PS126 Primer on Weapons of Mass Destruction (WMD):

Nuclear, Radiological, Chemical, and Biological Weapons

Source: Globalsecurity.org

Biological Weapons

Throughout history, infectious diseases contracted naturally have had a significant impact on military operations. The intentional dissemination of disease adds a new dimension to threats that are posed by infectious and toxic agents traditionally transmitted only by natural routes. Biological agents reportedly have been employed to a limited extent during recent military conflicts (for example, dispersion of plague bacilli during World War II and use of trichothecene mycotoxins ("yellow rain" in South East Asia); however, their use actually dates from antiquity.

The qualitative and quantitative impact of biological warfare, or the threat of such warfare, on military forces and urban communities has changed markedly in the past 20 years. Improved production techniques have resulted in more virulent strains of organisms and the genetic modification of non-pathogenic organisms to pathogenic strains with virulent characteristics. The implications of genetic engineering for chemical and biological warfare are far-reaching. Genetic engineering provides the potential for improved virulence by the incorporation of genes (i.e., specific strands of DNA) permitting increased production of a pathogen or toxin. Thus, as much as 100 times more pathogen or toxin could be produced per cell than that which could be produced by naturally occurring strains. Cells that normally do not produce toxins may be altered to produce toxins for biological weapon development. Conversely, known pathogens or toxins may be genetically inactivated for vaccine countermeasure development. Cells can also be modified to produce antibodies directly for passive immunization against specific infectious agents. As with the human immune system, many current biowarfare detection kits depend on antibodies reacting with the antigenic surface coatings of pathogenic bacteria or viruses. Thus, modified non-pathogens can be used to mask the agent from the immune-based detector and, potentially, from the human immune system itself to increase the agent's effectiveness.

General robustness or survivability of a pathogen under the environmental stresses of temperature, ultraviolet (UV) radiation, and desiccation (drying) can also be genetically improved to promote stability during dissemination; nutrient additives are used to enhance survival of selected biological agents in aerosols. Controlled persistence of a pathogen to permit survivability under specified environmental conditions may eventually be possible. The potential also exists for the development of so-called "conditional suicide genes," which could program an organism to die off following a predetermined number of replications in the environment. Thus, an affected area may be safely reoccupied after a predetermined period of time.

Biological agents which may be used as weapons can be classified as follows:

Bacteria. Bacteria are small free-living organisms, most of which may be grown on solid or liquid culture media. The organisms have a structure consisting of nuclear material, cytoplasm, and cell membrane. They reproduce by simple division. The diseases they produce often respond to specific therapy with antibiotics.

Viruses. Viruses are organisms which require living cells in which to replicate. They are therefore intimately dependent upon the cells of the host which they infect. They produce diseases which generally do not respond to antibiotics but which may be responsive to antiviral compounds, of which there are few available, and those that are available are of limited use.

Rickettsiae. Rickettsiae are microorganisms which have characteristics common to both bacteria and viruses. Like bacteria, they possess metabolic enzymes and cell membranes, utilize oxygen, and are susceptible to broadspectrum antibiotics. They resemble viruses in that they grow only within living cells.

Chlamydia. Chlamydia are obligatory intracellular parasites incapable of generating their own energy source. Like bacteria, they are responsive to broad-spectrum antibiotics. Like viruses, they require living cells for multiplication.

Fungi. Fungi are primitive plants which do not utilize photosynthesis, are capable of anaerobic growth, and draw nutrition from decaying vegetable matter. Most fungi form spores, and free-living forms are found in soil. The spore forms of fungi are operationally significant. Fungal diseases may respond to various antimicrobial.

Toxins. Toxins are poisonous substances produced and derived from living plants, animals, or microorganisms; some toxins may also be produced or altered by chemical means. Toxins may be countered by specific antisera and selected pharmacologic agents.

Intrinsic features of biological agents which influence their potential for use as weapons include: infectivity; virulence; toxicity; pathogenicity; incubation period; transmissibility; lethality; and stability. Unique to many of these agents, and distinctive from their chemical counterparts, is the ability to multiply in the body over time and actually increase their effect.

II. Biological Threats Stemming From Human Activity

A. Accidental.

Civilian R&D such as research on dangerous pathogens; the field testing of genetically organisms; the marketing of products that eventually cause negative side effects; and/or the accidental spillage of contaminated materials into the environment.

B. Deliberate.

1. R&D in military or civilian laboratories for the purpose of producing a biological weapon. Two components - pathogen + delivery system

a. Low Tech System - the pathogen [usually an easily obtained pathogen or its bio toxin]; and a low tech delivery system [i.e. sealed glass container].

b. High Tech System - any naturally existing or man-made pathogen [modified in virulence and ability to survive adverse conditions]; and a high tech delivery system [i.e. missile].

c. Delivery via Living System - Human, Animal or Plants deliberately infected for the purpose of spreading disease.

2. Commercial Contamination

a. Deliberate infection of, or failure to cleanse, a food, hygiene, medical, etc. product; and the eventual dispersement of that infected product to unknowing individuals.

b. Deliberate violation of a public health law knowing full well that the act may cause the spread of disease [i.e. illegal dumping of untreated materials known to contain biohazards; the illegal disposing of biohazard material such as used syringes; etc.].

III. Zoonotic Etiology

This category may be natural or the result of human activity. It is recognized that the reservoirs of several emerging infectious diseases are animals. Among these are Sin Nombre (a hantavirus), and hemorrhagic fevers such as Marburg, Ebola and Lassa. Others are zoonoses -- diseases that affect both animals and humans. Rabies is probably the best known zoonosis. Recently emerging zoonotic diseases are (1)West Nile virus, which has now been discovered in the United States and has killed both wild birds and caused disease in humans; (2) Nipah virus, which emerged in Malayasia killings pigs and humans; and (3) in Australia, Hendra virus, which can kill horses and humans.

Anthrax is a zoonotic disease caused by *Bacillus anthracis*. There are two types of this disease: cutaneous anthrax and inhalation anthrax. About 95% of the human anthrax cases in the United States have been in the former category. Cutaneous anthrax develops when a bacterial organism from infected animal tissues becomes deposited under the skin. When a patient contracts cutaneous anthrax, he develops a small elevated lesion on his skin which becomes a skin ulcer, frequently surrounded by swelling or edema. The lymph gland near the lesion may also swell from the infection. If the lesion occurs on the

neck or on or about the eye, it may cause complications. The incubation period for cutaneous anthrax is from one to seven days. When a patient does not receive an effective antibiotic, the mortality rate for cutaneous anthrax is 10-20%. With treatment, the mortality rate falls to less than 1%.

Inhalation anthrax develops when the bacterial organism is inhaled into the lungs. A progressive infection follows. Since inhalation anthrax is usually not diagnosed in time for treatment, the mortality rate in the United States is 90-100%. A biological warfare attack with anthrax spores delivered by aerosol would cause inhalation anthrax, an extraordinarily rare form of the naturally occurring disease.

A lethal dose of anthrax is considered to be 10,000 spores; 80 percent of a population that inhaled such a dose would die. Less than one millionth of a gram is invariably fatal within five days to a week after exposure. According to an estimate by the US Congress's Office of Technology Assessment, 100 kilograms of anthrax, released from a low-flying aircraft over a large city on a clear, calm night, could kill one to three million people.

The disease begins after an incubation period varying from 1-6 days, presumably dependent upon the dose of inhaled organisms. Onset is gradual and nonspecific, with fever, malaise, and fatigue, sometimes in association with a nonproductive cough and mild chest discomfort. In some cases, there may be a short period of improvement. The initial symptoms are followed in 2-3 days by the abrupt development of severe respiratory distress with dyspnea, diaphoresis, strider, and cyanosis. Physical findings may include evidence of pleural effusions, edema of the chest wall, and meningitis. Chest x-ray reveals a dramatically widened mediastinum, often with pleural effusions, but typically without infiltrates. Shock and death usually follow within 24-36 hours of respiratory distress onset.

An epidemic of inhalation anthrax in its early stage with nonspecific symptoms could be confused with a wide variety of viral, bacterial, and fungal infections. Progression over 2-3 days with the sudden development of severe respiratory distress followed by shock and death in 24-36 hours in essentially all untreated cases eliminates diagnoses other than inhalation anthrax. The presence of a widened mediastinum on chest x-ray, in particular, should alert one to the diagnosis. Other suggestive findings include chest-wall edema, hemorrhagic pleural effusions, and hemorrhagic meningitis. Other diagnoses to consider include aerosol exposure to SEB; but in this case onset would be more rapid after exposure (if known), and no prodrome would be evident prior to onset of severe respiratory symptoms. Mediastinal widening on chest x-ray will also be absent. Patients with plague or tularemia pneumonia will have pulmonary infiltrates and clinical signs of pneumonia (usually absent in anthrax).

