Veterans Health Initiative

Health Effects from Chemical, Biological and Radiological Weapons

Independent Study Course Released: October 2003

Sponsored by
Department of Veterans Affairs
Employee Education System

This is a Veterans Health Administration System-Wide Training Program sponsored by the Veterans Affairs Employee Education System and the Office of Public Health and Environmental Hazards, Department of Veterans Affairs. It is produced by the Employee Education System.

Department of Veterans Affairs

Employee Education System

DEPARTMENT OF VETERANS AFFAIRS
UNDER SECRETARY FOR HEALTH
WASHINGTON DC 20420

A MESSAGE FROM THE UNDER SECRETARY FOR HEALTH

Dear Colleagues in Quality Health Care:

I am very pleased to present the enclosed Veterans Health Initiative (VHI) independent study guide on the basics of "Health Effects from Chemical, Biological and Radiological (CBR) Weapons". "Health Effects from Chemical, Biological and Radiological Weapons" is designed and written by VA physicians and experts in chemical, biological, and radiological warfare and treatment. Clinicians treating our nation's Veterans must be aware of the specific conditions that may confront individuals with injuries associated with CBR. Since some of the Veterans the VA receives may have already experienced the exposure to one of the agents contained in these weapons, it is important that VA health care providers are aware of the need to know the best way to treat these life-threatening problems. Greater general awareness of the specialized health issues facing persons with CBR injuries is needed to assure therapeutically appropriate clinical processes.

The Education Contact at your medical center has the necessary information so you can receive continuing medical education credits for studying this book and successfully completing the accompanying test. It is my expectation that every practitioner in the VA system will complete this course. I hope that you will keep this book available for reference when you have the opportunity to provide care for veterans with CBR injuries in the future. This ensures that provisions are made for quality health care across the continuum of acute care, rehabilitative care, to extended care. VA may see Veterans with CBR injury and being prepared to handle these injuries in a variety of health care settings, ensures the best care possible. The Veterans are counting on you to provide the best care possible. We owe them nothing less.

Robert H. Roswell, M.D.

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Independent Study Outline

Purpose

The recent crises in Afghanistan and then Iraq, and the terrorist attacks in the U.S in September 2001 have resulted in a very unstable political and military situation around the globe. This situation has required that the VA and DoD review and update it's information on chemical, biological, and radiological (CBR) weapons and agents. This VHI provides essential information for health care providers about the CBR threat in the U.S. and abroad.

Background

This independent study module is a part of the Veterans Health Initiative (VHI). The VHI is a comprehensive program of continuing education designed to improve recognition and treatment of health problems related to military service, specifically health issues related to chemical, biological, and radiological weapons and agents.

Objectives

After completing this independent study, participants will be able to:

1. describe the long-term effects from the military experiments involving human subjects exposed to chemical, biological, and radiation weapons and agents;
2. explain the history of the U.S. military programs involving chemical, biological, and radiation as military weapons;
3. identify the psychological effects of being involved in human experiments with these military weapons;
4. identify how various classes of chemical agents are absorbed and eliminated from the body;
5. list the typical signs and symptoms of exposure to various classes of chemical warfare agents and to their pesticide counterparts, where relevant;
6. differentiate the signs and symptoms one might observe following infection with common biological weapon agents, including anthrax, botulism, plague, smallpox, tularemia, and viral hemorrhagic fever (VHF);
7. outline briefly the 3 categories of biological agents as defined by CDC;
8. describe how a "dirty bomb" can produce radiation exposure in a victim;
9. describe the signs and symptoms of acute radiation exposure; and
10. list the VA programs developed to care for casualties from attacks with chemical, biological, and radiological weapons.

Outcome

The expected outcomes of this independent study are to improve the quality of health care provided to military personnel who place themselves in harm's way. Drug treatments and dosages provided in this study guide should be double-checked prior to prescribing therapy.

Independent Study Outline

Target Audience

This independent study is designed for Department of Veterans Affairs and Department of Defense clinicians and interested health care staff. Other health care providers, especially those working in veterans and military health care facilities in the U.S. also are encouraged to complete this independent study module.

Format

This program is available in booklet form and on the Web at: http://www.va.gov/vhi.

Program Description

This Program Includes:

- Independent study written material
- Test for CME credits
- Program evaluation

This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of VA Employee Education System and Department of Veterans Affairs Office of Public Health and Environmental Hazards. The VA Employee Education System is accredited by the ACCME to provide continuing medical education for physicians.

Content Materials

Part 1

U.S. Chemical Warfare Agent Human Experimentation and Long-Term Veteran's Health

History of U.S. Chemical Warfare Agent Human Experimentation

A Growing Awareness

Long-Term Health Effects amongst Experimental Subjects

Part 2

Health Effects from Chemical and Biological Agents and Radiological Weapons

Chemical Warfare Agents

Toxic Pesticide Agents

Biological Warfare Agents

Radiological Warfare Weapons

VA Programs to Prepare for Casualties from Attacks with Chemical, Biological, and Radiological Weapons

Appendices

References

Additional Readings

Independent Study Questions for CME Credit

Independent Study Program Registration/Answer Sheet/Participation Satisfaction Form

Program Implementation and VA Application Procedure

To receive credit for this course:

1. Read the independent study materials.
2. Complete the CME test questions. A passing score of 70% or higher on the CME test is required to receive credit. This test may be retaken.
3. Complete the program evaluation.
4. The estimated study time for this program is 3 hours.

