hypochlorite with 9 parts water)

Triage seriously ill based on Respiratory, Cardiovascular and CNS symptoms (START)

Triage walking wounded based on presence of pinpoint pupils (with vapor exposure)

Activate and follow mass casualty plan

Control hysteria

Recognize when you are in over your head

Resources

Information:

Emergency Management _____

Regional Poison Center _____

Supplies: Who is your Radar O'Reilly?

Antidotes needed: Atropine, Pralidoxime, Valium

Where is the atropine stored? Veterinarians, ophthalmologic, glycopyrolate for peripheral effects

Major Pitfalls

Delay in recognizing the cause

Mass Hysteria and Medical Mass Hysteria

Secondary contamination of you, your staff, or hospital

The Challenge: The most important requirement of management of chemical agent casualties is KNOWLEDGE

“The health care provider’s job begins once the attack takes place, and that job is caring for casualties. Each person reading this should ask what would happen if such an attack occurred in the area of his or her hospital. Could we properly take care of the casualties? If the answer is no, perhaps the reader should ponder why.”

“The most important, and often neglected, requirement of management of chemical-agent casualties is knowledge on the part of the health care provider. How many health care providers, from the first responder on the ambulance to the emergency physician in the hospital, feel intellectually equipped to manage a sarin casualty or a casualty from another military agent? How many feel qualified to triage more than 5,000 people to find the 1,200 or so needing medical care, as the Japanese did? There has been little training for this type of casualty in the past”

“We in the United States must stop being so complacent. This type of incident can happen here. We do not like to think about it, and too often this means we do not want to hear about it and do not want to know about it. **But we must think about it, we must hear about it, and we must know about it.**”

“The Japanese medical community is to be commended for their response to the Tokyo incident. **How well will we do when faced with this new form of terrorism?”**

Sidell FR: Chemical agent terrorism. *Ann Emerg Med* August 1996;28:223-224.

Chemical Warfare Agents

•Nerve Agents	Sarin, Soman, VX
•Cyanide	Hydrogen Cyanide
•Pulmonary Intoxicants	Phosgene, Chlorine
•Vesicants	Mustard, Lewisite
•Riot Control Agents	Pepper Spray, Mace
•Incapacitating Agents	Hallucinogens

Recognition of Potential Terrorist Acts

Recognizing High Risk Situations

Reports from the scene of an *explosion* with dispersion of mists, liquids or gas or *paraphernalia* such as spray devices, leaking packages

Mass casualties at *potential targets* (government buildings, mass gatherings, mass transportation)

Mass casualties *without* obvious *trauma*

Mass casualties with *toxic syndromes*

Recognizing HazMat Toxic Syndromes

- Irritant gas syndrome
- Chemical burns
- Metabolic poisoning
- Acetylcholinesterase poisoning
- Psychogenic illness

Irritant Gas Syndrome

- Signs and Symptoms
 - Mucous membrane irritation, painful, burning skin
 - Cough, dyspnea, wheezing, pulmonary edema
- Examples: Chlorine, phosgene, ammonia, isocyanates, Hydrofluoric acid, hydrogen chloride, Riot control agents, pepper spray

Chemical Burns

- Signs and Symptoms
 - Painful, burning skin, bulla, blisters, or reddened skin
 - Mucous membrane irritation
 - Systemic effects
- Examples: Acid and alkaline corrosives, Hydrocarbons, Mustard agents, Lewisite

Metabolic Poison

- Signs and Symptoms
 - Nausea, vomiting, dysrhythmias, hypotension
 - Headache, syncope, seizures, coma, metabolic acidosis
 - Knocked down - cardiac arrest
- Examples: Cyanide, Hydrogen sulfide, azides, phosphine, Nerve agents

Acetylcholinesterase Poisoning

- Signs and Symptoms: SLUDGE syndrome
 - Pinpoint pupils, eye pain
 - Dyspnea, wheezing, pulmonary edema
 - Headache, weakness, seizures, coma
- Examples: Nerve agents: sarin, soman, tabun, VX; Organophosphate insecticides

Psychogenic Illness

- Signs and Symptoms
 - Nausea, vomiting
 - Headache, dizziness, faintness
 - Weakness, extremity numbness
 - Chest tightness, hyperventilation
- Examples: Often indistinguishable from many serious toxic exposures