Almost all cases of inhalation anthrax in which treatment was begun after patients were symptomatic have been fatal, regardless of treatment. Historically, penicillin has been regarded as the treatment of choice, with 2 million units given intravenously every 2 hours. Tetracycline and erythromycin have been recommended in penicillin-sensitive patients. The vast majority of anthrax strains are sensitive in vitro to penicillin. However, penicillin-resistant strains exist naturally, and one has been recovered from a fatal human

case. Moreover, it is not difficult to induce resistance to penicillin, tetracycline, erythromycin, and many other antibiotics through laboratory manipulation of organisms. All naturally occurring strains tested to date have been sensitive to erythromycin, chloramphenicol, gentamicin, and ciprofloxacin.

Vaccines are available against some forms of anthrax, but their efficacy against abnormally high concentrations of the bacteria is uncertain. A licensed, alum-precipitated preparation of purified *B.anthracis* protective antigen (PA) has been shown to be effective in preventing or significantly reducing the incidence of inhalation anthrax. Limited human data suggest that after completion of the first three doses of the recommended six-dose primary series (0, 2, 4 weeks, then 6, 12, 18 months), protection against both cutaneous and inhalation anthrax is afforded. As with all vaccines, the degree of protection depends upon the magnitude of the challenge dose; vaccine-induced protection is undoubtedly overwhelmed by extremely high spore challenge.

If there is information indicating that a biological weapon attack is imminent, prophylaxis with ciprofloxacin (500 mg po bid), or doxycycline (100 mg po bid) is recommended. If unvaccinated, a single 0.5 ml dose of vaccine should also be given subcutaneously. Should the attack be confirmed as anthrax, antibiotics should be continued for at least 4 weeks in all exposed.

Ebola Haemorrhagic Fever

Ebola Haemorrhagic Fever is one of the most virulent viral disease known to humankind, causing death in 50-90% of all clinically-ill cases. Consequently, it has figured prominently in popular discussions of biological warfare, although its practical appli cations as an biological warfare agent remain speculative. The disease has its origins in the jungles of Africa and Asia and several different forms of Ebola virus have been identified and may be associated with other clinical expressions, on which further research is required.

The Ebola virus is transmitted by direct contact with the blood, secretions, organs or semen of infected persons. Transmission through semen may occur up to 7 weeks after clinical recovery, as with Marburg haemorrhagic fever. Health care workers have frequently been infected while attending patients. In the 1976 epidemic in Zaire, every Ebola case caused by contaminated syringes and needles died.

After an incubation period of 2 to 21 days, Ebola is often characterised by the sudden onset of fever, weakness, muscle pain, headache and sore throat. This is followed by vomiting, diarrhoea, rash, limited kidney and liver functions, and both internal and external bleeding. Specialized laboratory tests on blood specimens (which are not commercially available) detect specific antigens or antibodies and/or isolate the virus. These tests present an extreme biohazard and are only conducted under maximum containment conditions.

No specific treatment or vaccine exists for Ebola haemorrhagic fever. Severe cases require intensive supportive care, as patients are frequently dehydrated and in need of intravenous fluids. Experimental studies involving the use of hyperimmune sera on animals demonstrated no long-term protection against the disease after interruption of therapy.

Suspected cases should be isolated from other patients and strict barrier nursing techniques practised. All hospital personnel should be briefed on the nature of the disease and its routes of transmission. Particular emphasis should be placed on ensuring that high-risk procedures such as the placing of intravenous lines and the handling of blood, secretions, catheters and suction devices are done under barrier nursing conditions. Hospital staff should have individual gowns, gloves and masks. Gloves and masks must not be reused unless disinfected. Patients who die from the disease should be promptly buried or cremated.

As the primary mode of person-to-person transmission is contact with contaminated blood, secretion or body fluids, any person who has had close physical contact with patients should be kept under strict surveillance, i.e. body temperature checks twice a day, with immediate hospitalization and strict isolation recommended in case of temperatures above 38.3 C (101 F). Casual contacts should be placed on alert and asked to report any fever. Surveillance of suspected cases should continue for three weeks after the date of their last contact. Hospital personnel who come into close contact with patients or contaminated materials without barrier nursing attire must be considered exposed and put under close supervised surveillance.

The Ebola virus was first identified in a western equatorial province of Sudan and in a nearby region of Zaire in 1976 after significant epidemics in Yamkubu, northern Zaire, and Nzara, southern Sudan. Between June and November 1976 the Ebola virus infected 284 people in Sudan, with 117 deaths. In Zaire there were 318 cases and 280 deaths in September and October. An isolated case occurred in Zaire in 1977, a second outbreak in Sudan in 1979. In 1989 and 1990, a filovirus, named Ebola-Reston, was isolated in monkeys being held in quarantine in a laboratory in Reston (Virginia), Alice (Texas) and Pennsylvania. In the Philippines, Ebola-Reston infections occurred in the quarantine area for monkeys intended for exportation, near Manila. A large epidemic occurred in Kikwit, Zaire in 1995 with 315 cases, 244 with fatal outcomes. One human case of Ebola haemorrhagic fever and several cases in chimpanzees were confirmed in Côte d'Ivoire in 1994-95. In Gabon, Ebola haemorrhagic fever was first documented in 1994 and recent outbreaks occurred in February 1996 and July 1996. In all, nearly 1,100 cases with 793 deaths have been documented since the virus was discovered. The natural reservoir of the Ebola virus seems to reside in the rain forests of Africa and Asia but has not yet been identified.

Different hypotheses have been developed to try to uncover the cycle of Ebola. Initially, rodents were suspected, as is the case with Lassa Fever whose reservoir is a wild rodent (Mastomys). Another hypothesis is that a plant virus may have caused the infection of vertebrates. Laboratory observation has shown that bats experimentally infected with Ebola do not die and this has raised speculation that these mammals may play a role in

maintaining the virus in the tropical forest.

Ricin

Ricin is a glycoprotein toxin (66,000 daltons) from the seed of the castor plant. It blocks protein synthesis by altering the rRNA, thus killing the cell. Ricin's significance as a potential biological warfare agent relates to its availability world wide, its ease of production, and extreme pulmonary toxicity when inhaled.

Overall, the clinical picture seen depends on the route of exposure. All reported serious or fatal cases of castor bean ingestion have taken approximately the same course: rapid onset of nausea, vomiting, abdominal cramps and severe diarrhea with vascular collapse; death has occurred on the third day or later. Following inhalation, one might expect nonspecific symptoms of weakness, fever, cough, and hypothermia followed by hypotension and cardiovascular collapse. The exact cause of death is unknown and probably varies with route of intoxication. High doses by inhalation appear to produce severe enough pulmonary damage to cause death.

In oral intoxication, fever, gastrointestinal involvement, and vascular collapse are prominent, the latter differentiating it from infection with enteric pathogens. With regard to inhalation exposure, nonspecific findings of weakness, fever, vomiting, cough, hypothermia, and hypotension in large numbers of patients might suggest several respiratory pathogens.

Therapy is supportive and should include maintenance of intravascular volume. Standard management for poison ingestion should be employed if intoxication is by the oral route. There is presently no antitoxin available for treatment.

There is currently no prophylaxis approved for human use. Active immunization and passive antibody prophylaxis are under study, as both are effective in protecting animals from death following exposure by intravenous or respiratory routes.

Small Pox

Smallpox virus, an orthopoxvirus with a narrow host range confined to humans, was an important cause of morbidity and mortality in the developing world until recent times. Eradication of the natural disease was completed in 1977 and the last human cases (laboratory infections) occurred in 1978. The virus exists today in only 2 laboratory repositories in the U.S. and Russia. Appearance of human cases outside the laboratory would signal use of the virus as a biological weapon. Under natural conditions, the virus is transmitted by direct (face-to face) contact with an infected case, by fomites, and occasionally by aerosols. Smallpox virus is highly stable and retains infectivity for long periods outside of the host. A related virus, monkeypox, clinically resembles smallpox and causes sporadic human disease in West and Central Africa.

