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GENERAL GUIDELINES FOR MEDICALLY SCREENING MIXED POPULATION GROUPS POTENTIALLY EXPOSED TO NERVE OR VESICANT AGENTS

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FOREWORD

When confronted with the possibility of managing a potentially agent-exposed population, some state and local health officials have considered blood sampling for cholinesterase (ChE) activity determination in the event of a possible nerve agent exposure. Urine sampling for thiodiglycol (a metabolite of sulfur mustard) has been considered by these same health officials as a screen in the event of a possible mustard agent exposure. The brief analysis that follows has been collaboratively developed for the Chemical Stockpile Emergency Preparedness Program (CSEPP) by the authors to

- document why such population exposure screening analysis is discouraged, and
- provide alternate guidelines that have proved useful in practice

This analysis has been approved for release by the CSEPP Reentry and Restoration Subcommittee.

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ABSTRACT

A number of state and local planners have requested guidance on screening protocols and have expressed interest in sampling body fluids from exposed or potentially exposed individuals as a means of estimating agent dose. These guidelines have been developed to provide a clear statement that could be used by state and local emergency response personnel in the event of a nerve or vesicant agent incident resulting in off-post contamination; maximum protection from harm is the goal. The assumption is that any population group so exposed would be heterogeneous for age, gender, reproductive status, and state of health.

GENERAL SCREENING GUIDELINES

In all cases, emergency response and medical personnel should wear protective clothing, and take special precautions to avoid self-contamination (i.e., butyl rubber gloves and aprons, etc.), cross-contamination, or contamination of medical equipment and transport vehicles. Undiluted household bleach is particularly suited for immediate decontamination of gloves or small equipment items possessing smooth surfaces (e.g., scissors).

1) **Individuals exhibiting any signs/symptoms** should be immediately segregated, treated according to observed severity of toxic response (see Table 1), stripped, and decontaminated to reduce further exposure via potentially contaminated skin, hair, or clothing (see Table 2 and Sidell 1990).

2) **All individuals potentially exposed to liquid agent** in the form of splash, direct droplet/aerosol deposition, or skin contact with potentially contaminated surfaces should undergo decontamination and change into fresh, clean clothing.

3) **Special precautions for a sulfur mustard incident.** Immediate decontamination to reduce the potential for sulfur mustard exposure is imperative for several reasons:

a) There can be a delay of several hours' duration between exposure to sulfur mustard agents and onset of skin/eye irritation or pain.

b) There is no specific antidote for sulfur mustard poisoning; severity of symptoms is governed by absorbed dose.

c) Sulfur mustard agents are known human carcinogens. Any exposure poses some calculated risk of cancer induction.

4) **For those individuals NOT exhibiting signs/symptoms.**

a) If a vesicant agent release is involved, decontaminate any potentially exposed individual and dress him (her) out in fresh, clean clothing

b) If a nerve agent release is involved, decontaminate any potentially exposed individual and dress him/her out in fresh, clean clothing. Employ a buddy system or medical personnel to keep potentially exposed individuals under strict observation for at least 60 minutes and close observation for 24 hours. Sign or symptom levels such as "blurred vision only, pupillary constriction (with or without blurred vision) only" do not usually require treatment and will resolve without medical intervention. Most signs and/or symptoms of organophosphate poisoning will usually present within an hour after initial exposure; however, effects are well known to occur as long as 4 to 8 hours after percutaneous exposure. Some cases did not display symptoms until 18 hours post-exposure. Note that the smaller the exposure, the longer the time to symptom onset; effects that occur many hours later are usually non-lethal. If signs and/or symptoms other than those outlined immediately above develop, the exposed individual should be immediately segregated and treated with antidotes as outlined in Table 1. Upon release, asymptomatic individuals should be counseled to undergo no further exposure to OP or carbamate insecticides (e.g., rose dust, flea and tick control products for family pets, etc.) for a period of 3 to 4 weeks.

Blood and Urine Samples

We recommend emergency medical management of exposed or suspect populations on the basis of classical signs and symptoms. Determination of blood ChE activity (for nerve agents) or urine thiodiglycol (a metabolite of sulfur mustard) concentration would be best used as a diagnostic confirmation of severe exposure and as a monitor of recovery.

We do not recommend ChE activity determination as a population screen for several reasons:

1) **Lack of baseline ChE data for individuals in sample population.** Most individuals, unless they are part of a closely monitored agricultural worker group, do not have regular determinations of baseline ChE activity performed. Normal human ChE activity values represent a wide range that may be further altered by such factors as disease, reproductive and nutritional status, and drug or alcohol use. Age and gender may also be factors. Without a baseline determination on the same individual, it is impossible to sort out differences in ChE activity due to sources of biological variability vs. nerve agent exposure. Note that RBC-ChE activity is a more stable indicator of OP exposure than plasma ChE activity.