If you are using the Independent Study Registration/Answer/Evaluation Form (two sided) at the back of the independent study booklet, please send the completed form within two weeks after reading the material to:

Employee Education Resource Center
Attn: SDU
Medical Forum, Suite 500
950 North 22nd Street
Birmingham, AL 35203-5300

If you have attained a passing score of 70% or higher, a certificate will be mailed to you approximately 6-8 weeks after your test has been graded. The test may be retaken.

NOTE: Scantron forms cannot be photocopied. For additional copies of this independent study Scantron forms or other VHI independent study modules, please contact your facility education contact person.

The CME test and program evaluation can be completed using the VA Internet. The address is: http://www.ees-learning.net

After you take the test, you will receive immediate feedback as to pass or fail. You will be allowed to retake the test. Upon passing the test and completing the program evaluation, you will be able to immediately print your certificate according to instructions.

NOTE: If you experience difficulty reaching this Web site, please contact the Help Desk via e-mail at eeslibrixhelp@lrn.va.gov, or call 1-866-496-0463. You may also contact your local computer support staff or librarian for assistance.

NOTE: In order to complete the CME test and Evaluation, your computer must have Internet Explorer 4.0 or Netscape 4.0 or higher.

If you have questions or special needs concerning this independent study, please contact:

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This program will no longer be authorized for CME credit after June 2005.

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AMA and ANCC Continuing Education Credits

Accreditation

Accreditation Council for Continuing Medical Education (ACCME)

The VA Employee Education System is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

American Nurses Credentialing Education

VA Employee Education System is accredited as a provider of continuing education in nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Continuing Education Credit

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The VA Employee Education System designates this educational activity for a maximum of 3 hours in Category 1 credit towards the American Medical Association Physician's Recognition Award. Each physician should claim only those hours he/she actually spent in the educational activity.

Association of Social Work Boards (ASWB)

VA Employee Education System, Provider Number 1040, is approved as a provider for social work continuing education by the Association of Social Work Boards (ASWB), (1-800-225-6880) through the Approved Continuing Education (ACE) program. VA Employee Education System maintains responsibility for the program. Social workers will receive 3 continuing education clock hours for participating in this course.

American Nurses Credentialing Education

VA Employee Education System designates this educational activity for 3.6 contact hours in continuing nursing education.

The Employee Education System maintains responsibility for the program. A certificate of attendance will be awarded to participants and accreditation records will be on file at the Employee Education System. In order to receive a certificate from EES, you must read the material, complete and pass the CME test with a 70% or higher, and complete a program evaluation.

Report of Training

It is the program participant's responsibility to ensure that this training is documented in the appropriate location according to his/her locally prescribed process.

AMA and ANCC Continuing Education Credits

Disclosure Statement

The Employee Education System (EES) must insure balance, independence, objectivity, and scientific rigor for all EES sponsored educational activities. The intent of this disclosure is not to prevent faculty with a significant financial or other relationship from presenting materials, but rather to provide the participant with information on which they can make their own judgments.

It remains for the participant to determine whether the faculty interests or relationships influence the materials presented with regard to exposition or conclusion. When an unapproved use of a FDA approved drug or medical device, or an investigational product not yet FDA approved for any purpose is mentioned, EES requires disclosure to the participants.

Faculty have provided the following information:

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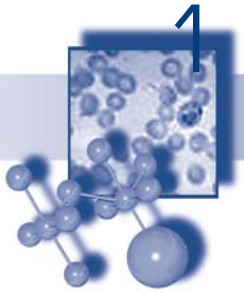
Larry Flesh, MD
No disclosable relationships or FDA issues

Lawrence Deyton, MD
Recommendations for several treatment or prophylaxis strategies in this lecture are based on consensus recommendations developed with HHS, CDC, NIH, and FDA involvement. These recommendations have been widely published (JAMA) and presented by CDC and other Federal Agencies as currently recommended treatment or prophylaxis for response to bioterror use of these infectious agents. These recommendations are based on the best available evidence for biologic activity against these agents of bioterrorism, but do not represent uses currently approved by the FDA.

Mark Brown, PhD
Use of drugs to treat health effects from chemical, biological or radiological warfare agents in general cannot be approved by the FDA, since the required clinical trials to show safety and efficacy can not be ethically conducted. However, based on animal studies and some limited clinical evidence, we do have basic information showing efficacy of commonly prescribed treatments for casualties exposed to these agents.

Americans with Disabilities Act Policy

The Employee Education System wishes to ensure no individual with a disability is excluded, denied services, segregated, or otherwise treated differently from other individuals participating in this independent study because of the absence of auxiliary aids and services. If you require any special arrangements to fully participate in this independent study, please contact Bob Smith, EdD, MCP, Program Manager, at 205-731-1812 extension 317, or e-mail bob.smith@lrn.va.gov.