The incubation period is typically 12 days (range, 10-17 days). The illness begins with a prodrome lasting 2-3 days, with generalized malaise, fever, rigors, headache, and backache. This is followed by defervescence and the appearance of a typical skin eruption characterized by progression over 7-10 days of lesions through successive stages, from macules to papules to vesicles to pustules. The latter finally form crusts and, upon healing, leave depressed depigmented scars. The case fatality rate is approximately 35% in unvaccinated individuals. Permanent joint deformities and blindness may follow recovery. Vaccine immunity may prevent or modify illness.

The eruption of chickenpox (varicella) is typically centripetal in distribution (worse on trunk than face and extremities) and characterized by crops of lesions in different stages on development. Chickenpox papules are soft and superticial, compared to the firm, shotty, and deep papules of smallpox. Chickenpox crusts fall off rapidly and usually leave no scar. Monkeypox cannot be easily distinguished from smallpox clinically. Monkeypox occurs only in forested areas of West and Central Africa as a sporadic, zoonotic infection transmitted to humans from wild squirrels. Person-to-person spread is rare and ceases after 1-2 generations. Mortality is 15%. Other diseases that are sometimes confused with smallpox include typhus, secondary syphilis, and malignant measles. Skin samples (scrapings from papules, vesicular fluid, pus, or scabs) may provide a rapid identification of smallpox by direct electron microscopy, agar gel immunoprecipitation, or immunofluorescence.

There is no specific treatment available although some evidence suggests that vaccinia-immune globulin may be of some value in treatment if given early in the course of the illness.

Vaccinia virus is a live poxvirus vaccine that induces strong crossprotection against smallpox for at least 5 years and partial protection for 10 years or more. The vaccine is administered by dermal scarification or intradermal jet injection; appearance of a vesicle or pustule within several days is indication of a "take." Vaccinia-immune human globulin at a dose of 0.3 mg/kg body weight provides $\geq$70% protection against naturally occurring smallpox if given during the early incubation period. Administration immediately after or within the first 24 hours of exposure would provide the highest level of protection, especially in unvaccinated persons. The antiviral drug, n-methylisatin ß-thiosemicarbazone (Marboran®) afforded protection in some early trials, but not others, possibly because of noncompliance due to unpleasant gastrointestinal side effects.

Patients with smallpox should be treated by vaccinated personnel using universal precautions. Objects in contact with the patient, including bed linens, clothing, ambulance, etc.; require disinfection by fire, steam, or sodium hypochlorite solution.

Nuclear Weapons

Since their introduction in 1945, nuclear explosives have been the most feared of the weapons of mass destruction, in part because of their ability to cause enormous instantaneous devastation and of the persistent effects of the radiation they emit, unseen and undetectable by unaided human senses. The Manhattan Project cost the United States $2 billion in 1945 spending power and required the combined efforts of a continent-spanning industrial enterprise and a pool of scientists, many of whom had already been awarded the Nobel Prize and many more who would go on to become Nobel Laureates. This array of talent was needed in 1942 if there were to be any hope of completing a weapon during the Second World War. Because nuclear fission was discovered in Germany, which remained the home of many brilliant scientists, the United States perceived itself to be in a race to build an atomic bomb.

When the Manhattan Project began far less than a microgram of plutonium had been made throughout the world, and plutonium chemistry could only be guessed at; the numbers of neutrons released on average in U-235 and Pu-239 fissions were unknown; the fission cross sections (probabilities that an interaction would occur) were equally unknown, as was the neutron absorption cross section of carbon. Although talented people are essential to the success of any nuclear weapons program, the fundamental physics, chemistry, and engineering involved are widely understood; no basic research is required to construct a nuclear weapon. Therefore, a nuclear weapons project begun in 1996 does not require the brilliant scientists who were needed for the Manhattan Project.

For many decades the Manhattan Project provided the paradigm against which any potential proliferator's efforts would be measured. Fifty years after the Trinity explosion, it has been recognized that the Manhattan Project is just one of a spectrum of approaches to the acquisition of a nuclear capability. At the low end of the scale, a nation may find a way to obtain a complete working nuclear bomb from a willing or unwilling supplier; at the other end, it may elect to construct a complete nuclear infrastructure including the mining of uranium, the enrichment of uranium metal in the fissile isotope U-235, the production and extraction of plutonium, the production of tritium, and the separation of deuterium and 6 Li to build thermonuclear weapons. At an intermediate level, the Republic of South Africa constructed six quite simple nuclear devices for a total project cost of less than $1 billion (1980's purchasing power) using no more than 400 people and indigenous technology.

Fissile materials can produce energy by nuclear fission, either in nuclear reactors or in nuclear weapons. A country choosing to join the nuclear weapons community must acquire the necessary weapons (fissile) material (U-235 U or Pu-239). It is generally recognized that the acquisition of fissile material in sufficient quantity is the most formidable obstacle to the production of nuclear weapons. Fissile material production consumes the vast majority of the technical, industrial, and financial resources required to produce nuclear weapons. For example, production of fissile materials —- highly enriched uranium (HEU) and plutonium —- accounted for more than 80 percent of the $1.9 billion (1945 dollars) spent on the Manhattan Project.

Some analysts believe that the difficulties of enriching uranium are offset by the simpler weapon designs which enriched uranium allows. In the United States, HEU is considered less expensive to use in a weapon than plutonium. Operation of a reactor to produce plutonium requires the extraction and purification of uranium and, in some cases, at least modest enrichment. Given international safeguards on reactors using enriched uranium obtained from another nation or heavy water moderated reactors, a proliferant may be forced in any case to construct an enrichment facility. The choice is likely to be determined by the indigenous availability of uranium and the national surplus (or shortage) of electricity.

Acquisition of a militarily significant nuclear capability involves, however, more than simply the purchase or construction of a single nuclear device or weapon. It requires attention to issues of safety and handling of the weapons, reliability and predictability of entire systems, efficient use of scarce and valuable special nuclear material (SNM) (plutonium and enriched uranium), chains of custody and procedures for authorizing the use of the weapons, and the careful training of the military personnel who will deliver weapons to their targets.

In contrast, a nuclear device used for terrorism need not be constructed to survive a complex stockpile-to-target sequence, need not have a predictable and reliable yield, and need not be efficient in its use of nuclear material. Although major acts of terrorism are often rehearsed and the terrorists trained for the operation, the level of training probably is not remotely comparable to that necessary in a military establishment entrusted with the nuclear mission.

The United States has developed a complex and sophisticated system to ensure that nuclear weapons are used only on the orders of the President or his delegated representative. Some elements of the custodial system are the "two-man rule," which requires that no person be left alone with a weapon; permissive action links (PALs), coded locks which prevent detonation of the weapon unless the correct combination is entered; and careful psychological testing of personnel charged with the custody or eventual use of nuclear weapons. In addition, U.S. nuclear weapons must be certified as "one point safe," which means that there is less than a one-in-a-million chance of a nuclear yield greater than the equivalent of four pounds of TNT resulting from an accident in which the high explosive in the device is detonated at the point most likely to cause a nuclear yield.

It is believed to be unlikely that a new proliferator would insist upon one point safety as an inherent part of pit design; the United States did not until the late 1950's, relying instead upon other means to prevent detonation (e.g., a component of Little Boy was not inserted until after the Enola Gay had departed Tinian for Hiroshima). It is also unlikely that a new actor in the nuclear world would insist upon fitting PALs to every (or to any) nuclear weapon; the United States did not equip its submarine-launched strategic ballistic missiles with PALs until, at the earliest, 1996, and the very first U.S. PALs were not introduced until the mid-1950's, when American weapons were stationed at foreign bases where the possibility of theft or misuse was thought to be real.

Nonetheless, any possessor of nuclear weapons will take care that they are not used by unauthorized personnel and can be employed on the orders of duly constituted authority. Even -— or, perhaps, especially -— a dictator such as Saddam Hussein will insist upon a

fairly sophisticated nuclear chain of command, if only to ensure that his weapons cannot be used by a revolutionary movement. It is also quite likely that even the newest proliferator would handle his weapons with care and seek to build some kind of safety devices and a reliable SAFF system into the units. On the basis of experience, one might expect to observe significant nuclear planning activity and the evolution of situation-specific nuclear doctrine on the part of a new proliferator who would have to allocate carefully the "family jewels." The development of a nuclear strategy might be visible in the professional military literature of the proliferator.

