

Chapter 1

NERVE AGENTS

Summary

NATO Codes: GA, GB, GD, GF, VX

Signs and Symptoms:

Vapor, small dose: miosis, rhinorrhea, mild difficulty breathing.

Vapor, large dose: sudden loss of consciousness, convulsions, apnea, flaccid paralysis, copious secretions, miosis.

Liquid on skin, small to moderate dose: localized sweating, nausea, vomiting, feeling of weakness.

Liquid on skin, large dose: sudden loss of consciousness, convulsions, apnea, flaccid paralysis, copious secretions.

Field Detection: Joint Chemical Agent Detector (JCAD), M256A1 Chemical Agent Detector Kit, M18A2 Chemical Agent Detector Kit, M8 Chemical Agent Detector Paper, M9 Chemical Agent Detector Paper, Improved Chemical Agent Monitor (ICAM), M93 series Fox Reconnaissance System, M21 Remote Sensing Chemical Agent Alarm (RSCAAL), M90 Chemical Warfare Agent Detector, M22 Automatic Chemical Agent Detection Alarm (ACADA).

Decontamination: Reactive Skin Decontamination Lotion, soap and water, 0.5% hypochlorite solution.

Management: Administer three Antidote Treatment Nerve Agent Autoinjectors (ATNAAs) and one Convulsive Antidote, Nerve Agent (CANA) to severe casualties; support airway for respiratory distress.

Overview

Nerve agents are the primary chemical warfare agent threat because of their high toxicity and effectiveness through multiple routes of entry. They are absorbed through the eyes, respiratory tract, and skin.

Toxicity

The classic nerve agents are tabun (GA), sarin (GB), soman (GD), GF, and VX. Tables 1-1 and 1-2 show the toxicities of the nerve agents by inhalation and skin exposure.

The Ct product, or C (concentration) × t (time), is a marker of the vapor or aerosol dose to which someone has been exposed. The agent’s weight is used for C and period of exposure in minutes for t. A person exposed to a high concentration for a short time may have the same dose as someone exposed to a low concentration for a longer time.

The LCt₅₀ is the Ct of agent vapor that will be lethal (L) to half of the population exposed to it. The ICt₅₀ is the Ct that will incapacitate (I) half of those exposed to it. Table 1-1 shows the estimated LCt₅₀, ICt₅₀, and Ct that will cause pinpoint pupils (miosis) in half of the exposed population (MCt₅₀).

Table 1-1. Comparative Nerve Agent Vapor Toxicity*

Agent	LCt ₅₀	ICt ₅₀	MCt ₅₀
GA	400	300	2–3
GB	100	75	3
GD	70	Unknown	< 1
GF	Unknown	Unknown	< 1
VX	50	35	0.04

*For this table, one concentration of VX = 50, and one concentration of GB = 100, meaning it would take 2 times more GB to have the same median lethal dose as one concentration of VX.

LCt₅₀: median lethal concentration/time

ICt₅₀: median incapacitation concentration/time

MCt₅₀: median first noticeable effect (of miosis) concentration/time

Table 1-2. Comparative Median Lethal Dose Values on Skin*

Agent	Amount
GA	100
GB	170
GD	5
GF	3
VX	1

*Refer to FM 3-11.9, *Potential Military Chemical/Biological Agents and Compounds*, for specific LD₅₀ information. For this table, one dose of VX = 1, and 170 doses of GB = 170, meaning it would take 170 times more GB to have the same median lethal dose as one dose of VX.

The LD₅₀ is the dose (D) of agent liquid or solid that is lethal (L) to half of the population exposed to it. The LD₅₀ of VX is the size of a droplet as wide as two columns of the Lincoln Memorial on a Lincoln penny. Table 1-2 compares median lethal values of nerve agents when placed on the skin.

Mechanism of Action

Nerve agent poisons block the action of the enzyme acetylcholinesterase (AChE). The normal function of acetylcholinesterase is to break down (hydrolyze) the chemical messenger, or neurotransmitter, acetylcholine (ACh).

The nervous system is made up of electrically conducting cells called neurons (nerve cells). Neurons convey information by electrical signals, called action potentials. When an electrical signal reaches the end of the neuron, the information must be conveyed to the next cell by means of a chemical messenger, or neurotransmitter. Cholinergic neurons use ACh as the neurotransmitter to communicate with other cells. When an electrical signal reaches the end of a cholinergic neuron, the neuron releases packets of ACh. These cross a space, called a synaptic cleft, to the next cell in the series, another neuron, gland cell, or muscle cell. There they interact with specialized proteins called synaptic receptors. The interaction of enough molecules of

ACh with postsynaptic receptors, or receptors on the second cell, causes a new electrical signal that conveys the communication into the second cell.