1 U.S. Chemical Warfare Agent Human Experimentation and Long-Term Veteran's Health

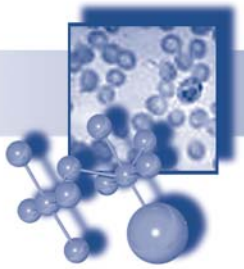
Introduction

The U.S. has maintained an active biological and chemical warfare program since World War I. Today, this program is essentially only defensive. However, in the past, part of this large-scale program involved the manufacture and stockpiling of chemical and biological warfare agents and munitions. As of the early 1990s, the U.S. chemical weapon stockpile included an estimated 25,000 tons of chemical warfare agents including organophosphorus nerve agents, vesicant (blister) agents including mustard and Lewisite. By law, most of this stockpile is slated for destruction. Similarly, the offensive biological weapons program was ordered to cease by President Nixon in 1969, and all biological weapons were subsequently destroyed.

In addition to past weapons development and manufacture, another part of this program involved human experimentation with "soldier volunteers." Human experiments were part of this program virtually from its inception. The scope of the program, including the number of service members involved and the specific chemical warfare agents tested have all changed greatly over time. Experiments involving human exposure to various agents were conducted until 1975. Many of the experiments focused upon developing defensive chemical warfare capabilities, such as tests of protective clothing or respiratory masks. Other experiments were designed to evaluate the impact of various agents upon the operational readiness of military personnel who might be exposed to chemical warfare agents. For example, many experiments were designed to test the effectiveness of experimental incapacitating agents and devices.

Although all of these experiments were originally conducted in secret, today we have available to us a great deal of information about them in the open literature. Sources include congressional hearings on the topic, and media accounts. Perhaps the most detailed information on these experiments is from a series of reports by the National Research Council/National Academy of Sciences (NAS) requested by both the Departments of Veterans Affairs and Defense (VA and DoD.) These reports have focused primarily upon the long-term health consequences to those involved in experiments where they were exposed to various chemical warfare agents. The NAS reports also provide an enormous amount of historical data on what really went on during this period.

Even though the details of these experiments are no longer secret, many health care providers are not aware of this history, and how it may have affected their veteran patients today. This Veterans Health Initiative (VHI) was written in part to acquaint health care providers who may see as patients some of the veterans who were subjects or who participated in these experiments. In fact, to date the most likely source of any significant exposure to a chemical warfare agent to a U.S. veteran is participation in these experiments. Use of this VHI will help ensure that VA and DoD health care providers have all of the relevant clinical data they might need to treat their patients. Perhaps more important, this guide will let health care providers understand the reality of this history, and that the feelings and reactions of their patients to these past events really do have a firm historical basis.



History of U.S. Chemical Warfare Agent Human Experimentation

World War II Human Experiments

Military use of the chemical warfare agent sulfur mustard (or just "mustard agent") caused nearly 400,000 casualties during World War I, more than from any other chemical agent used during the war (NAS 1993). In response, the U.S. developed its own chemical warfare program, including a secret research program intended to develop better military protective equipment. From relatively small beginnings, the U.S. military chemical warfare program expanded significantly during World War II, driven largely by the need to develop protection against the chemical warfare agents mustard and Lewisite (two examples of blister agents) known to be possessed by Axis forces. During World War II, Germany was known to possess these agents, and in fact used them against the Poles in 1939 (NAS 1993). Ultimately, the U.S. military concluded that animal studies were not an adequate substitute for human studies, and in 1942, U.S. military chemical weapons program managers initiated formal authority to recruit and use volunteer subjects.

Experimental Procedures

By the end of World War II, over 60,000 U.S. service members had been used as human subjects in the U.S. chemical warfare defense research program (NAS 1993). This mostly secret research focused upon the development of better weapons and better methods for protecting against these weapons. At least 4,000 subjects were used in tests involving exposure to high concentrations of mustard agents or Lewisite, in gas chambers or in field exercises over contaminated ground areas.

Human subjects were exposed to mustard agents or Lewisite using a wide variety of exposure protocols. Experimental treatments ranged from exposure to a small drop of agent on the arm or clothing, to quite severe exposures, such as from repeated gas chamber trials, occasionally without the benefit of protective clothing (NAS 1993). In these later instances, subjects were repeatedly placed in gas chambers filled with mustard agent or Lewisite vapor until their skin reddened as an indication of exposure or until their protective suit failed (NAS 1993).

In general, three types of exposure procedures were used in these experiments.

1. Patch, or drop tests were the most common and were used to assess the efficacy of various protective agents, treatments for mustard agents and Lewisite burns, effects of multiple exposures on sensitivity, and the effects of physical exercise on the severity of chemical warfare agent burns. Drop application with mustard agents was also commonly used in basic training to raise single blisters to impress trainees.
2. Chamber tests were conducted to test the effectiveness of protective clothing.
3. Field tests involved contamination of large or small areas of land with sulfur mustard or Lewisite; human subjects were used in field tests to test protective clothing (NAS 1993).

Various procedures were used that involved exposure of subjects in gas chambers. Some of these involved duration testing, for example:

- to determine how long;
- under what conditions; and
- at what exposures could subjects remain protected by protective clothing (NAS 1993).