Signatures

Every stage of nuclear weapon development, from material production to deployment, can generate signatures that provide some indication of a weapon program's existence or status, although only a few of them point fairly unambiguously to a nuclear weapon program. The difficulty of producing fissile materials limits the rate at which a country could field nuclear weapons. If only a very small number of weapons were at hand, they might be reserved for strategic rather than battlefield use, thus reducing the need to conduct military exercises that anticipated combat in a nuclear environment. Furthermore, the weapons might be stored unassembled and their components kept at various locations. They might also be kept under the control of a small military or quasi-military unit outside of the regular military forces. It might be very difficult to detect a nuclear force still in its infancy solely by relying only on observable changes in deployment, storage facilities, or military operations. Materials production of nuclear weapons would still provide the greatest opportunities for detecting such a program.

Effects

Nuclear detonations are the most devastating of the weapons of mass destruction. To make this point one need only recall the pictures from Hiroshima or the international furor over the accidental but enormous radiation release from the Chernobyl power plant. The contamination from Chernobyl was significantly larger than would have been expected from a nuclear detonation of about 20 kT at ground level, but was comparable in extent to what might result from a "small" nuclear war in which a dozen or so weapons of nominal yield were exploded at altitudes intended to maximize blast damage.

A nuclear detonation creates a severe environment including blast, thermal pulse, neutrons, x- and gamma-rays, radiation, electromagnetic pulse (EMP), and ionization of the upper atmosphere. Depending upon the environment in which the nuclear device is detonated, blast effects are manifested as ground shock, water shock, "blueout," cratering, and large amounts of dust and radioactive fallout. All pose problems for the survival of friendly systems and can lead to the destruction or neutralization of hostile assets.

The energy of a nuclear explosion is transferred to the surrounding medium in three distinct forms: blast; thermal radiation; and nuclear radiation. The distribution of energy among these three forms will depend on the yield of the weapon, the location of the burst, and the characteristics of the environment. For a low altitude atmospheric

detonation of a moderate sized weapon in the kiloton range, the energy is distributed roughly as follows:

50% as blast;

35% as thermal radiation; made up of a wide range of the electromagnetic spectrum, including infrared, visible, and ultraviolet light and some soft x-ray emitted at the time of the explosion; and

15% as nuclear radiation; including 5% as initial ionizing radiation consisting chiefly of neutrons and gamma rays emitted within the first minute after detonation, and 10% as residual nuclear radiation. Residual nuclear radiation is the hazard in fallout.

Considerable variation from this distribution will occur with changes in yield or location of the detonation.

*Table 3-I. Radii of Effects of Nuclear Weapons**

Effect	1 Kt	10 Kt	100 Kt	1000 Kt
Ionizing radiation (50% immediate transient ineffectivenss)	600m	950m	1400m	2900m
Ionizing radiation (50% latent lethality)	800m	110m	1600m	3200m
Blast (50% casualties)	140m	360m	860m	3100m
Thermal radiation (50% casualties, second degree burns under fatigue uniform)	369m	110m	3190m	8020m

* HOB 60W $^{1/3}$

Because of the tremendous amounts of energy liberated per unit mass in a nuclear detonation, temperatures of several tens of million degrees centigrade develop in the immediate area of the detonation. This is in marked contrast to the few thousand degrees of a conventional explosion. At these very high temperatures the nonfissioned parts of the nuclear weapon are vaporized. The atoms do not release the energy as kinetic energy but release it in the form of large amounts of electromagnetic radiation. In an atmospheric detonation, this electromagnetic radiation, consisting chiefly of soft x-ray, is absorbed within a few meters of the point of detonation by the surrounding atmosphere, heating it to extremely high temperatures and forming a brilliantly hot sphere of air and gaseous weapon residues, the so-called fireball. Immediately upon

formation, the fireball begins to grow rapidly and rise like a hot air balloon. Within a millisecond after detonation, the diameter of the fireball from a 1 megaton (Mt) air burst is 150 m. This increases to a maximum of 2200 m within 10 seconds, at which time the fireball is also rising at the rate of 100 m/sec. The initial rapid expansion of the fireball severely compresses the surrounding atmosphere, producing a powerful blast wave.

As it expands toward its maximum diameter, the fireball cools, and after about a minute its temperature has decreased to such an extent that it no longer emits significant amounts of thermal radiation. The combination of the upward movement and the cooling of the fireball gives rise to the formation of the characteristic mushroom-shaped cloud. As the fireball cools, the vaporized materials in it condense to form a cloud of solid particles. Following an air burst, condensed droplets of water give it a typical white cloudlike appearance. In the case of a surface burst, this cloud will also contain large quantities of dirt and other debris which are vaporized when the fireball touches the earth's surface or are sucked up by the strong updrafts afterwards, giving the cloud a dirty brown appearance. The dirt and debris become contaminated with the radioisotopes generated by the explosion or activated by neutron radiation and fall to earth as fallout.

The relative effects of blast, heat, and nuclear radiation will largely be determined by the altitude at which the weapon is detonated. Nuclear explosions are generally classified as air bursts, surface bursts, subsurface bursts, or high altitude bursts.

Air Bursts. An air burst is an explosion in which a weapon is detonated in air at an altitude below 30 km but at sufficient height that the fireball does not contact the surface of the earth. After such a burst, blast may cause considerable damage and injury. The altitude of an air burst can be varied to obtain maximum blast effects, maximum thermal effects, desired radiation effects, or a balanced combination of these effects. Burns to exposed skin may be produced over many square kilometers and eye injuries over a still larger area. Initial nuclear radiation will be a significant hazard with smaller weapons, but the fallout hazard can be ignored as there is essentially no local fallout from an air burst. The fission products are generally dispersed over a large area of the globe unless there is local rainfall resulting in localized fallout. In the vicinity of ground zero, there may be a small area of neutron-induced activity which could be hazardous to troops required to pass through the area. Tactically, air bursts are the most likely to be used against ground forces.

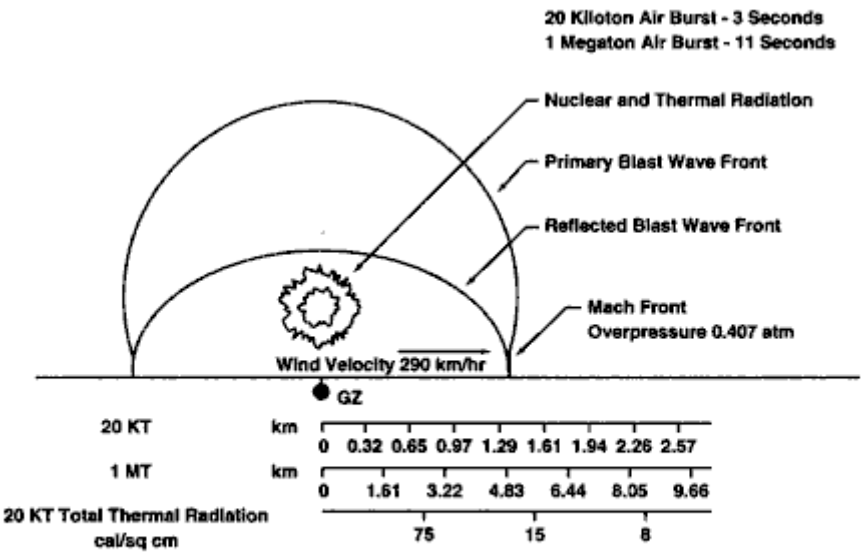

Figure 3-I. Chronological Development of an Air Burst

Surface Burst. A surface burst is an explosion in which a weapon is detonated on or slightly above the surface of the earth so that the fireball actually touches the land or water surface. Under these conditions, the area affected by blast, thermal radiation, and initial nuclear radiation will be less extensive than for an air burst of similar yield, except in the region of ground zero where destruction is concentrated. In contrast with air bursts, local fallout can be a hazard over a much larger downwind area than that which is affected by blast and thermal radiation.

Subsurface Burst. A subsurface burst is an explosion in which the point of the detonation is beneath the surface of land or water. Cratering will generally result from an underground burst, just as for a surface burst. If the burst does not penetrate the surface, the only other hazard will be from ground or water shock. If the burst is shallow enough to penetrate the surface, blast, thermal, and initial nuclear radiation effects will be present, but will be less than for a surface burst of comparable yield. Local fallout will be very heavy if penetration occurs.

High Altitude Burst. A high altitude burst is one in which the weapon is exploded at such an altitude (above 30 km) that initial soft x-rays generated by the detonation dissipate energy as heat in a much larger volume of air molecules. There the fireball is much larger and expands much more rapidly. The ionizing radiation from the high altitude burst can travel for hundreds of miles before being absorbed. Significant ionization of the upper atmosphere (ionosphere) can occur. Severe disruption in communications can occur following high altitude bursts. They also lead to generation of an intense electromagnetic pulse (EMP) which can significantly degrade performance of or destroy sophisticated electronic equipment. There are no known biological effects of EMP; however, indirect effects may result from failure of critical medical equipment.