2) **Logistics.** Handling/tracking large numbers of blood samples from asymptomatic individuals would require resources that could be better utilized on more immediate emergency activities.

3) **Lab turnaround.** Large numbers of samples would generate a backlog in most labs, and data would likely not be available for several days after blood draw. This interval is too great to be of any practical assistance in diagnosis or treatment of populations during an emergency.

Depending on analytical and staffing capability, throughput rates are rarely in excess of 20/day for the Michel method. Other methods, such as the Dupont ACA, are faster and more efficient. To our knowledge, Army labs use the Michel method for human ChE determination. The availability of commercial clinical lab capability is largely location-specific and should be determined beforehand in the event that large-scale blood ChE activity determinations are expected.

4) **Analytical variability between diagnostic laboratories.** Round-robin analysis of duplicate blood samples by diagnostic labs following the same protocol can provide results that vary as much as 24% (Harlin and Ross 1990). Variability this large does not permit reliable determination of clinically significant ChE depression when data from several labs are being used.

5) **Kinetics of cholinesterase depression.** Depending on OP dose, route of exposure, and ChE assay used, ChE may not reach its minimum value for several hours. This is especially true for the red blood cell (RBC) cholinesterase (Morgan 1989). Note, however, that inhalation doses of nerve agent vapor can rapidly depress ChE activity; minimum values should be attained within 15-30 minutes post exposure.

We do not recommend urine thiodiglycol determination as a population screen for two reasons:

1) **Urine thiodiglycol monitoring as a measure of sulfur mustard exposure is an experimental technique** that is not suited for wide-scale application as a routine screen for potential exposure. It has proved useful as a recovery monitor in a recent case of occupational sulfur mustard exposure to a chemical munitions worker, wherein 24-hour urine samples were examined for a 3-4 week period. Abnormally high concentrations of thiodiglycol were observed in the worker's urine for 1 week post-exposure.

2) **Logistics of obtaining 24-hour urine samples.** To reduce the variability characterizing urinalysis that relies on single, demand samples, 24-hour urine samples for thiodiglycol determination are necessary.

Table 1. Antidote Treatment Guidelines for Nerve and Vesicant Agent Exposure[a]

Nerve Agents (GA, GB, VX)	
Symptom Level	Treatment
Convulsions, coma, severe respiratory distress, muscle fasciculations (other than at site of contact).	•6 mg atropine IM. Repeat 2 mg doses IV every 5-15 minutes as needed. No IV atropine if patient hypoxic. Ventilation. Pediatric: 25-40 ug/kg. Infant: 25 ug/kg.[b] •1-2 gm 2-PAM-Cl (Protopam®) in 100 mL saline IV over 15-30 min for initial dose with careful monitoring of blood pressure throughout infusion. Second dose after 1 h if symptoms indicate. Pediatric: 15-25 mg/kg. Infant: try 15 mg/kg. • ≥ 10 mg diazepam (Valium®) to control seizure activity and reduce possibility of resultant brain damage. •Support respiration.
Abdominal cramping, diffuse sweating, mild respiratory hypersecretions, diarrhea.	•2 mg atropine IM. Repeat 2 mg doses IM or IV every 5-15 minutes as needed. Pediatric: 15-25 ug/kg. Infant: 15 ug/kg.[b] •1-2 gm 2-PAM-Cl (Protopam®) in 100 mL saline IV over 15-30 min for initial dose with careful monitoring of blood pressure throughout infusion. Second dose after 1 h if symptoms indicate. Pediatric: 15-25 mg/kg. Infant: try 15 mg/kg.
Pupillary constriction (e.g., miosis), runny nose and shortness of breath	•2 mg atropine IM repeated at 5 min intervals until breathing is "comfortable." •1 gm 2-PAM-Cl (Protopam®) in 100 mL saline IV over 15-30 min.
Blurred vision only, pupillary constriction (e.g. miosis) (with or without blurred vision) only.	•Observe without treatment.

[a]See footnotes at end of table.
[b]See footnotes at end of table.