Commonly, subjects were given protective equipment including a gas mask, and then placed in chambers from 60 minutes to 4 hours. Twenty-four hours following such exposures, subjects were examined for reddening of the skin (erythema), i.e., evidence that the vapor had penetrated the protective clothing. Subjects were required to repeat the procedure and enter the chambers either every day or every other day until they developed moderate to intense erythema. Most subjects apparently experienced intense erythema widespread over their bodies, especially in moist areas of skin folds, such as:

- behind the knees and under the arms;
- in large areas of the chest and shoulders; and
- on their arms and legs.

Some of the experiments conducted during this period involved subjects who were not provided with complete protective equipment. In those cases, exposures could be much higher, and some of these subjects experienced burns to the genital areas, including instances of crusted lesions to the scrotum that were characterized by researchers as severe (NAS 1993).

Other World War II Chemical Warfare Agent Exposures

Human experimental subjects were not the only individuals who were injured by chemical warfare agents during this period. Preparations for actual chemical warfare combat before and during World War II involved many military and civilian personnel in the production, handling, shipping, and training to use this form of weapon (NAS 1993).

By the end of World War II, the U.S. had produced more than 87,000 tons of sulfur mustard, 20,000 tons of Lewisite, and 100 tons of nitrogen mustard at Edgewood Arsenal, MD; Huntsville Arsenal, AL; Pine Bluff Arsenal, AR; and Rocky Mountain Arsenal, CO (NAS 1993). Not surprisingly, producing these large amounts of materials for the U.S. military required tens of thousands of workers, both military and civilian. Many military service members were trained to handle these weapons or were assigned to jobs that put them in contact with mustard agents or Lewisite (NAS 1993).

The number of documented injuries among those involved with this program was initially "quite high" (NAS 1993). According to the NAS, one study of accidental injuries among this group reported over 1,000 cases over a 2-year period at Edgewood Arsenal of mustard poisoning resulting in eye, ear, nose and throat symptoms.

By the end of World War II, there was only a single military incident involving these weapons. A German bombing attack in December 1943 on U.S. ships loaded with mustard agent docked in the Italian harbor of Bari, Italy, released mustard agent into the air and water. This incident resulted in thousands of injuries and hundreds of deaths among U.S. service members and others in the area. In the immediate area of the harbor, over 600 victims of mustard poisoning were treated, 83 died (NAS 1993). Close to 1,000 civilians from the nearby town also died. Because the presence of the mustard agent in these ships was secret, many of the victims did not receive rapid appropriate decontamination, and thus, severe exposures continued over many hours. Even though there are such examples of humans exposed to levels of chemical warfare agents sufficient to cause immediate injury and even death, the IOM commented in their review of potential long-term health consequences from such exposures that there were virtually no long-term studies available for these populations.

Post-World War II: New Agents — New Experiments

The close of World War II led to a reduced interest in human experimentation with mustard agents and Lewisite (NAS 1993). However, by the 1950s, the U.S. military again became interested in human testing, this time with a focus upon newer chemical warfare agents including:

- OrganoPhosphorus nerve agents such as sarin and VX, and
- incapacitating agents including:
  - tear gas; and
  - psychoactive agents such as:
    - LSD;
    - PCP; and
    - synthetic cannabis analogs (NAS 1993, NRC 1982).

These new classes of chemical warfare agents were seen as providing much more flexibility in chemical warfare compared to the older chemical warfare agents sulfur mustard and Lewisite.

Renewed interest led to renewed human testing by the Department of Defense (DoD), although ultimately on a much smaller scale. Thus, between 1950 and 1975, about 6,720 soldiers took part in experiments involving exposures to 254 different chemicals, conducted at U.S. Army Laboratories at Edgewood Arsenal, MD (NRC 1982, NRC 1984, NAS 1993). Congressional hearings into these experiments in 1974 and 1975 resulted in disclosures, notification of subjects as to the nature of their chemical exposures, and ultimately to compensation for a few families of subjects who had died during the experiments (NAS 1993).

These experiments were conducted primarily to learn how various agents would affect humans (NRC 1982). Other agencies including the CIA and the Special Operations Division of the Department of the Army were also reportedly involved in these studies (NAS 1993). Only a small number of all the experiments done during this period involved mustard agents or Lewisite. Records indicate that between 1955 and 1965, of the 6,720 soldiers tested, only 147 human subjects underwent exposure to mustard agent at Edgewood (NRC 1982).

According to the 1984 NRC review, human experiments at DoD's Edgewood Arsenal involved about 1,500 subjects who were experimentally exposed to irritant and blister agents including:

- lachrymatory agents, e.g., CN;
- riot control agents, e.g., CS;
- chloropicrin (PS);
- Diphenylaminochlorarsine (DM, Adamsite);
- other ocular and respiratory irritants; and
- mustard agents.

For example, from 1958 to 1973 at least 1,366 human subjects underwent experimental exposure specifically with the riot control agent CS at Edgewood Arsenal (NRC 1984). Of those involved in the experiments:

- 1,073 subjects were exposed to aerosolized CS;
- 180 subjects were exposed dermally;
- 82 subjects had both skin applications and aerosol exposures; and finally
- 31 subjects experienced ocular exposure via direct CS application to their eyes.

Most of these experiments involved tests of protective equipment and of subjects' ability to perform military tasks during exposure.