AChE, which is present on postsynaptic membranes, serves as the turn-off switch for this process; the reaction is stopped when AChE hydrolyzes ACh. Nerve agents act directly upon AChE. When a nerve agent inhibits AChE, it cannot perform its normal function of hydrolyzing ACh. ACh then accumulates, and the target cell's action continues uncontrolled, producing a clinical syndrome called cholinergic crisis.

Effects

The primary concern of the care provider when treating patients poisoned by nerve agents is to provide correct, timely, and lifesaving care. The first step in providing this care is to understand the effects that vapor or liquid nerve agent exposure has on the patient.

Nerve agent produces cholinergic crisis by inhibiting AChE and thus prolonging the action of ACh. The parts of the body that are affected by excessive ACh accumulation are:

- eyes
- nose (glands)
- mouth (glands)
- respiratory tract
- gastrointestinal tract
- cardiac muscle
- sweat glands
- skeletal muscles
- central nervous system

Eyes

Direct contact with a nerve agent vapor or aerosol produces effects on the eyes. When the agent's route of entry is through the skin or by ingestion, the effect on the eyes is delayed or may not occur. The main effect of the agent is to cause miosis, or pinpointing of the pupils. One or both pupils may be pinpointed and

unresponsive to light or darkness. Pinpoint pupils cause a complaint of dim vision that is more pronounced in low light conditions; soldiers may complain that everything “looks black,” even in the middle of the day. Frontal headache, mild aching around the eye, or severe eye pains are common complaints in a soldier exposed to a moderate concentration of agent. About one patient in ten may complain of nausea. Twitching of the eyelids may be observed through the protective mask, and the eyes may be reddened. When a light source is used to test for pupillary response, the patient may complain of an ache behind the eyes due to light sensitivity.

Nose and Mouth

The secretory glands of the nose and mouth are as sensitive as or more sensitive than the eyes to nerve agent vapor or aerosol. If a soldier is poisoned by nerve agent liquid on the skin or through ingestion, the nose will become affected, but only in response to the whole body's (systemic) involvement. But if the patient is exposed to a nerve agent vapor or aerosol, the nose will begin to run immediately. This effect has been described by patients recovering from accidental nerve agent vapor exposure as “worse than a cold or hay fever” and “like a leaking faucet.” Even after low concentrations of agent, runny nose (rhinorrhea) may be severe. The mouth will secrete saliva so copious that watery secretions run out the corners of the mouth.

Respiratory Tract

Inhalation of a small amount of nerve agent vapor will cause the patient to complain of tightness in the chest or shortness of breath (dyspnea). This occurs because the excessive ACh stimulates the muscles in the airways to contract and constrict the airways (bronchoconstriction). As the concentration increases, breathing difficulty will become severe (feeling like a severe asthma attack). One or two breaths of a high concentration of nerve agent vapor will cause gasping and irregular respirations within seconds to minutes. Cessation of breathing (apnea) can occur within minutes after exposure to a large amount of nerve agent, through either liquid on the skin or vapor inhalation.

Excessive bronchial and upper airway secretions (bronchorrhea) caused by stimulation of the airway glands by the excessive ACh will compound breathing difficulty. These secretions can obstruct the airway and cause difficulty in moving air into and out of the lungs.

Gastrointestinal Tract

After exposure to a large but sublethal concentration of vapor, the patient will complain of nausea and may vomit. Nausea and vomiting may also be the first effects from liquid nerve agent exposure on the skin. The patient may also complain of “heartburn” and pain in the abdomen, and he or she may belch frequently and have diarrhea or involuntary defecation and urination. These effects usually occur within several minutes after vapor exposure. However, after liquid agent exposure on the skin, these effects may lag in onset for as long as 18 hours after a sublethal exposure.

Cardiac Muscle

The heart rate can either increase or decrease after nerve agent exposure. Generally, blood pressure will increase, but blood pressure can rarely be determined in a contaminated area because the casualty and the care provider are in protective gear. The patient’s heart rate will not aid the care provider in choosing the treatment for nerve agent poisoning.