Table 1. Antidote Treatment Guidelines for Nerve and Vesicant Agent Exposure[a] (Continued)

Vesicant Agents (H, HD, HT, L)

Symptom Level	Treatment
Mustards: Chemicals burns/blisters, pulmonary distress, immunosuppression/bone marrow damage, eye damage	•Ventilatory support with O_2 and PEEP[c], some fluids, dark room; follow burn regimen for large blisters (do not unroof), asepsis. Do not overhydrate. No specific therapy proven in man[d,e]
Lewisite: Chemical burns/blisters, tissue blanching, dead skin, coughing and pulmonary secretions, GI symptoms of emesis and diarrhea, eye damage. Pain.	•BAL in oil injection, 0.5 mL/25 lbs. body wt. deep IM (to max. of 4 mL). •Repeat BAL injection every 4 h to a total of 4 doses. Shorten interval to 2 h for severe cases. BAL ophthalmic ointment if eye exposure.
Mustards: Eye irritation (red eyes or photophobia); respiratory irritation; itching, reddening of skin with small blisters.	•Antihistamines and corticosteroids may relieve skin and eye irritation; protect eyes from light with dark glasses, dark room or patch(es). Guard against infections
Lewisite: Stinging pain and reddening, itching and irritation of skin. Pain, reddening and swelling of eye tissues. Small blisters.	•BAL in oil injection, 0.5 mL/25 lbs. body wt. deep IM (to max of 4 mL). Repeat as needed every 4 h; 4 doses unlikely. BAL ophthalmic ointment if eye exposure.

[a]For more detailed description of casualty therapy, see Sidell, 1990 (USAMRICD TM 90-1).

[b]Provide atropine until signs of "atropinization" occur (secretions are dry and ventilation is easy; comfortable breathing in conscious patients); use until signs of improvement are observed and then taper off dose (Leffingwell, 1990; Sidell 1986, 1988, 1990).

[c]Positive End-Expiratory Pressure.

[d]An experimental therapy, consisting of high doses of sodium thiosulfate (3000 mg/kg to react with mustard), Vit E (20 mg/kg to scavenge free radicals) and a corticosteroid (dexamethasone at 8 mg/kg) within 30 min after exposure permitted lab rats to survive 3 LD_{50} of mustard (Vojvodic et al. 1985).

[e]Cortisone injections plus hydrocortisone ointment decreased the depth of skin injury in dermally exposed rabbits. However, this corticosteroid treatment did not speed healing (Vogt et al. 1984).

Table 2. General Decontamination Guidelines for Nerve and Vesicant Agents[a]

1. For best results, VICTIM MUST BE DECONNED WITHIN MINUTES OF INITIAL EXPOSURE

2. For staff, must be before exit from a "dirty" or potentially contaminated area. Mustard agents and VX are particularly problematic

3. Staff need protective equipment, clothing, etc., particularly before entry to confined space

4. Flush exposed EYES with copious quantities of water only (DO NOT USE BLEACH OR ANY OTHER DECON SOLUTION ON EYE OR ANY OTHER MUCOUS TISSUE)

5. For best results, decon skin with undiluted Clorox® (5% NaClO). This treatment will be irritating to wounds. Use copious quantities of clear water as rinse.

6. Blot (do not swab or wipe) skin with decon solution

7. In the absence of chlorine solutions, use available alkaline substance such as washing or baking soda, ammonia, etc.; or soap and lukewarm water followed by copious quantities of clear water; etc.

8. Decon clothing, instruments with high test hypochlorite [HTH, 15% Ca $(ClO)_2$] or Clorox® [5% (NaClO)]. SUPER TROPICAL BLEACH (STB, chlorinated lime and calcium oxide) suitable for SURFACES ONLY.

9. Dispose of potentially contaminated clothing in plastic bag(s). Twist, tape, fold over, tape again. Double-bag, remove from occupied area, and hold for disposal. Contents should be disposed of in an environmentally acceptable manner.

[a]More detailed decontamination guidelines are compiled in "Standards for Decontamination for the Chemical Stockpile Emergency Preparedness Program" by B. Shumpert and A. Watson, ORNL (Draft of September 1991 in Steering Committee review).

REFERENCES

Harlin, K. S. and P. F. Ross (1990). "Enzymatic-spectrophotometric method for the determination of cholinesterase activity in whole blood: collaborative study." J. Assoc. Off. Anal. Chem. 73: 616-621.

Leffingwell, S.S. (1990). "Health effects of incidents," handout and oral presentation, Technical Orientation Workshop, Landmark Inn, Park City, Utah, Sept. 5-7, 1990. Sponsored by Automation Subcommittee, Chemical Stockpile Emergency Preparedness Program.

Morgan, D.P. (1989). *Recognition and management of pesticide poisonings*, 4th Ed. EPA-540/9-88-001. U.S. Environmental Protection Agency, Washington, DC.

Munro, N.B., et al (1990). "Treating exposure to chemical warfare agents:implications for health care providers and community emergency planning," Environmental Health Perspectives 89: 205-215.

Munro, N.B., et al (1991). "Cholinesterase activity levels in domestic animals as a potential biomonitor for nerve agent and other organophosphate exposure," J. Amer. Vet. Med. Assoc. 199(1): 103-115.

Sidell, F.R. (1986). "General guidelines for therapy of acetylcholinesterase intoxication," (Course handout). Biomedical Laboratory, Medical Research Division, Aberdeen Proving Ground, MD 21010-5425.