Similarly, cholinesterase reactivators antidotes such as 2-PAM were tested on about 750 subjects. These agents are still used today as antidotes to organophosphorus nerve agent poisoning, including accidental poisoning by organophosphorus pesticides. About 260 subjects were experimentally exposed to various psychochemicals including phencyclidine (PCP), and 10 related synthetic analogs of the active ingredient of cannabis (NRC 1984). The NRC report also mentions human experiments involving exposure of 741 soldiers to LSD (NRC 1984). Finally, from 1962 to 1972, a total of 123

irritant chemicals were tested on only two subjects each exposed using a wind tunnel (NRC 1984). These irritant chemicals were selected for human testing following preliminary animal studies.

Shipboard Hazards and Defense (SHAD) and Project 112 Tests

From 1963 through the early 1970's, DoD conducted tests to determine the effectiveness of shipboard detection and protective measures against both chemical and biological warfare agents, and less toxic simulants for these agents. The tests were conducted under the broad heading of Shipboard Hazard and Defense (SHAD), which was part of a larger activity DoD called Project 112 that also included similar land-based tests.

Until recently, all information about these tests was classified. However, in 2001, responding to a request from Secretary of Veterans Affairs Anthony J. Principi, DoD began sharing information with VA as it became declassified. Since May 2002, using declassified information provided by DoD, the VA has been notifying veterans who took part in the SHAD and Project 112 tests. These notified veterans were encouraged to go to a VA medical facilities (VAMC) if they have any health concerns related to these tests.

DoD has stated that the military personnel involved in these tests were not actually test subjects, but were rather only involved as test conductors. DoD offered the reassurance that procedures were taken during the tests to protect these test conductors from hazardous exposures, and that no veteran became ill during these experiments. Despite these assurances, there has been a perception by some that some military personnel may have been the unwitting subjects of secret military experiments involving their deliberate exposure to hazardous agents.

Based on DoD's declassification efforts, it is now known that a wide range of chemical and biological warfare agents, less-harmful simulants, and disinfectant agents were used as part of SHAD and Project 112. The biological warfare agents tested by DoD included:

- *Coxiella burnetii;*
- *Francisella tularensis; and*
- *Staphylococcal* Enterotoxin B.

Much less, hazardous biological agent simulants were also tested, which have been widely used as relatively non-toxic stand-ins for actual biological warfare agents. These included:

- *Bacillus globigii (BG);*
- *E. coli; and*
- *Serratia marcscens.*

Although these biological simulants were felt to be safe, it is understood today that these simulants can be opportunistic pathogens under certain unusual circumstances; circumstances that are probably not relevant to most active duty personnel.

DoD has also indicated that during these tests, they used most of the chemical warfare nerve agents that were in the U.S. arsenal at that time, including:

- Sarin;
- VX;
- Tabun; and
- Soman (all organophosphorus nerve agents).

Most tests involved chemical agent simulants; materials with similar physical properties, such as vapor pressure, but without the lethal toxicity of the actual chemical warfare agents. This included materials such as Methylacetoacetate and sulfur dioxide.

DoD also used a number of common chemicals to sterilize surfaces, presumably following experiments with biological agents, including:

- ß-propiolactone;
- Ethyl alcohol;
- Lysol®;
- Peracetic acid;
- Potassium and sodium hydroxide; and
- Sodium hypochlorite (i.e., common bleach).

Lastly, DoD used a couple of relatively non-toxic chemicals as simulants for biological agents; chemicals that also have similar physical properties as the biological agents, but without the hazard, such as zinc cadmium sulfide.

VA's own review of the literature on long-term health concerns from biological agents used in SHAD and Project 112 indicate that long-term health effects are unlikely in the absence of any observable health problems at the time of exposure (in the Under Secretary for Health Information Letter IL 10-2002-016, August 26, 2002, available at: http://www.va.gov/SHAD).

This is in part because these infectious agents do not cause latent infections without symptomatic disease. Similarly, in general, the chemical agents used in project SHAD and Project 112 are most likely to have produced long-term health effects if they caused clinically significant illnesses during or shortly after exposure. However, there are few good, long-term studies of the health effects of exposure to low levels of the agents used in these tests.

Biological Agent Human Experiments

This VHI describes major events in the U.S. chemical warfare agent test program. However, similar experiments involving tests with biological warfare agents and human subjects were also carried out during this period. For example, beginning in 1954 and over the next 18 years, about 2,300 military draftees, most of them stationed at Ft. Detrick, MD, and most Seventh-Day Adventists, volunteered for Operation Whitecoat (Washington Post 2003). Operation Whitecoat involved 153 tests over the period 1955 to 1973.

Experiments conducted at Ft. Detrick apparently exposed subjects to a variety of biological warfare agents including:

- Tularemia;
- Venezuelan equine encephalitis; and
- Sandfly fever.

Tests also involved human exposure to Q fever at Dugway Proving Ground, Utah, in 1955. Although many of the experimental subjects became ill from these exposures, apparently none of the Whitecoat volunteers is known to have died as a result of these tests. However, Army officials acknowledge that little is known about what happened to these test subjects over the long-term.

Strikingly, all volunteers in these experiments reportedly signed consent forms prior to testing (Washington Post 2003).