Although some nuclear weapons effects (NWE) such as blast and cratering have analogs in the effects of conventional weapons, many NWE are unique to nuclear use. In addition, blast and other "common" weapons effects are likely to be much more powerful in the nuclear case than in the realm of conventional weapons. NWE are so severe that combinations of two or more simultaneously (as in a real event) may not add linearly, complicating the design and construction of physical simulators or the writing and validation of computer simulation codes.

Although thermal radiation, EMP, and ionizing radiation from a nuclear blast are all damage producing, at yields below about a megaton the blast and shock produced by a nuclear weapon are the predominant means of damaging a target. For some targets, such as underground bunkers and missile silos, blast and shock are virtually the only effective destructive mechanisms.

The intensity of thermal radiation decreases only as the inverse square of the distance from a nuclear detonation, while blast, shock, and prompt ionizing radiation effects decrease more rapidly. Thus, high-yield weapons are primarily incendiary weapons, able to start fires and do other thermal damage at distances well beyond the radius at which they can topple buildings or overturn armored vehicles.

Nuclear effects on electromagnetic signal propagation, which affects command, control, communications, computers, and intelligence (C 4 I), are of concern to countries expected to use nuclear weapons, particularly those which intend to explode a weapon at great altitudes or those which expect to have to defend against such a nuclear attack. C3I technology is primarily affected by high-altitude nuclear effects that could interrupt satellite-to-satellite communications, satellite-to-aircraft links, or satellite-to-ground links. Most nations will hope that signals from Global Positioning System (GPS) satellites and ground-based differential GPS transmitters will be usable shortly after a nuclear explosion, as well as traditional communications channels which must be protected.

The electromagnetic pulse generated by the detonation of a single nuclear weapon at high altitudes can be a threat to military systems located as much as a thousand miles away. HEMP can disable communications systems and even power grids at enormous distances from the burst. This type of threat could be used by a third world country that has the capability to launch a rocket carrying a high-yield device (about 1 megaton or more) a few hundred kilometers into the upper atmosphere and a few thousand kilometers from its own territory (to avoid damaging its own systems).

CHEMICAL WEAPONS

Chemical weapons use the toxic properties of chemical substances rather than their explosive properties to produce physical or physiological effects on an enemy.

Although instances of what might be styled as chemical weapons date to antiquity, much of the lore of chemical weapons as viewed today has its origins in World War I. During that conflict "gas" (actually an aerosol or vapor) was used effectively on numerous occasions by both sides to alter the outcome of battles. A significant number of battlefield casualties were sustained. The Geneva Protocol, prohibiting use of chemical weapons in warfare, was signed in 1925. Several nations, the United States included, signed with a reservation forswearing only the first use of the weapons and reserved the right to retaliate in kind if chemical weapons were used against them (the United States did not ratify the Protocol until 1975). Chemical weapons were employed in the intervening period by Italy (in Ethiopia) and Japan (in Manchuria and China). Both nations were signatories to the Geneva Convention. Chemical weapons were never deliberately employed by the Allies or the Axis during World War II, despite the accumulation of enormous stockpiles by both sides. Instances of employment of chemical weapons in the local wars since then are arguable, although they were definitely used in the Iran-Iraq conflict of 1982–87.

Development of chemical weapons in World War I was predominantly the adaptation of a chemical "fill" to a standard munition. The chemicals were commercial chemicals or variants. Their properties were, for the most part, well known. The Germans simply opened canisters of chlorine and let the prevailing winds do the dissemination. Shortly thereafter the French put phosgene in a projectile and this method became the principal means of delivery. In July 1917, the Germans employed mustard shells for the first time and simultaneously attempted to use a solid particulate emetic, diphenyl chloroarsine, as a mask breaker. Mustard, an insidious material, penetrates leather and fabrics and inflicts painful burns on the skin.

These two themes, along with significant increases in toxicity, represent a large segment of the research and development of chemical weapons that nations have pursued over the years. There is first the concept of agents that attack the body through the skin, preferably also through clothing, and more preferably through protective clothing. Along with that concept is the idea of penetrating or "breaking" the protective mask so that it no longer offers protection for the respiratory system. Increasing the toxicity of the chemical agent used would theoretically lower the amounts required to produce a battlefield effect. Unless this increase is significant, however, it can be masked by the inefficiencies of disseminating the agent. Consequently, later development has focused on the methods for delivering the agent efficiently to the target.

The chemicals employed before World War II can be styled as the "classic" chemical weapons. They are relatively simple substances, most of which were either common industrial chemicals or their derivatives. An example is phosgene, a choking agent (irritates the eyes and respiratory tract). Phosgene is important in industry as a

chlorinating material. A second example is hydrogen cyanide, a so-called blood agent (prevents transfer of oxygen to the tissues), now used worldwide in the manufacture of acrylic polymers. The classic chemical agents would be only marginally useful in modern warfare and generally only against an unsophisticated opponent. Moreover, large quantities would be required to produce militarily significant effects, thus complicating logistics.

Blister agents or vesicants are an exception to the limited utility of classic agents. Although these materials have a relatively low lethality, they are effective casualty agents that inflict painful burns and blisters requiring medical attention even at low doses. The classic mustard is the most popular among proliferant nations since it is relatively easy to make. Mustard is generally referred to as the "king" of agents because of its ease of production, low cost, predictable properties, persistence, and ability to cause resource-devouring casualties rather than fatalities. Its insidious nature is both an advantage and a disadvantage. Mustard on the skin causes no immediate sensation and symptoms normally do not appear until several hours after exposure. At incapacitating levels this may be as long as 12 hours. (Contrary to the normal expectation, horrible fatalities occurred in the Iran-Iraq War because Iranian soldiers, feeling no effects, continued to wear mustard soaked clothing and inhale its fumes.)

To produce immediate effects, an arsenical vesicant known as lewisite was developed in the United States. Much of the former Soviet Union vesicant stocks were mixtures of lewisite and sulfur mustard. Between the world wars the development of chemical weapons included adaptation to aircraft delivery (bombs) and exploitation of lewisite, since the more potent mustard was, from a battlefield perspective, slow in producing casualties. Independent experiments in several countries led them to consider/adopt mixtures of mustard and lewisite as fills for chemical munitions.

The Italians, Hungarians, Japanese, French, English, Russians, and Americans, as well as the Germans, all perfected mustard, phosgene, and similar agents during World War II. Although never used in the conflict, these nations amassed such huge quantities of chemical munitions that their disposal presented a practical problem, one that would be virtually insurmountable in today's more environmentally conscious world. In those more naive times, however, the munitions simply found their way to the bottoms of almost all the world's oceans in the holds of expendable ships.

Nerve gases are liquids, not gases, which block an enzyme (acetylcholinesterase) that is necessary for functions of the central nervous system. Nerve agents are generally divided rather arbitrarily into G- and V-agents, although there are numerous structural variants that are potent cholinesterase inhibitors. Nerve agents known to date to have been produced for chemical warfare purposes are all organo-phosphorus compounds and are liquids at room temperature. Similar in action to many pesticides, they are lethal in much lower quantities than classic agents. The nerve gases are effective when inhaled or when absorbed by the skin (percutaneous), or both, although there are differences in effectiveness. In general, the lower the material's volatility (and hence its inhalation threat) the greater its percutaneous toxicity.

Nerve gases, or anticholinesterase agents, were discovered by the Germans in the 1930's and developed during World War II. In 1936 during studies of possible pesticides, the German chemist Gerhard Schrader discovered what he called "tabun" or GA. Two years later Schrader discovered the even more toxic "sarin" or GB. These compounds are orders of magnitude more toxic than those used in World War I and thus represent the significant toxicity increase that changed the concept of employment. Fortunately for the Allies, the Germans never exploited their technological advantage, although they did produce a large number of tabun-filled munitions.

After World War II the victors took an interest in exploiting the potential of the remarkably potent "nerve" agents. The British, in particular, had captured small stocks of sarin (GB) and set about investigating its potential. The Soviets removed the Germans' GB production plant to the Soviet Union. GB turned out to be perhaps the best of the respiratory agents, being volatile as well as exceedingly toxic. The United States designed a cluster bomb to exploit the characteristics of GB and followed this with a litany of adaptations of munitions. Artillery rockets were produced as were bombs, projectiles, and spray tanks. Many of these used the basic design of high-explosive weapons and simply changed the fill to GB. In the instance of the spray tank, it was necessary to use a polymeric thickening material so that the liquid would form large droplets and not evaporate before it reached the ground.