Nerve Agent Poisoning

Chemical Properties

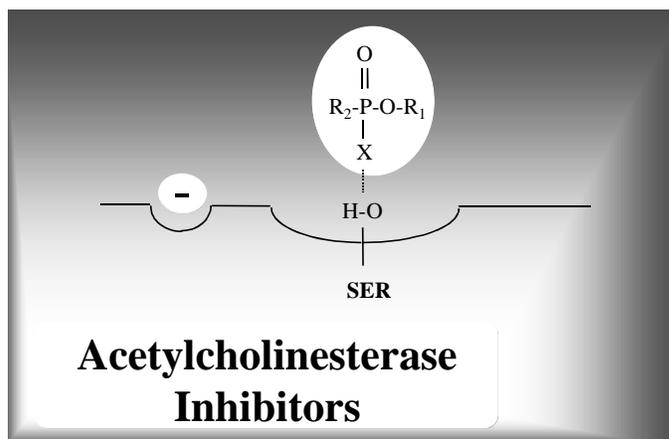
- NOT "nerve gases"
- Sarin is most volatile (volatility similar to water)
- Potency greater than organophosphate insecticides
- Heavier than air (tends to sink into low lying areas such as valleys, trenches and basements)

Mechanism of Toxicity

Acetylcholine is a neurotransmitter that activates muscarinic and nicotinic receptors found at:

- Central Nervous System
- Parasympathetic and Sympathetic autonomic ganglia
- Postganglionic Parasympathetic Nervous System
- Sympathetic Sweat Glands
- Skeletal Muscle End Plate

Acetylcholinesterase regulates acetylcholine activity in the synaptic cleft



Nerve agents, like organophosphate insecticides, inhibit acetylcholinesterase preventing the inactivation of acetylcholine

Results in excess acetylcholine stimulation at muscarinic and nicotinic receptors

- **Cholinergic Storm**
- **SLUDGE Syndrome**

Clinical Effects

- **Muscarinic**
 - Salivation
 - Lacrimation
 - Urination
 - Defecation
 - Gastroenteric cramping
 - Emesis
 - Bronchospasm/Bronchorrhea
 - Bradycardia
 - Miosis
- **Nicotinic**
 - Muscle fasciculations, twitching, cramping
 - Muscle paralysis
 - Tachydysrhythmias, hypertension
- **Central Nervous System**
 - Anxiety, restlessness, ataxia
 - Seizures
 - coma

Clinical Effects by System

Respiratory

- *Respiratory failure is the major cause of death*
- Causes of Respiratory Failure:
 - 1) Increased Airway Resistance
 - 2) Bronchorrhea
 - 3) Neuromuscular Paralysis
 - 4) Depression of Central Respiratory Centers

Central Nervous System

- Central mediated respiratory failure leading to apnea
- Rapid progression to coma
- Grand mal seizures

Seizure Mechanisms

- Cholinergic Overstimulation *Triggers* Seizures (Predominately Muscarinic)
 - Anticholinergics terminate seizures
 - No Neuropathology
- Excitatory AA Neurotransmitters *Reinforce* Seizure Activity
 - Anticholinergics less effective
- Non-Cholinergic Phase (Prolonged Seizures)
 - Refractory to Anticholinergics
 - Benzos and NMDA antagonists effective***
 - Neuropathology Evident
 - Excessive Calcium Influx
 - Prolonged NMDA stimulation

Ophthalmologic

- Lacrimation
- Miosis
- Unable to Dark Adapt
- Dim Vision
- Ciliary Spasm, Ocular Pain

Musculoskeletal System

- Muscular weakness
 - Fasciculations
 - Paralysis
- ** *similar to succinylcholine*