Ionizing Radiation Human Experiments

In addition to the chemical warfare agent and biological test programs, similar experiments involving radiation exposures were also conducted during this period. For example, in 1993, former Department of Energy Secretary Hazel O'Leary disclosed that some early radiation experiments might not have conformed to current policies and procedures for written informed consent and protection of human subjects. Subsequently a Presidential Advisory Committee on Human Radiation Experiments (ACHRE) was established to investigate these issues and consider corrective action.

Many veterans and family members were concerned about these disclosures and the VA received over 1700 radiation-related inquiries. Most of these inquiries were related to ionizing radiation exposure during military service.

DoD Human Radiation Exposure Research Projects

Between 1945 when the first nuclear detonation occurred at Alamogordo, NM, and 1963 when the limited test ban was implemented, the U.S. conducted over 200 atmospheric nuclear weapons tests. Over 200,000 U.S. service personnel participated in these tests and are included in the term "Atomic Veterans".

According to the ACHRE final report, about 2000 to 3000 military personnel served as actual research subjects in conjunction with these nuclear weapons tests. Examples of studies included:

- psychological and physiological testing;
- testing of volunteers as close as under one mile from the nuclear weapon detonation;
- flash-blindness experiments (the only experiments in which immediate injury was recorded);
- research on protective clothing (including having personnel walk

or crawl over contaminated ground as soon as 4 hours after the nuclear weapon detonation);
- cloud-penetration activities; and
- decontaminating aircraft involved in these nuclear tests.

Most of the participants in these research projects apparently were not volunteers, nor did they sign consent forms. Other Atomic Veterans who were not then considered "research subjects" were nevertheless engaged in similar activities.

Radiation doses received by many of the participants in this research associated with nuclear weapons tests are not available today. Nevertheless, records show that some participants in cloud-penetration studies received radiation doses of 15 Rem (R) or higher, which is about 3 times or more of the current annual whole-body occupational dose limit of 5 R mandated by the U.S. Nuclear Regulatory Commission.

According to the DoD Defense Threat Reduction Agency (DTRA), the average external radiation dose for all U.S. atmospheric nuclear weapons test participants was 0.6 Rem, and less than 1 percent had doses exceeding 5 Rem. Based upon a recent National Research Council report that raised questions about the accuracy of some DTRA dose reconstructions, DTRA is taking certain corrective action that address those concerns.

VA Radiation Research Projects

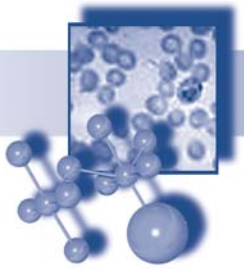
VA researchers have conducted research projects involving radiation. Based on responses from VAMCs, 53 projects at 17 VAMCs conducted during the period of 1947 to 1980 were reviewed in early 1995 by an expert committee including specialists in:

- nuclear medicine;
- health physics/radiation safety;
- radiation oncology; and
- radiation dosimetry.

Analysis of this group of early VA experiments suggests that there was no widespread exposure of veterans to excessive doses of ionizing radiation. Almost all the research was conducted exclusively for medical purposes to improve diagnosis or treatment of diseases and primarily involved "tracer" amounts of radiation. Of these early VA research programs reviewed, only one project (involving a study of strontium as a component nuclear fallout) appears to have been done primarily for military purposes.

Additional Information

The related VHI program "Veterans and Radiation" may be obtained from the VAMC library or accessed at: http://www.va.gov/VHI



A Growing Awareness

Introduction

Most of the soldier volunteer subjects of these experiments conducted by the U.S. military were told at the time that they should never reveal the nature of the experiments, and apparently, almost to a man, they kept this secret for the next 40 or more years (NAS 1993). Nevertheless, the experiments began to generate public attention as some World War II veterans began to seek compensation from VA for health problems that they believed were caused by their experimental exposures to mustard agents or Lewisite.

World War II Era Experiments

Because of the secrecy in which these experiments were conducted, veterans faced significant difficulties in obtaining the documentation they needed to support their disability claims for long-term health problems resulting from the experiments. Commonly, the periods of time spent, as volunteers in the World War II mustard agents and Lewisite experiments were unaccounted for in official service records. Veterans seeking compensation claims therefore had significant difficulty providing any documentation of their participation (NAS 1993). Further, many of these veterans experienced the denial of government agencies that such tests and related activities had actually ever occurred (NAS 1993). Compounding veterans' difficulties, there was little scientific or medical information on long-term health effects from exposure to the chemical warfare agents used in these experiments; existing literature focused almost exclusively on short-term effects.

During their investigation into the history of World War II era experiments, the 1993 IOM committee complained:

- "an atmosphere of secrecy still exists to some extent regarding the World War II testing program."
- "As a result, the committee often had great difficulty obtaining information."
- "The committee is certain that other relevant information exists that was never obtained."
- "It is also clear that there may be many exposed veterans and workers who took an oath of secrecy . . . and remain true to that oath even today."

The task of examining the history behind these experiments was compounded by the secrecy oath taken by the veteran subjects, which they generally kept for nearly 5 decades (NAS 1993).