The French, British, and Canadians all built small-scale facilities to produce the GB for testing. The United States, however, entered into full-scale production of GB, as did the Russians just a little later. The Russians also produced soman (GD), an agent the U.S. developers had decided to forswear because of its properties of being refractory to treatment above a single lethal dose.

In the late 1950's, UK scientists discovered another category of nerve agents, the V-agents. These were particularly interesting in that most of them were very effective percutaneously and represented an effective way to circumvent the ubiquitous gas mask. The United States and the UK pursued a form of V-agent called VX, although they produced it by entirely different processes. The Russians exploited another structural analog that proved more adaptable to their industrial processes.

The 1960's saw continued development in nonlethal agents, or riot control agents, first used in World War I. These materials, most notably CS, are strong irritants of the mucous membranes with very high safety ratios. The letters "CS" are code letters for a solid powder classified as a riot-control agent (O-chlorobenzylmalonitrile). This compound is a highly effective irritant of the mucous membranes with an exceedingly high safety ratio (~63,000). The purpose of CS and similar materials is temporary incapacitation without permanent harm. CS was developed and first used by the UK. It was quickly adopted and used extensively by the United States and since has been produced and employed by many nations. CS is a solid at room temperature and presents a problem for effective dissemination in useful particle sizes. Particulate CS, like most solids, tends to develop an electrostatic charge which causes the particles to agglomerate into larger particles. Much development effort during the 1960's was spent on finding effective dissemination techniques.

The work on particulate CS could be extrapolated to another type of chemical agent that was of extreme interest in the 1960's: incapacitating agents. These were initially seen by some as a panacea to make warfare safe and humane. Thousands of potential compounds were screened, obtained from government sources in the United States and from commercial pharmaceutical companies around the world. Although there were several promising materials, primarily mental incapacitants, only BZ was ever standardized. The problem of incapacitants, or incapacitating agents, is complex. The use of incapacitants in warfare is considered to be prohibited by the Chemical Weapons Convention even though only a single agent, BZ (3-Quinuclidinyl benzilate), and its immediate precursors are included as listed compounds (Schedule 2) in that Treaty. In retrospect, while BZ was the only incapacitating agent formally accepted (i.e., type classified) by the United States, it was a poor choice and is now obsolete. It remained in U.S. stocks for only a short period of time. The substance is a mental rather than a physical incapacitant with long-onset time and unpredictable symptoms. The victim becomes confused and is likely to be incapable of acting decisively. The confusion, however, may not be readily apparent. The duration of action is long, about 48 hours, making prisoner management difficult. There are, moreover, hundreds of compounds more potent, faster acting, and with shorter duration of effect.

Mental incapacitants are predominantly glycolates, whereas some of the more potent candidates for physical incapacitants have come from research on improved anesthetics. Indeed, almost all potential incapacitants are byproducts of the pharmaceutical industry and have legitimate pharmaceutical uses. The defining technologies for such incapacitating weapons, then, are the production of a physiologically effective compound in greater than practical pharmaceutical quantities and incorporation of the material in weapons. It is probable that the physical state of an incapacitant will be a particulate solid and that the practical route for effective use is by inhalation.

Binary chemical weapons use toxic chemicals produced by mixing two com-pounds immediately before or during use. Binary weapons do not necessarily employ new toxic chemicals. In U.S. parlance, relatively innocuous precursors were stored separately and reacted to form the toxic chemical agent en route to the target. In principle, the binary concept could also be used to produce highly lethal but unstable compounds or mixtures of compounds unsuitable for long-term storage. The U.S. type classified and produced a GB (sarin) binary nerve agent weapon, the M687 projectile (a 155-mm artillery shell), and was in the late stages of development of two other binary weapons when its offensive CW program was terminated. The Russians have been publicly accused by dissidents within their own agencies of developing new binary agents, and the Iraqis are known to have constructed binary bombs and missile warheads, albeit with crude manual mixing of the reactants.

Other possibilities for chemical agents include toxins and allergens which also have been, at times, considered biological agents. Although not living organisms them-selves, these materials are usually products of living organisms with complex molecu-lar structures. A wide variety of toxins with an equally broad spectrum of chemical, physical, and physiological properties exists.

Until the recent attempts at terrorism by the Japanese cult Aum Shinrikyo, virtually all uses of chemical weapons have been as tactical weapons by nations. These have ranged from attempts to break the stalemate in World War I to the recent use by Iraq to blunt Iranian human wave attacks in the Iran-Iraq War (1982–87). Chemical weapons were not employed by the major protagonists in World War II. Between World Wars I and II, two signatories of the Geneva Protocol (Italy and Japan) employed chemical weapons. Typically, nations have employed them against unprotected targets and not against an equally well-armed nation; chemical weapons are therefore arguably an example of mutual deterrence. Although there have been charges of chemical weapon use in virtually every conflict in recent decades, most have not been substantiated by clinical or physical evidence.

Nerve Agents

The nerve agents are a group of particularly toxic chemical warfare agents. They were developed just before and during World War II and are related chemically to the organophosphorus insecticides. The principle agents in this group are:

GA (Tabun)
GB (Sarin)
GD (Soman)
GF
VX (methylphosphonothioic acid)

The "G" agents tend to be non-persistent whereas the "V" agents are persistent. Some "G" agents may be thickened with various substances in order to increase their persistence, and therefore the total amount penetrating intact skin. At room temperature GB is a comparatively volatile liquid and therefore non-persistent. GD is also significantly volatile, as is GA though to a lesser extent. VX is a relatively non-volatile liquid and therefore persistent. It is regarded as presenting little vapour hazard to people exposed to it. In the pure state nerve agents are colorless and mobile liquids. In an impure state nerve agents may be encountered as yellowish to brown liquids. Some nerve agents have a faint fruity odour.

The effects of the nerve agents are mainly due to their ability to inhibit acetylcholinesterase throughout the body. Since the normal function of this enzyme is to hydrolyse acetylcholine wherever it is released, such inhibition results in the accumulation of excessive concentrations of acetylcholine at its various sites of action. These sites include the endings of the parasympathetic nerves to the smooth muscle of the iris, ciliary body, bronchial tree, gastrointestinal tract, bladder and blood vessels; to the salivary glands and secretory glands of the gastrointestinal tract and respiratory tract; and to the cardiac muscle and endings of sympathetic nerves to the sweat glands.

The sequence of symptoms varies with the route of exposure. While respiratory symptoms are generally the first to appear after inhalation of nerve agent vapour, gastrointestinal symptoms are usually the first after ingestion. Tightness in the chest is an

early local symptom of respiratory exposure. This symptom progressively increases as the nerve agent is absorbed into the systemic circulation, whatever the route of exposure. Following comparable degrees of exposure, respiratory manifestations are most severe after inhalation, and gastrointestinal symptoms may be most severe after ingestion.

The lungs and the eyes absorb nerve agents rapidly. In high vapour concentrations, the nerve agent is carried from the lungs throughout the circulatory system; widespread systemic effects may appear in less than 1 minute.

- The earliest ocular effect which follows minimal symptomatic exposure to vapour is miosis. The pupillary constriction may be different in each eye. Within a few minutes after the onset of exposure, there also occurs redness of the eyes. Following minimal exposure, the earliest effects on the respiratory tract are a watery nasal discharge, nasal hyperaemia, sensation of tightness in the chest and occasionally prolonged wheezing
- Exposure to a level of a nerve agent vapour slightly above the minimal symptomatic dose results in miosis, pain in and behind the eyes and frontal headache. Some twitching of the eyelids may occur. Occasionally there is nausea and vomiting.
- In mild exposures, the systemic manifestations of nerve agent poisoning usually include tension, anxiety, jitteriness, restlessness, emotional lability, and giddiness. There may be insomnia or excessive dreaming, occasionally with nightmares.
- If the exposure is more marked, the following symptoms may be evident: headache, tremor, drowsiness, difficulty in concentration, impairment of memory with slow recall of recent events, and slowing of reactions. In some casualties there is apathy, withdrawal and depression.
- With the appearance of moderate systemic effects, the casualty begins to have increased fatiguability and mild generalised weakness which is increased by exertion. This is followed by involuntary muscular twitching, scattered muscular fasciculations and occasional muscle cramps. The skin may be pale due to vasoconstriction and blood pressure moderately elevated.
- If the exposure has been severe, the cardiovascular symptoms will dominate and twitching (which usually appear first in the eyelids and in the facial and calf muscles) becomes generalised. Many rippling movements are seen under the skin and twitching movements appear in all parts of the body. This is followed by severe generalised muscular weakness, including the muscles of respiration. The respiratory movements become more laboured, shallow and rapid; then they become slow and finally intermittent.
- After moderate or severe exposure, excessive bronchial and upper airway secretions occur and may become very profuse, causing coughing, airway obstruction and respiratory distress. Bronchial secretion and salivation may be so profuse that watery secretions run out of the sides of the mouth. The secretions may be thick and tenacious. If the exposure is not so overwhelming as to cause death within a few minutes, other effects appear. These include sweating, anorexia, nausea and heartburn. If absorption of nerve agent has been great enough, there may follow abdominal cramps, vomiting, diarrhoea, and urinary frequency. The casualty perspires profusely, may have involuntary defecation and urination and may go into cardiorespiratory arrest followed by death.