Sweat Glands

The skin is very permeable to nerve agent. When penetration occurs after either liquid or vapor exposure, localized sweating occurs and progressively spreads over the surrounding skin area as nerve agent is absorbed. The likelihood that the care provider will be able to observe this localized sweating is minimal.

Skeletal Muscles

After exposure to a moderate or large amount of nerve agent, the patient will complain of weakness and twitching of muscle groups. The twitching can first be noticed at the site of a liquid

droplet on the skin. The muscles may show a rippling effect (fasciculation). As the nerve agent effect progresses, muscles can go into a prolonged contraction. However, instead of prolonged contraction, the large muscle groups may begin unsynchronized contractions that cause the arms and legs to flail about. The hyperactivity of the muscles in these instances leads to muscle fatigue and flaccid paralysis (being limp or unable to move). Without aggressive care, such a casualty will not survive.

The twitching caused by the direct effect of nerve agents on skeletal muscle may be difficult to distinguish from the tonicoclonic movements of convulsive seizures, but it is not a seizure. Seizures are caused by electrical discharges in the brain. A nerve-agent-poisoned patient who has been treated, has normal mental status, and is talking appropriately, but still has twitching, is most likely not seizing but suffering the skeletal muscle effects only.

Additionally, the skeletal muscle effects of nerve agents can worsen the patient's respiratory status by weakening or paralyzing the muscles of respiration, especially the diaphragm.

Central Nervous System

The effects of a large inhalation or liquid exposure on the brain and spinal cord are rapid and usually fatal under battlefield conditions. The soldier almost immediately loses consciousness, followed seconds later by seizure activity. Several minutes later, respiration ceases. Without immediate care, such soldiers will not survive to reach Role 1 treatment. Seizures may be present without motor activity, especially in a patient who has been either twitching or seizing for long enough that he or she has depleted the muscles of energy in the form of adenosine triphosphate.

When exposed systemically to low amounts of nerve agent, the soldier may complain of generalized weakness. Some people who survived low-dose exposures complained of nonspecific symptoms for weeks and have been described as having "post-neuro-syndrome." These symptoms include change in sleep pattern, mild memory losses, and new headaches. Some symptoms may be reflective of or indistinguishable from posttraumatic stress disorder.

Treatment

The most important care the casualty receives is given within the first several minutes after exposure (self-aid, buddy aid). Tables 1-3 and 1-4 show nerve agent effects, the onset time of these effects, and the required self-aid and buddy aid. These tables show the typical time course for mild, moderate, and severe nerve agent exposure. Immediate care, including administration of antidotes, can mean the difference between survival and death in a soldier exposed to a nerve agent. If aggressive care is not given to the patient exposed to a lethal concentration, death can result within 5 minutes after the appearance of symptoms.

It is imperative that every care provider understands the effects of nerve agents, the time in which effects occur, and the correct steps to treat the exposed soldier. The care provider must rapidly determine the following:

- extent of the poisoning,
- what medications have been administered,

Table 1-3. Nerve Agent Effects: Vapor Exposure

Mild <ul style="list-style-type: none">• Eyes: miosis, dim vision, headache• Nose: rhinorrhea• Mouth: salivation• Lungs: dyspnea (tightness in the chest)• Time of onset: seconds to minutes after exposure	Immediate Treatment <ul style="list-style-type: none">• <i>Self-aid:</i> one ATNAA• <i>Buddy aid:</i> stand by
Severe <p>All of the above, plus</p> <ul style="list-style-type: none">• Severe breathing difficulty or cessation of respiration• Generalized muscular twitching, weakness, or paralysis• Convulsions• Loss of consciousness• Loss of bladder and bowel control• Time of onset: seconds to minutes after exposure	Immediate Treatment <ul style="list-style-type: none">• <i>Self-aid:</i> none; soldier will be unable to help self• <i>Buddy aid:</i> three ATNAAs and diazepam immediately

ATNAA: antidote treatment nerve agent autoinjector

Table 1-4. Nerve Agent Effects: Liquid on Skin**Mild to Moderate**

- Muscle twitching at site of exposure
- Sweating at site of exposure
- Nausea, vomiting
- Feeling of weakness
- Time of onset: 10 minutes to 18 hours after exposure

Immediate Treatment

- *Self-aid*: one to two ATNAAs, depending on severity of symptoms
- *Buddy aid*: stand by

Severe

- All of the above, plus
- Severe breathing difficulty or cessation of breathing
 - Generalized muscular twitching, weakness, or paralysis
 - Convulsions
 - Loss of consciousness
 - Loss of bladder and bowel control
 - Time of onset: minutes to an hour after exposure

Immediate Treatment

- *Self-aid*: none; soldier will be unable to help self
- *Buddy aid*: three ATNAAs and diazepam immediately

ATNAA: antidote treatment nerve agent autoinjector

- complications induced by the poisoning and/or resulting from conventional wounds, and
- if possible, route of exposure, liquid or vapor; liquid poisoning can delay onset of effects.