Skin

- Profuse Sweating
- Erythema

Gastrointestinal System

- Exocrine Gland Secretions
- Increased Motility
- Relaxation of Sphincters

Genitourinary System

- Detrusor Muscle Contraction
- Relaxation of Sphincters

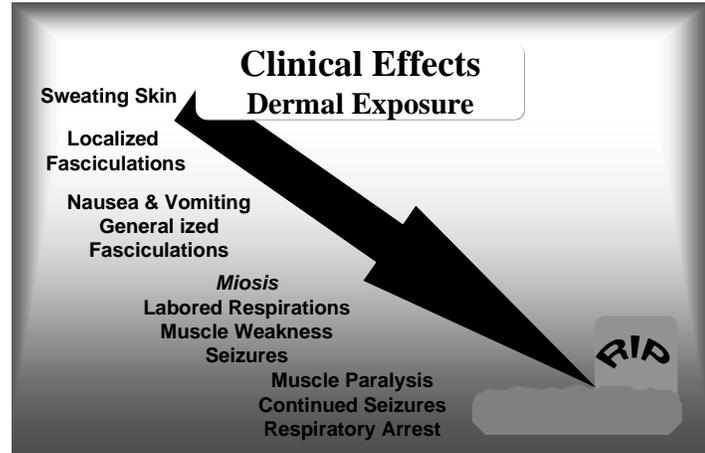
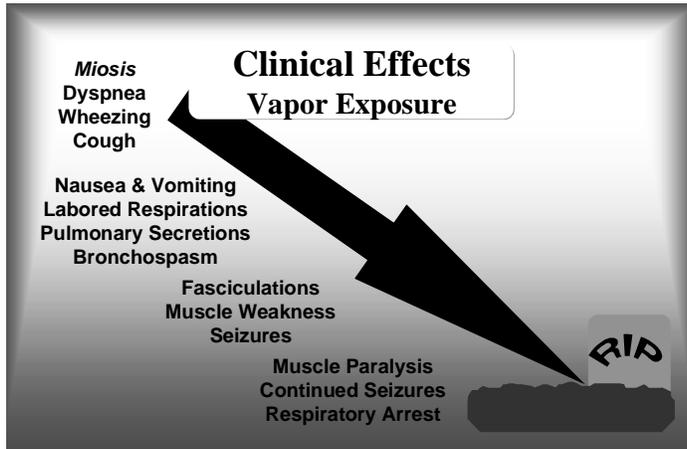
Cardiovascular System

- Sinus Tachydysrhythmias
- Bradydysrhythmias
- QT prolongation and subsequent torsades

Tokyo Subway Sarin Attack Toxic Effects

Miosis	99%
Headache	75%
Dyspnea/Cough	63%
Nausea/Vomiting	60
Eye Pain/Blurred Vision	45
Weakness/Fasciculations	37
Running Nose	25

Clinical Course of Vapor and Dermal Exposure Route of Exposure Determines Signs and Symptoms



Is it Hysteria or Poisoning?

Nerve Agent Poisoning	Hysteria
Chest Tightness Dyspnea Tachycardia Nausea/Vomiting Abdominal Cramps Involuntary Urination Fasciculations Headache Coma Diaphoresis	Chest Tightness Dyspnea Tachycardia Nausea/Vomiting Abdominal Cramps Involuntary Urination Tremor Headache Syncope Diaphoresis

Laboratory Principles

- Useful to Confirm Exposure
 - Poor Correlation with Local Effects of Vapor Exposure
 - Systemic Effects with RBC-ChE inhibited to 20% of normal
- Preferential Inhibition: RBC over Plasma
 - VX: 70%:20%
 - Sarin: 80%:30%
 - Activity Reduced to 0 after Large Exposure

Treating Nerve Agent Poisoning

- **Use the Simple Triage and Rapid Treatment System to Sort Patients**
What is the Respiratory Status? 0/>30/normal
What is the Perfusion Status? No radial pulse/cap refill >2 sec/ cap refill < 2 sec
What is the Neurologic Status? normal/altered/coma
Was the Exposure Vapor or Liquid Exposure?
Are the pupils pinpoint (vapor exposure)
- **Terminating Exposure**
Decontamination/ Self Protection
Rapidly Remove from Exposure
Remove Clothing
Soap and Water Shower with Specific Attention to Cleansing Hair
If available – household bleach diluted 1:10
- **Supportive Care**
Ventilation
Patients Die a Respiratory Death
Why do the Seizures Stop so Quickly?
- **Antidotes**
 - Atropine
Dose determined by improved oxygenation and ease of ventilation
 - Oximes
 - Benzodiazapines

Alternative Sources of Atropine

Powdered Multidose Atropine
EMS Stockpiles
Veterinary Atropine
Ophthalmic Atropine
Last Resort: Jimson Weed Tea

Indications for Ocular Atropine

Distressing Ocular Pain
Need for Full Dark Adaptation
Treatment Causes Cycloplegia
Options: Ophthalmic Atropine or Cyclopentolate