- If absorption of nerve agent has been great enough, the casualty becomes confused and ataxic. The casualty may have changes in speech, consisting of slurring, difficulty in forming words, and multiple repetition of the last syllable. The casualty may then become comatose, reflexes may disappear and generalised convulsions may ensue. With the appearance of severe central nervous system symptoms, central respiratory depression will occur and may progress to respiratory arrest.
- After severe exposure the casualty may lose consciousness and convulse within a minute without other obvious symptoms. Death is usually due to respiratory arrest requires prompt initiation of assisted ventilation to prevent death. If assisted ventilation is initiated , the individual may survive several lethal doses of a nerve agent.
- If the exposure has been overwhelming, amounting to many times the lethal dose, death may occur despite treatment as a result of respiratory arrest and cardiac arrhythmia. When overwhelming doses of the agent are absorbed quickly, death occurs rapidly without orderly progression of symptoms.

Nerve agent poisoning may be identified from the characteristic signs and symptoms. If exposure to vapour has occurred, the pupils will be very small, usually pin-pointed. If exposure has been cutaneous or has followed ingestion of a nerve agent in contaminated food or water, the pupils may be normal or, in the presence of severe systemic symptoms, slightly to moderately reduced in size. In this event, the other manifestations of nerve agent poisoning must be relied on to establish the diagnosis. No other known chemical agent produces muscular twitching and fasciculations, rapidly developing pin-point pupils, or the characteristic train of muscarinic, nicotinic and central nervous system manifestations.

The rapid action of nerve agents call for immediate self treatment. Unexplained nasal secretion, salivation, tightness of the chest, shortness of breath, constriction of pupils, muscular twitching, or nausea and abdominal cramps call for the immediate intramuscular injection of 2 mg of atropine, combined if possible with oxime.

- GB and VX doses which are potentially life-threatening may be only slightly larger than those producing least effects. Death usually occurs within 15 minutes after absorption of a fatal VX dosage.
- Although only about half as toxic as GB by inhalation, GA in low concentrations is more irritating to the eyes than GB. Symptoms appear much more slowly from a skin dosage than from a respiratory dosage. Although skin absorption great enough to cause death may occur in 1 to 2 minutes, death may be delayed for 1 to 2 hours. Respiratory lethal dosages kill in 1 to 10 minutes, and liquid in the eye kills almost as rapidly.

Blister or Vesicants

Blister or vesicant agents are likely to be used both to produce casualties and to force opposing troops to wear full protective equipment thus degrading fighting efficiency, rather than to kill, although exposure to such agents can be fatal. Blister agents can be thickened in order to contaminate terrain, ships, aircraft, vehicles or equipment with a persistent hazard.

Vesicants burn and blister the skin or any other part of the body they contact. They act on the eyes, mucous membranes, lungs, skin and blood-forming organs. They damage the respiratory tract when inhaled and cause vomiting and diarrhoea when ingested.

The vesicant agents include:

- HD - sulphur mustard (Yperite)
- HN - nitrogen mustard
- L - Lewisite (arsenical vesicants may be used in a mixture with HD)
- CX - phosgene [properties and effects are very different from other vesicants]

HD and HN are the most feared vesicants historically, because of their chemical stability, their persistency in the field, the insidious character of their effects by attacking skin as well as eyes and respiratory tract, and because no effective therapy is yet available for countering their effects. Since 1917, mustard has continued to worry military personnel with the many problems it poses in the fields of protection, decontamination and treatment. It should be noted that the ease with which mustard can be manufactured and its great possibilities for acting as a vapour would suggest that in a possible future chemical war HD will be preferred to HN.

Due to their physical properties, mustards are very persistent in cold and temperate climates. It is possible to increase the persistency by dissolving them in non-volatile solvents. In this way thickened mustards are obtained that are very difficult to remove by decontaminating processes.

Exposure to mustard is not always noticed immediately because of the latent and sign-free period that may occur after skin exposure. This may result in delayed decontamination or failure to decontaminate at all. Whatever means is used has to be efficient and quick acting. Within 2 minutes contact time, a drop of mustard on the skin can cause serious damage. Chemical inactivation using chlorination is effective against mustard and Lewisite, less so against HN, and is ineffective against phosgene oxime.

- In a single exposure the eyes are more susceptible to mustard than either the respiratory tract or the skin. The effects of mustard on the eyes are very painful. Conjunctivitis follows exposure of about 1 hour to concentrations barely perceptible by odour. This exposure does not effect the respiratory tract significantly. A latent period of 4 to 12 hours follows mild exposure, after which there is lachrymation and a sensation of grit in the eyes. The conjunctival and the lids become red. Heavy exposure irritates the eyes after 1 to 3 hours and produces severe lesions.
- The hallmark of sulphur mustard exposure is the occurrence of a latent symptom and sign free period of some hours post exposure. The duration of this period and the severity of the lesions is dependent upon the mode of exposure, environmental temperature and probably on the individual himself. High temperature and wet skin are associated with more severe lesions and shorter latent periods.

- If only a small dose is applied to the skin, the skin turns red and itches intensely. At higher doses blister formation starts, generally between 4 and 24 hours after contact, and this blistering can go on for several days before reaching its maximum. The blisters are fragile and usually rupture spontaneously giving way to a suppurating and necrotic wound. The necrosis of the epidermal cells is extended to the underlying tissues, especially to the dermis. The damaged tissues are covered with slough and are extremely susceptible to infection. The regeneration of these tissues is very slow, taking from several weeks to several months.
- Mustard attacks all the mucous membranes of the respiratory tract. After a latent period of 4 to 6 hours, it irritates and congests the mucous membranes of the nasal cavity and the throat, as well as the trachea and large bronchi. Symptoms start with burning pain in the throat and hoarseness of the voice. A dry cough gives way to copious expectoration. Airway secretions and fragments of necrotic epitheliums may obstruct the lungs. The damaged lower airways become infected easily, predisposing to pneumonia after approximately 48 hours. If the inhaled dose has been sufficiently high the victim dies in a few days, either from pulmonary oedema or mechanical asphyxia due to fragments of necrotic tissue obstructing the trachea or bronchi, or from superimposed bacterial infection, facilitated by an impaired immune response.

The great majority of mustard gas casualties survive. There is no practical drug treatment available for preventing the effects of mustard. Infection is the most important complicating factor in the healing of mustard burns. There is no consensus on the optimum form of treatment.

Protection against these agents can only be achieved by a full protective ensemble. The respirator alone protects against eye and lung damage and gives some protection against systemic effects. No drug is available for the prevention of the effects of mustard on the skin and the mucous membranes caused by mustards. It is possible to protect the skin against very low doses of mustard by covering it with a paste containing a chlorinating agent, e.g., chloramine. The only practical prophylactic method is physical protection such as is given by the protective respirator and special clothing.

In a pure form lewisite is a colorless and odourless liquid, but usually contains small amounts of impurities that give it a brownish colour and an odour resembling geranium oil. It is heavier than mustard, poorly soluble in water but soluble in organic solvents. L is a vesicant (blister agent), also, it acts as a systemic poison, causing pulmonary edema, diarrhea, restlessness, weakness, subnormal temperature, and low blood pressure. In order of severity and appearance of symptoms, it is: a blister agent, a toxic lung irritant, absorbed in tissues, and a systemic poison. When inhaled in high concentrations, may be fatal in as short a time as 10 minutes.

- Liquid arsenical vesicants cause severe damage to the eye. On contact, pain and blepharospasm occur instantly. Oedema of the conjunctival and lids follow rapidly and close the eye within an hour. Inflammation of the iris usually is evident by this

time. After a few hours, the oedema of the lids begins to subside, while haziness of the cornea develops.