Sidell, F.R. (1988). "Medical aspects of nerve agent exposure," pp.3-8 In: Medical Bulletin of the U.S. Army Medical Department, PB-88-8, 7th Army Medical Command, Heidelberg, Germany.

Sidell, F.R. (1990). "Clinical notes on chemical casualty care." Pamphlet USAMRICD TM 90-1, U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD 21010-5425.

Van Hooidonk, C., et al. (1983). "CW agents and the skin. Penetration decontamination." pp. 153-160, in *Proc. of the International Symposium on Protection Against Chemical Warfare Agents*, Stockholm, FOA Reports C40171-C2-C3.

Vogt, R. et al (1984). " Pathogenesis of skin lesions caused by sulfur mustard," Fundam. Appl. Toxicol. 4:571-583

Vojvodic, V., et al. (1985). "The protective effect of different drugs in rats poisoned by sulfur and nitrogen mustards," Fundam. Appl. Toxicol. 5: S160-S168.

GLOSSARY

asepsis -- prevention of septic infection by use of sterilized dressings, instruments, etc.

atropine -- an antidote to organophosphate insecticide and nerve agent poisoning; acts by blocking stimulation from excess acetylcholine at parasympathetic receptor sites; relieves smooth muscle constriction in lung and GI tract and reduces glandular paralysis; dries up respiratory tract secretions.

BAL -- British Anti-Lewisite; the synthetic dithiol 2,3-dimercapto-1-propanol developed as a Lewisite antidote by British toxicologists in the years immediately prior to WWII. If given to victim within 1 h of exposure, can prevent skin vesication; also enhances urinary excretion of systemic arsenic resulting from Lewisite exposure.

cholinesterase (ChE) -- a normally occurring enzyme that inhibits the acetylcholine neurotransmitter found at nerve endings. Cholinesterase prevents excessive accumulation of acetylcholine, which (accumulation) results in uncontrolled impulse transmission and toxic signs such as drooling, miosis, cardiac arrythmia, convulsions, etc. The toxicity of organophosphate compounds results from their ability to inhibit cholinesterase and permit excess quantities of acetylcholine to accumulate at synapses.

Dupont ACA -- a commercial analytical method that utilizes the colorimetric determination of thiocholine to quantify plasma cholinesterase activity. A direct method with results in U/mL; 10 min per sample.

fasciculations -- isolated areas of uncontrolled muscle twitching described by some as looking like "a bag of worms." A sign of organophosphate nerve agent exposure.

GI -- gastrointestinal (tract). When used to describe nerve agent exposure, refers to diarrhea, abdominal cramping, vomiting, etc.

kg -- kilogram (approx. 2.2 lb).

Lewisite -- an organic arsenical vesicant, dichloro(2-chlorovinyl) arsine. More volatile than the sulfur mustard agents; causes immediate severe pain upon skin or eye contact. Stockpiled only at Tooele Army Depot, Utah.

μg -- microgram, or 1 millionth of a gram (i.e., 10^{-6} g).

mg -- milligram, or 1 thousandth of a gram (i.e., 10^{-3} g).

miosis -- pupil pin-pointing, an early sign of OP exposure.

Michel method -- a once-popular analytical method for determining red blood cell cholinesterase activity. Employs the change in pH of the assay mixture as a result of the enzymatic hydrolysis of acetylcholine. An indirect method with results in ΔpH/mL/h; 90 min per sample.

organophosphate (OP) -- insecticides and nerve agents that contain carbon, oxygen, and phosphorous atoms plus other moieties. All inhibit cholinesterase enzymes and result in a "short-circuit" of normal nervous system control of the muscles, some glands and the central nervous system. The result is over-stimulation and malfunction. At increasing doses, signs include pupil pin-pointing (miosis), frontal headache, abdominal cramping, diarrhea, respiratory distress, uncontrolled muscle twitching, copious respiratory secretions, convulsions and respiratory arrest. Commercial OP insecticides include malathion, diazinon, and guthion; OP nerve agents in the unitary stockpile include GA, GB, and VX. Nerve agents are approximately 10^3 to 10^4 times more potent than commercially available OP insecticides.

2-PAM-Cl -- protopam chloride; 2-pyridine aldoxime methyl chloride. An antidote to organophosphate insecticide and nerve agent poisoning; acts by removing OP from ChE and restores normal control of skeletal muscle contraction. Most effective when given with atropine.

sulfur mustard -- a group of vesicant agents (H, HD, HT) that are various formulations of bis(2-chloroethyl) sulfide. Produces skin blisters and damage to eyes and respiratory tract; human carcinogen; mutagenic in cellular assays.

vesicant -- term describing blister agents; those agents (H, HD, HT, Lewisite) that produce vesicles or blisters on skin and damage both eyes and mucous membranes.