Disposition

- Observation for ?
 - Vapor = 1 hour
 - Liquid = Up to 18 hours
- Consider Treatment if progressive symptoms - Especially Dyspnea
- Pinpoint Pupils may persist for >45 days

Pitfalls of Nerve Agent Poisoning Management

- Not Recognizing Cholinergic Excess Syndrome
- Not Understanding the Concept of Self-Protection
- Not Recognizing Delayed Effects of Dermal Exposure
- Becoming a Psychological Casualty

Caring for Mass Casualties



Dealing with Mass Casualties

- Information Management
- Resource Management
 - People
 - Antidotes
 - Decontamination Supplies
- Patient Management

The Event: Tokyo Subway Sarin Attack

- March 20, 1995
- 7:55 am Subway Capacity 200%
- Diluted Sarin Solution in Plastic Bags Punctured by Umbrella Tip
- 5,500 Affected
 - 4300 with No Signs of Exposure/ Sent Home
 - 1200 Requiring Hospitalization
 - 12 Fatalities
 - Patients presented to over 200 Hospitals and clinics w/in hours of the incident
- St. Lukes International Hospital
 - 640 Patients on day of attack
 - 1,410 Patients in week following attack

Communications

Information Sources: A Timeline

- 7:55 am Release of Sarin in Subway
- 8:16 am FD reports of Gas Explosion at a Subway Station
- 8:25 am Patient arrives by foot
First Victim is Hospitals "best" Information Source
Complaining of eye pain and visual darkness
- 8:40 am First Ambulance Arrives
- 8:43 am Cardiac Arrest arrives by private car
- More than 500 Victims Arrive over next one hour
*"We suspected the victims' illness was some form of OP agent exposure.
We were puzzled as to why it had happened in the subway"*
- 9:40 am Cholinesterase Levels reported very Low
- 9:40 am FD reports **Acetonitrile** Detected by on Scene Monitoring Equipment
- 10:30 Press Conference by Self Defense Forces Hospital "Sarin Suspected"
- 11:00 am TV News reports Police Confirmed Cause to be Sarin (No direct information from Police)
- 12:00 noon Doctors Conference held to Standardize Triage and Treatment

EMS Response

"The wounded were brought from the field in wagons, carriages, ambulances, litters, and, in fact, every conveyance which could be brought into requisition." Denney Civil War Medicine 1995

Transportation from Scene to Hospitals

- EMTs Transported 688 Victims
- >4000 Reached Hospitals by: Foot, Taxis (25%), Private Vehicles (2/3 Cardiac Arrests)
- Unable to Obtain Hospital Availability Information, therefore, Victims Concentrated at Closest Hospital (St. Luke's)

Victims from Tokyo Subway Sarin Attack

Summary of Patients treated at St Lukes Hospital

- Total = 640
- Mild = 528 (82.5%)
Miosis, Eye pain, Dim vision
- Moderate = 107 (16.7%)
Systemic signs e.g.. Weakness, Fasciculations, Convulsions, and Difficulty Breathing
- Severe = 5 (0.78%)
Required Intubation and Ventilatory Support

Secondary Exposure to EMTs

- No Decontamination at the Scene
- No Respiratory Protection
- Developed Symptoms During Transport
- 1,364 EMTs - 135 (9.9%) developed acute symptoms, received treatment that compromised their rescue work
- Vaporized Sarin from Victim's Clothing

Secondary Exposure Symptoms Hospital Workers **110/472 (23%) with Acute Poisoning Symptoms**

Eye Symptoms	66 (14.0%)
Headache	52 (11.0%)
Throat Pain	39 (8.3%)
Dyspnea	25 (5.3%)
Nausea	14 (3.0%)
Dizziness	12 (2.5%)
Nose Pain	9 (1.9%)

Lessons Learned from Tokyo Subway Sarin Attack

Hospital Response Problems

- Hardware
 - Structural Deficit of Hospital Building Ventilation
 - Lack of Decontamination Facilities
- Software
 - Chemical Disaster Planning
- Transmission
 - Communication Difficulties

Transmission: Correcting Communication Problems

- Organizations acted Independently with Little Communication between Organizations
- Lack of Efficient Chemical Disaster Information Network
- Poison Information Center Participation
 - During an Event Provide Acute Toxicologic Information
 - Regional Mediators of all Toxicologic Information
 - Disaster Drills
- Need Education on the Toxicological Aspects of Chemical Disasters

Nerve Agent Poisoning Summary

- Nerve Agents are *BAD* Poisons
- Effects are Similar to Organophosphate Insecticide Poisoning

Differences Between Nerve Agents and OP Insecticides.