Self-Aid and Buddy Aid

All military personnel must know the signs and symptoms of nerve agent poisoning and the correct first aid in order to evaluate exposures and provide the appropriate self-aid and buddy aid. Timely and correct determination of the type of agent and route of entry causing the signs or symptoms is critical if the poisoned soldier is to survive to reach definitive medical care. Nerve agents will, under most field conditions, be encountered in both the vapor and liquid forms. When nerve agents are encountered and soldiers have donned protective equipment, a hasty self-evaluation for signs or symptoms of poisoning must be conducted. This self-evaluation implies that soldiers know the signs and symptoms of mild and severe nerve agent poisoning,

as well as the correct first aid. Decontamination eliminates nerve agents on the skin surface that could continue to be absorbed, causing a “time release” effect of symptoms.

Take the following steps for self-aid and buddy aid:

1. First, protect yourself by donning **mission-oriented protective posture (MOPP) level 4**.
2. Next, assist the casualty in **decontamination** of exposed skin in the following order:
 - a. face
 - b. neck area
 - c. chest area
 - d. abdomen
 - e. arms and hands
 - f. other exposed skin areas
3. **Administer drugs** following the guidelines below.

Drug Therapy

Atropine is the drug of choice for treating nerve agent poisoning. It will dry secretions (including those in the airways), reduce bronchoconstriction, and decrease gastrointestinal motility. (Note: use of atropine in the absence of nerve agent will cause the casualty to experience inhibition of sweating and heat storage problems in a warm climate.) Atropine will not relieve miosis, muscle twitching, or spasms, or increase diaphragm effort.

Pralidoxime chloride (2-PAM Cl) is the second drug for use in nerve agent poisoning cases. The 2-PAM Cl removes nerve agent (except soman) from AChE. This drug must be used as early as possible. Each ATNAA includes autoinjectors of 2.1 mg atropine and 600 mg 2-PAM Cl. Giving one ATNAA means injecting both drugs into the patient (Figure 1-1).

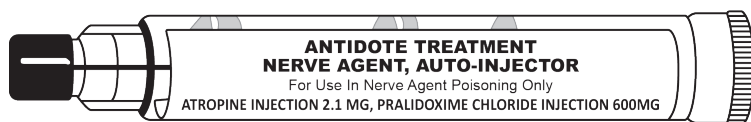


Figure 1-1. Antidote Treatment Nerve Agent Autoinjector (ATNAA).

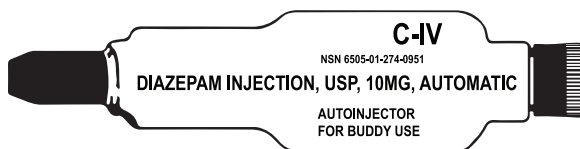


Figure 1-2. Convulsive Antidote, Nerve Agent (CANA) autoinjector.

Diazepam in the 10-mg autoinjector (CANA) is the drug adopted by the US military for use in controlling convulsing patients (Figure 1-2). If symptoms are severe, involving two or more organ systems (for example, the lungs and gastrointestinal tract), all three ATNAAs and one CANA should be given immediately to lessen the convulsive activity the soldier may experience. The key to increasing diazepam's effectiveness is administering it before convulsions begin. Diazepam is not for self-use. It should be given only to severe casualties via buddy aid. See illustrations for self and buddy aid in Figures 1-3 through 1-6.