Nevertheless, mounting pressure from veterans, the press, and Congress on VA to resolve these issues led the Secretary of VA, Edward J. Derwinski on June 11, 1991 to announce new guidelines for compensation of veterans who had been subjects of the World War II mustard agents and Lewisite experiments. These new guidelines were helpful for these veterans because they loosened the normal requirements for documentation of participation in such activities, and clearly identified certain specific illnesses that VA acknowledged as being long-term effects from exposure to the chemical warfare agents involved. These specific illnesses recognized as connected to participation in these experiments included:

- asthma;
- chronic laryngitis;
- chronic bronchitis;
- emphysema;
- corneal opacities;
- chronic conjunctivitis; and
- keratitits (of the eye).

As part of this overall response, in 1991 VA's Secretary also requested that the IOM conduct their 1993 review of the relevant medical literature on human health effects from exposure to mustard agents and Lewisite experiments conducted by the U.S. military during World War II. This request was based upon concerns about possible long-term health effects to over 60,000 U.S. service members used as subjects in these early experiments.

Post-World War II Experiments

In an earlier response to growing concerns, in the early 1980s, DoD also requested the National Research Council (NRC) review possible long-term health effects to the 6,720 servicemen who served as subjects in the post-World War II chemical warfare agent experiments conducted in U.S. Army Laboratories from 1958 to 1975. The request resulted in a series of three NRC reports collectively titled:

Possible Long-Term Health Effects of Short-Term Exposure to Chemical Agents

These three reports, included reviews of the medical and scientific literature on the possible long-term health effects from exposure to the specific agents used in the post-World War II experiments, and an epidemiological study of the participants.

1. Volume 1, published in 1982, subtitled "**Anticholinesterases and Anticholinergics,**" reviewed the health effects from exposure to 15 Anticholinesterases nerve agents including military organophosphorus chemical warfare agents, which were tested on

about 1,400 subjects. It also reviewed health effects from exposure to 24 cholinergic nerve poison ***antidotes***, including atropine, tested on about 1,800 subjects.

2. Volume 2, published in 1984, subtitled **"Cholinesterase Reactivators, Psychochemicals, and Irritants and Vesicants,"** reviewed the health effects from exposure to four different cholinesterase ***reactivators*** including 2-PAM, certain psychochemicals including phencyclidine (PCP) and a series of synthetic cannabis analogs, and some irritants including mustard agent, and various riot-control agents (tear gas) including CS.
3. Volume 3, published in 1985, **subtitled "Final Report: Current Health Status of Test Subjects,"** was a retrospective epidemiological study that examined both morbidity (via a questionnaire sent to all living subjects) and mortality of the participants in the post-World War II human experiments.

The results of these studies are discussed in detail in relevant portions of this VHI. In general, the NRC concluded that there was only a minimal likelihood of long-term health effects among the subjects of these experiments conducted from 1958 to 1975. However, they acknowledge that there remain significant gaps in available relevant literature on such long-term effects, making any conclusions necessarily tentative. Results of the epidemiological study were also generally negative.

Comparison to Modern Standards for Human Subjects Research

Standards for the protection of human subjects in research have come a long way since the earliest of these experiments with chemical agents.

The same 60-year period that encompasses World War II, the Cold War, the nuclear arms race, and the ongoing explosion of new developments in science, technology, and medicine produced the following documents:

- Nuremberg Code (1947)
- Declaration of Helsinki (1965)
- Belmont Report (1978)
- Common Rule (promulgated in 1981)
- A variety of pertinent legal decisions and ethical treatises

Expectations regarding human rights, patients' rights, research ethics, and government accountability have been debated, defined, and established in laws and regulations; these laws and regulations continue to evolve.

When veterans judge past events by today's standards, some who were (or who believe they were) exposed as research subjects to chemical or biological (or radiological) agents feel that they were unwitting "guinea pigs."

1. In hindsight, some of these experiments now appear to have been unduly dangerous, posing risks that might not withstand ethical review today.

2. Current scientific knowledge reveals that the level of risk associated with certain experimental agents was greater than was known at the time of the experiments.
3. In addition, contemporary risk assessments consider a more comprehensive list of potential adverse effects (e.g., including psychological ones).
4. Some veterans believe these studies do not live up to today's requirements to:
   - document protocols;
   - monitor outcomes;
   - avoid coercion in recruitment; and
   - ensure that subjects are fully informed.

The information given to subjects in these experiments conducted in the past varied significantly by experiment, and probably increased in studies that are more recent. However, some subjects did not (and some still do not) know for sure:

1. ***if*** they were exposed to harmful substances;
2. ***what*** or how much they were exposed to;
3. the purpose of the research; or
4. the potential short- and long-term effects on their health.

Furthermore, consideration of the autonomy of military personnel during wartime or the threat of war calls into question the claim that research participation was always voluntary (Howe & Martin, 1991). Moreover, the conditions of secrecy surrounding most of these experiments can reasonably be expected to fuel lingering suspicion or mistrust of the organizations and institutions that conducted or sponsored the experiments.

There is no question that the research protocols for experiments conducted decades ago fall short of subsequent ethical and legal standards related to human subjects protections. After all, termination of these research programs was due at least in part to findings of Congressional hearings and inquiries held in 1974 and 1975 that were critical of the programs. Minutes of the Senate Subcommittee on Health and the Subcommittee on Administrative Practice and Procedure, September 10-12, 1975, stated that the consent information for studies conducted by DoD between 1958 and 1975

> "was inadequate by current [i.e., 1975] standards" (NRC, 1982). Similarly, radiological experiments conducted by the Atomic Energy Commission during approximately the same period were later called "an enormous scandal for science and government…" (Makhijani, 1994).