- Liquid arsenical vesicants produce more severe lesions of the skin than liquid mustard. Stinging pain is felt usually in 10 to 20 seconds after contact with liquid arsenical vesicants. The pain increases in severity with penetration and in a few minutes becomes a deep, aching pain. Contamination of the skin is followed shortly by erythema, then by vesication which tends to cover the entire area of erythema. There is deeper injury to the connective tissue and muscle, greater vascular damage, and more severe inflammatory reaction than is exhibited in mustard burns. In large, deep, arsenical vesicant burns, there may be considerable necrosis of tissue, gangrene and slough.
- The vapours of arsenical vesicants are so irritating to the respiratory tract that conscious casualties will immediately put on a mask to avoid the vapour. No severe respiratory injuries are likely to occur except among the wounded who cannot put on masks and the careless, who are caught without masks. Lewisite is irritating to nasal passages and produces a burning sensation followed by profuse nasal secretion and violent sneezing. Prolonged exposure causes coughing and production of large quantities of froth mucus. Injury to respiratory tracts, due to vapor exposure is similar to mustard's; however, edema of the lung is more marked and frequently accompanied by pleural fluid.

An antidote for lewisite is Dimercaprol (British Anti-Lewisite (BAL)). This ointment may be applied to skin exposed to lewisite before actual vesication has begun. Some blistering is inevitable in most arsenical vesicant cases. The treatment of the erythema, blisters and denuded areas is identical with that for similar mustard lesions. Burns severe enough to cause shock and systemic poisoning are life-threatening. Even if the patient survives the acute effects, the prognosis must be guarded for several weeks.

CX - Phosgene oxime

Phosgene oxime [CX] is a white crystalline powder. It melts between 39-40° C, and boils at 129° C.By the addition of certain compounds it is possible to liquify phosgene oxime at room temperature. It is fairly soluble in water and in organic solvents. In aqueous solution phosgene oxime is hydrolyses fairly rapidly, especially in the presence of alkali. It has a high vapour pressure, its odour is very unpleasant and irritating. Even as a dry solid, phosgene oxime decomposes spontaneously and has to be stored at low temperatures.

In low concentrations, phosgene oxime severely irritates the eyes and respiratory organs. In high concentrations, it also attacks the skin. A few milligrams applied to the skin cause severe irritation, intense pain, and subsequently a necrotising wound. Very few compounds are as painful and destructive to the tissues.

Phosgene oxime also affects the eyes, causing corneal lesions and blindness and may affect the respiratory tract causing pulmonary oedema. The action on the skin is immediate:

phosgene oxime provokes irritation resembling that caused by a stinging nettle. A few milligrams cause intense pain which radiates from the point of application, within a minute the affected area turns white and is surrounded by a zone of erythema (skin reddening) which resembles a wagon wheel in appearance. In 1 hour the area becomes swollen and within 24 hours the lesion turns yellow and blisters appear. Recovery takes 1 to 3 months.

Choking Agents

Chemical agents which attack lung tissue, primarily causing pulmonary oedema, are classed as lung damaging agents. To this group belong:

CG phosgene
DP diphosgene
Cl chlorine
PS chloropicrin

The toxic action of phosgene is typical of a certain group of lung damaging agents. Phosgene is the most dangerous member of this group and the only one considered likely to be used in the future. Phosgene was used for the first time in 1915, and it accounted for 80% of all chemical fatalities during World War I.

Phosgene is a colorless gas under ordinary conditions of temperature and pressure. Its boiling point is 8.2°C, making it an extremely volatile and non-persistent agent. Its vapour density is 3.4 times that of air. It may therefore remain for long periods of time in trenches and other low lying areas. In low concentrations it has a smell resembling new mown hay.

The outstanding feature of phosgene poisoning is massive pulmonary oedema. With exposure to very high concentrations death may occur within several hours; in most fatal cases pulmonary oedema reaches a maximum in 12 hours followed by death in 24-48 hours. If the casualty survives, resolution commences within 48 hours and, in the absence of complicating infection, there may be little or no residual damage.

During and immediately after exposure, there is likely to be coughing, choking, a feeling of tightness in the chest, nausea, and occasionally vomiting, headache and lachrymation. The presence or absence of these symptoms is of little value in immediate prognosis. Some patients with severe coughs fail to develop serious lung injury, while others with little sign of early respiratory tract irritation develop fatal pulmonary oedema. A period follows during which abnormal chest signs are absent and the patient may be symptom-free. This interval commonly lasts 2 to 24 hours but may be shorter. It is terminated by the signs and symptoms of pulmonary oedema. These begin with cough (occasionally substernally painful), dyspnoea, rapid shallow breathing and cyanosis. Nausea and vomiting may appear. As the oedema progresses, discomfort, apprehension and dyspnoea increase and frothy sputum develops. The patient may develop shock-like symptoms, with pale, clammy skin, low blood pressure and feeble, rapid heartbeat. During the acute phase, casualties may have minimal signs and symptoms and the prognosis should be guarded. Casualties may very rapidly

develop severe pulmonary oedema. If casualties survive more than 48 hours they usually recover.

Incapacitating Agents

Fentanyl (FEN-ta-nil) belongs to the group of medicines called narcotic analgesics (nar-KOT-ik an-al-GEE-ziks). Narcotic analgesics are used to relieve pain. The transmucosal form of fentanyl is used to treat breakthrough cancer pain. Breakthrough episodes of cancer pain are the flares of pain which "breakthrough" the medication used to control the persistent pain. Transmucosal fentanyl is only used in patients who are already taking narcotic analgesics. Fentanyl acts in the central nervous system (CNS) to relieve pain. Some of its side effects are also caused by actions in the CNS.

An overdose can cause severe breathing problems (breathing may even stop), unconsciousness, and death. Serious signs of an overdose include very slow breathing (fewer than 8 breaths a minute) and drowsiness that is so severe that you are not able to answer when spoken to or, if asleep, cannot be awakened. Other signs of an overdose may include cold, clammy skin; low blood pressure; pinpoint pupils of eyes; and slow heartbeat.

First synthesized in Belgium in the late 1950s, fentanyl, with an analgesic potency of about 80 times that of morphine, was introduced into medical practice in the 1960s as an intravenous anesthetic under the trade name of Sublimaze®. Thereafter; two other fentanyl analogues were introduced; alfentanil (Alfenta®), an ultra-short (5-10 minutes) acting analgesic, and sufentanil (Sufenta®), an exceptionally potent analgesic (5 to 10 times more potent than fentanyl) for use in heart surgery.

Today, fentanyls are extensively used for anesthesia and analgesia. Duragesic®, for example, is a fentanyl transdermal patch used in chronic pain management, and Actiq® is a solid formulation of fentanyl citrate on a stick that dissolves slowly in the mouth for transmucosal absorption. Actiq® is intended for opiate-tolerant individuals and is effective in treating breakthrough pain in cancer patients. Carfentanil (Wildnil®) is an analogue of fentanyl with an analgesic potency 10,000 times that of morphine and is used in veterinary practice to immobilize certain large animals.

Illicit use of pharmaceutical fentanyls first appeared in the mid-1970s in the medical community and continues to be a problem in the United States. To date, over 12 different analogues of fentanyl have been produced clandestinely and identified in the U.S. drug traffic. The biological effects of the fentanyls are indistinguishable from those of heroin, with the exception that the fentanyls may be hundreds of times more potent. Fentanyls are most commonly used by intravenous administration, but like heroin, they may also be smoked or snorted.

Fentanyl has an extremely low therapeutic index. Narrow therapeutic index drugs are those pharmaceuticals having a narrowly defined range between risk and benefit. Such drugs have less than a twofold difference in the minimum toxic concentration and minimum effective concentration in the blood or are those drug product formulations that exhibit limited or

erratic absorption, formulation-dependent bioavailability, and wide intrapatient pharmacokinetic variability that requires blood-level monitoring.

Narrow therapeutic Index is a term of art which has come into current use, but the term more correctly, is narrow therapeutic ratio. Narrow therapeutic ratio is defined in the regulations at 21 CFR 320.33(c). This subsection deals with criteria and evidence to assess actual or potential bioequivalence problems. Under Section 320.33(c) of Code of Federal Register 21, the US FDA defines a drug product as having a narrow therapeutic ratio as follows: there is less than a 2-fold difference in median lethal dose and median Effective dose values, or there is less than 2-fold difference in the minimum toxic concentrations and minimum effective concentrations in the blood.