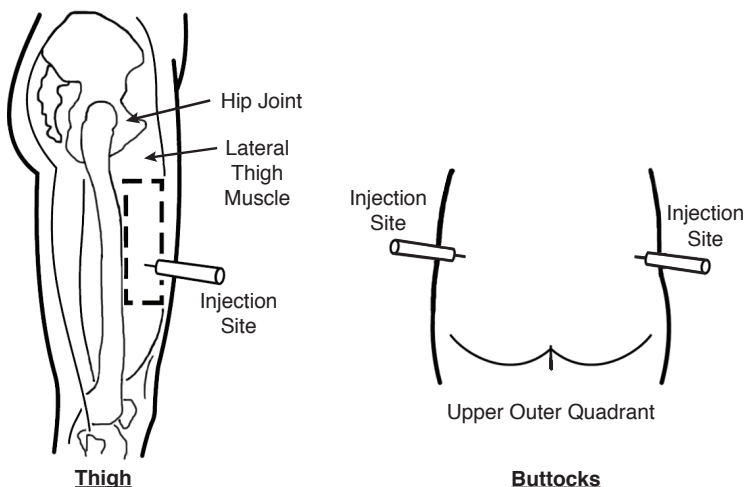


Figure 1-3. Primary (thigh) and secondary (buttocks) injection sites.



Figure 1-4. Self-aid injection.



Figure 1-5. Buddy aid injection.

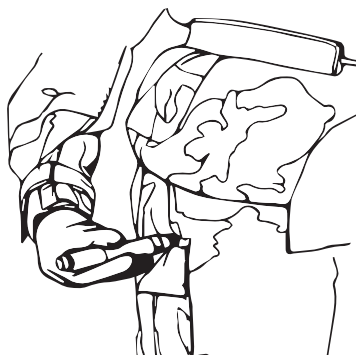


Figure 1-6. Hold the autoinjector like a pen.

Mild and Improving Symptoms (Especially Vapor-Only Exposure)

Observation is all that is needed for the casualty with mild symptoms, such as rhinorrhea, slight or recovering breathing difficulty, or excessive salivation that is decreasing. In the casualty with mild symptoms that appear to be clearing, one ATNAA administered during self-aid followed by observation for several hours, will normally be all that is needed.

In general, if there is suspicion that the patient may have had a liquid exposure, he or she should be observed for at least several hours and not returned to duty. The onset of symptoms after liquid exposures can be delayed by many hours.

Pain in the eyes, twitching of the eyelids, redness, and miosis cannot be treated in the field setting by the care provider. At the battalion aid station, eye pain can be controlled with atropine eye drops. These conditions, although annoying, are not life-threatening.

Severe Symptoms

When the effects progress to involve more than one organ system, the situation has changed from a mild to a severe exposure. Buddy aid in determining this transition is critical. As the change occurs, the remaining ATNAAs and one CANA autoinjector must be administered, as described above. Diazepam should always be administered when the three ATNAAs are given together. Self-aid or buddy aid must always be promptly followed with Role 1 medical care.

If the casualty is unconscious and in respiratory distress, ATNAAs and diazepam should be given immediately, followed by additional atropine. Atropine administered with the autoinjector will show some effectiveness in 3 to 5 minutes. Additionally, more atropine (2 mg) should be given every 2 to 5 minutes until the patient breathes easily without excess secretions complicating breathing. A total of 15 to 20 mg of atropine may be required in the first 1 to 3 hours after the onset of symptoms. Atropine will have a drying effect on salivation and rhinorrhea. During the time the atropine takes to reach maximum effect, the constriction and secretions in the airway and feeling of "tightness in the chest" will begin to decrease.

There is no upper bound to atropine use. Titrate for correction of breathing difficulties. At Role 2 and higher, more precise administration of additional doses of atropine will be possible through the intravenous (IV) route. Discontinue atropine when:

- Secretions of the mouth, nose, and lungs are minimized.
- The casualty says that breathing is easier, or it is easier to administer assisted ventilation.

If severe signs or symptoms persist 1 hour after using the three ATNAAs and the CANA, three additional 2-PAM Cl autoinjectors should be administered. The maximum 2-PAM Cl dose is six autoinjectors (3,600 mg) or two sets of three (6 total). IV 2-PAM Cl may be administered when available. Excess 2-PAM Cl may harm the casualty by dangerously raising blood pressure and causing laryngospasm. Never give more than three autoinjectors (or 2,000 mg IV) of 2-PAM Cl per hour. Discontinue the use of 2-PAM Cl after symptoms of respiratory distress have eased.

The doctrine for diazepam's use instructs the soldier to administer one CANA to his or her buddy immediately after using the third ATNAA in severe poisoning cases. The care provider may administer a second, third, or fourth CANA using the guidelines below.