Nerve Agents have:

- Higher Potency with Greater Lethality (Lower LCT_{50%} & LD_{50%})
- Extremely Rapid Onset of Effects & Aging
- Rapid Recovery After Acute Crisis (Hours)
 - Severe Poisoning has required *ONLY* 5 - 20 mg of Atropine
 - Atropine and 2PAM Infusions not Necessary

- Victims Die of Respiratory Failure
- Miosis is a CLUE to the Diagnosis in a Chaotic Mass Casualty Incident
- Learn Methods of SELF-Protection
- We are from the Poison Center, We are here to Help

Bibliography

- Anderson, D R, Harris L W, Bowersox S L, Lennox W J, Anders J C. Efficacy of injectable anticholinergic drugs against soman-induced convulsive/subconvulsive activity. *Drug Chem Toxicol.* 1994;17:139-148.
- Boxer, P.A. Occupational mass psychogenic illness. *J Occup Med.* 1985;27:867-872.
- Brown, J H, Taylor P. Muscarinic receptor agonists and antagonists. In: Hardman JG, Limbird LE, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics.* 9 ed. New York: McGraw-Hill; 1996:141-160.
- Burgess JL, Kirk MA, Borron SW, Cisek J: Emergency department hazardous materials protocol for contaminated patients. *Ann Emerg Med* 1999; 34:205-212.
- Cancio, L.C. Chemical casualty decontamination by medical platoons in the 82d Airborne Division. *Milit Med.* 1993;158:1-5.
- Compton, J A F: *Military Chemical and Biological Agents*, Caldwell: The Telford Press, 1987 :Pages.
- Grob, D, Harvey A M. The effects and treatment of nerve gas poisoning. *Am J Med.* 1953;14:52-63.
- Grob, D. The manifestations and treatment of poisoning due to nerve gas and other organic phosphate anticholinesterase compounds. *Arch Intern Med.* 1956;98:221-239.
- Grob, D, Johns R J. Treatment of anticholinesterase intoxication with oximes. *J A M A.* 1958;166:1855-1858.
- Holstege C, Kirk MA, Sidell FR: Chemical warfare: Nerve agent poisoning. *Critical Care Clinics* 1997, 13: 923-942.
- King, J.M., Frelin A.J. Impact of the chemical protective ensemble on the performance of basic medical tasks. *Milit Med.* 1984;149:196-201.
- Murphy, M R, Blick D W, Dunn M A, Fanton J W, Hartgraves S L. Diazepam as a treatment for nerve agent poisoning in primates. *Aviat, Space, Envir Med.* 1993;64:110-115.
- Ohbu, S, Yamashina A, Takasu N, et al. Sarin poisoning on Tokyo subway. *South Med J.* 1997;90:587-593.
- Okumura T, Suzuki K, Fukuda A, et al. The Tokyo subway sarin attack, Disaster management: Community emergency response, hospital response, national and international response. *Academic Emerg Med* 1998;5:613-628.
- Okumura, Tetsu, Takasu Nobukatsu, Ishimatsu Shinichi, et al. Report on 640 Victims of the Tokyo Subway Sarin Attack. *Ann Em Med.* 1996;28:129 - 224.
- Sidell, Frederick. Soman and sarin: Clinical manifestations and treatment of accidental poisoning by organophosphates. *Clin Tox.* 1974;7:1-17.
- Sidell, F R, Borak J. Chemical warfare agents: II. Nerve agents. *Ann Emerg Med.* 1992;21:865-871.
- Sidell, F R. Clinical considerations in nerve agent intoxication. In: Somani S, ed. *Chemical Warfare Agents.* San Diego: Academic Press, Inc; 1991:155-193.
- United States Army Medical Research Institute of Chemical Defense (USAMRIID). Medical response to chemical warfare and terrorism. Video presentation. 1999. Aberdeen Proving Grounds, MD.
- Van Biem, D. Prophet of Poison. *Time.* 1995. April 3:27-33.
- Yokoyoma, K, Yamada A, Mimura N. Clinical profiles of patients with sarin poisoning after the Tokyo subway attack. *Am Jour Med.* 1996;100:586.