The following synopsis serves as a brief review of PB, its function and mechanism.

**WHAT IS PB?**

- Pyridostigmine bromide is a chemical that blocks the nerve-signal-regulating enzyme acetylcholinesterase (AChE). It is given as a pill to military personnel during periods of high threat of chemical warfare attack to prevent death in the event of exposure to the nerve agent soman.
- It is used as an adjunct to postexposure administration of atropine and pralidoxime and confers no protection in the absence of these treatments.

**HOW NERVE AGENTS WORK**

- Soman, like other nerve agents, acts by inhibiting AChE, the enzyme that breaks down the body's acetylcholine (ACh), a neurotransmitter crucial to regulation of voluntary and involuntary muscles and to function of the brain.
- Once AChE is inhibited, ACh accumulates and may cause death from respiratory failure.
- In addition to spasms of the airways and reduced breathing drive, other effects of soman include slowed heart rate; increased secretions from the nose, eyes, intestines, salivary glands, sweat glands, and airways; increased movement of the intestines; twitching, weakness, and paralysis; loss of consciousness; and seizures.
HOW TRADITIONAL ANTI–NERVE AGENTS WORK

Atropine and Pralidoxime

- Atropine is the mainstay of postexposure antidote treatment for nerve agent exposure. Atropine opposes the effects of acetylcholine. (It opposes the “muscarinic effects”—see Chapter 3.) Rapid administration of atropine (by injection) is essential for severe nerve agent casualties.

- Pralidoxime (or other oximes), administered by injection, assists in post-exposure treatment. Oximes have the ability to cause nerve agents to be removed from AChE. However, they are ineffective once a process called “aging” occurs.

What Is Aging?

- Aging is a chemical change that happens to the AChE-nerve agent complex. Aging results in permanent inactivation of the AChE. Aging happens quickly in the case of the soman-AChE complex—half of complexed agents will have aged within a couple of minutes—whereas it takes hours for comparable aging to occur for other nerve agents, such as sarin.

- Once aging has occurred, oxime therapy is ineffective.

How PB Works

- PB is a carbamate compound that is thought to protect AChE by reversibly binding to (“carbamylating”) it, so that the nerve agent cannot bind to it. It may also assist in protection against nerve agent by “desensitizing” ACh receptors.

- PB is preferred over other carbamylators because it usually does not penetrate the central nervous system. Consequently, PB minimizes any harmful effects on brain function and does not significantly disable mental performance in those who take it.

PB Is Used When Soman Is a Danger

- PB is needed for adequate protection against soman: It takes only two minutes for 50 percent of the AChE-soman complexes to “age,” permanently inactivating AChE. Since this reaction time is so short, personnel do not have enough time after they have been exposed to soman to realize they have been exposed to a nerve agent, to take oxime, and to allow oxime to
pull nerve agent off AChE. Before all that can be done, most of the soman will have undergone aging, permanently inactivating the bound AChE. However, if personnel take PB in advance of exposure, soman will be prevented from binding to AChE in PB-bound AChE molecules, and aging cannot take place with permanent inactivation of these AChE molecules. The armed forces estimate that during a chemical attack, many personnel may be exposed to five times the lethal dose of nerve agent, so a “protective ratio” (the factor by which a treatment raises the lethal dose) of at least five is needed. Addition of PB allows the protective ratio to exceed five for soman, based on studies in monkeys.

- PB is not needed against sarin: It takes five hours for 50 percent of the AChE-sarin complexes to age. PB pretreatment does not confer an advantage against sarin, based on studies in animals; personnel have enough time to take oxime after exposure to this nerve agent before aging takes place, reactivating the AChE molecule. Indeed, soman is the only nerve agent for which PB is known to be necessary to produce an adequate protective ratio.