After the first injection (buddy aid):

- Observe the casualty for about 2 minutes.
- Ventilate if necessary.
- Turn the casualty on his or her side to facilitate breathing.
- Pad areas to prevent other injuries.
- Restrain if necessary.
- If still convulsing after 2 minutes, give the second, third, or fourth CANA to stop seizures. Enough diazepam must be given to stop the seizures as soon as possible. Seizures cause brain damage and interfere with breathing. The longer the seizures last, the more difficult they are to stop and the greater the tendency for seizures to return. If the seizures do return, CANAs must be readministered until they stop again.

Like atropine for breathing, CANAs are titrated to stop seizures and prevent brain damage. Medical officers may give more diazepam, either intramuscularly or IV, if they deem it necessary.

Ventilation

Some severe nerve agent casualties will need assisted ventilation. Aggressive airway maintenance and the use of assisted ventilation will greatly increase the casualty's chances for survival. Providing assisted ventilation in a contaminated environment is possible using the Resuscitation Device, Individual Chemical (RDIC). The RDIC is a bag valve mask device that has an M40-style filter attached and is protected by a butyl rubber covering. By using this device, a casualty can survive to reach a care facility where mechanical ventilation is available. The soldier will not survive without this aggressive resuscitation.

Pretreatment

The US military has adopted the policy of pretreating soldiers against nerve agents' effect on AChE with pyridostigmine. The Food and Drug Administration approved the use of pyridostigmine bromide as pretreatment against GD in 2003. Soldiers may be issued a 14-day package with two blister packs of pyridostigmine tablets (Figure 1-7). Each blister pack contains 21 tablets, and each tablet contains 30 mg of pyridostigmine. When ordered by the unit commander, one tablet is taken orally every 8 hours. If a scheduled dose is missed, it is not made up; the soldier will take one tablet at the earliest opportunity to begin the next 8-hour interval. The soldier will discontinue taking the tablets on order from the unit commander. Doctrine allows commanders to renew the order once, for a total of 28 days.

Pyridostigmine bromide shields the AChE enzyme from the full effects of GD by providing reserve AChE. It prevents GD from permanently and irreversibly binding the enzyme, which it would otherwise do in 2 minutes. Pyridostigmine enhances the efficacy of 2-PAM Cl in GD casualties. The pretreatment does not increase the effectiveness of treatment for GB, GF, or VX. These

Outer Wrapper

**NERVE AGENT PYRIDOSTIGMINE PRETREATMENT
TABLET SET
(NAPP)**

1. COMMENCE TAKING ONLY WHEN ORDERED BY YOUR COMMANDER.
2. TAKE 1 TABLET EVERY 8 HOURS AS DIRECTED.
3. IT IS DANGEROUS TO EXCEED THE STATED DOSE.

30-MG PYRIDOSTIGMINE BROMIDE X 21 TABLETS.

Blister Pack

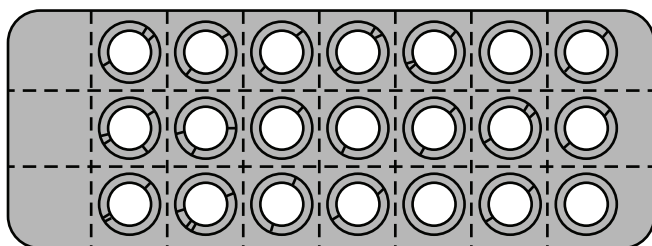


Figure 1-7. Blister pack of pyridostigmine tablets.

nerve agents also become irreversibly bound to AChE but require many hours to do so, and the binding does not affect therapy.

Pretreatment is not an antidote. Pretreatment alone will not protect the soldier and does not reduce the effects from the nerve agent. The effect of pyridostigmine bromide is to convert what would have been a lethal dose of GD into a dose that is survivable, but only if antidotes are promptly and correctly given. Instead of a dead soldier, pretreatment results in a sick one who requires treatment. When used in conjunction with ATNAA,

pyridostigmine enhances the effectiveness of ATNAA against GD only. It is critical that care providers understand that the effect of the pretreatment will have no effect on the severity of nerve agent poisoning symptoms. Therefore, an aggressive approach to care with antidotes is still warranted.

Common side effects of pyridostigmine bromide are increased bowel movements and abdominal cramping. In most cases these side effects decrease or resolve completely after a few days. If these or other symptoms persist, soldiers should see their care provider before going off the medication.