Indeed, referring to these studies, Energy Secretary Hazel O'Leary told *Newsweek* in 1993, "The only thing I could think of was Nazi Germany" (Makhijani, 1994).

Evolving Standards

Human subjects protections have evolved in two distinct ways, along what

the philosopher Allen Buchanan (who served as a consultant to the Advisory Committee on Human Radiation Experiments) called two "modes of moral progress" (Buchanan, 1996).

1. Compliance with standards has improved over time.
2. Better standards have emerged.

In the Operation Whitecoat experiments involving biological agents, between 1955 and 1973, all 2,300 draftees who participated reportedly signed consent forms. The 1982 NRC report says that the protocols used during the Edgewood Arsenal, MD experiments from 1958 to 1975:

> " . . . emphasized that voluntary consent of each human subject was absolutely essential. It was also stated that, in all experiments involving volunteer subjects, the subjects would be thoroughly informed of all procedures and of what might be expected as a result of each test. Furthermore, each volunteer would be free to determine whether he desired to participate in a given experiment."

These examples represent progress relative to earlier experimental protocols in which consent was not routinely obtained or not routinely "informed."

In addition to evolution of the concept of consent from "bare" consent to "informed" consent, it is now widely recognized that the ***quality*** of informed consent can vary. That is, some consents are more informed than others are, and that the goal should be "truly informed" consent. Evidence of this evolution includes the series of amendments to the World Medical Association Declaration of Helsinki's ***"Ethical Principles for Medical Research Involving Human Subjects"*** (five amendments from 1964 to 2000) and their national and local adaptations at organizations including VA. (See the References section for the VHA policy, amended multiple times between 1982 and 1992, is now planned for revision every two years, and also the DoD policy). Some of the newer ethical issues addressed in these documents include:

- adequate representation of women and minorities;
- research involving fetal tissue; and
- in research involving military personnel, the recruitment of subjects by their unit officers.
  1. Nevertheless, is "retrospective moral judgment"; assessing past actions by current standards appropriate?
  2. What is the appropriate response of VA health care providers to veterans who are worried, frustrated, or angry about their participation in old experiments involving chemical exposures?

Universal Ethical Standards

One thoughtful ethical analysis of these issues concluded that, regardless of changes in the social context and specific requirements for informed consent, it cannot be denied that these experiments violated very general principles that are ***not new*** (Buchanan, 1996). Relevant principles include:

- prohibitions against deceit;
- harming innocent persons without consent;
- using persons as a means to an end; and
- exploiting persons who may be vulnerable.

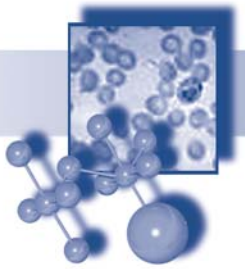
Put a little differently, the ethical norms that underlie current human subjects protections are not "uniquely contemporary"; rather, the concerns that led to federal oversight emerged long before, and "the elements of informed consent were in place long before the doctrine was formally named" (Crigger, 1994).

The special relationship between DoD and VA heightens the importance of acknowledging and embracing these ethical norms. Individuals who sustain injuries while on active military duty eventually become veterans who may be eligible for VA health care. The quality care that VA strives to provide demands compassion and respect. If participation in research conducted long ago results in illness today, VA health care providers must not only address a veteran's health care needs, but also acknowledge their anger at past apparent injustices.

In addition, VA health care providers should recognize that new ethical issues related to the conduct of human subjects research will continue to emerge as science and society change.

It would be naïve to assume that there will be no lapses in compliance with human subjects protections in future studies involving human subjects

Given what has happened in the past, we should not assume that current laws and standards intended for the protection of human experimental subjects have anticipated every risk to experimental subjects in the future. Health care providers, researchers, and policymakers need to be vigilant and open-minded and redouble their own effort to do whatever is possible to ensure that their own actions will pass the tests of the future.



Long-Term Health Effects Amongst Experimental Subjects

World War II Era Mustard Agents and Lewisite Experiments

The 1993 NAS review "Veterans at Risk: Health Effects of Mustard Gas and Lewisite," concluded that there was no doubt that some involved in those World War II era mustard agents and Lewisite chemical warfare agent experiments had been coping with serious and debilitating diseases for decades (NAS 1993). According to the earlier 1984 NRC report, records indicate that many human subjects exposed to mustard agents and Lewisite in these experiments sustained dermal injuries possibly severe enough to cause permanent scarring (NRC 1984). The NAS committee further complained that there were no epidemiological studies done of chemical weapons production workers, chemical warfare munitions handlers and trainers, or chemical weapon combat casualties from World War II (NAS 1993). Lack of relevant follow-up health assessments of the human subjects in these experiments severely limited assessment of long-term health consequences.

Immediate Health Effects

Recent actual military use of mustard agent, including during World War I and the Iran-Iraq war, provides some insights into the health effects from exposure to these chemical warfare agents. Probably the largest military application of mustard agent was during the 1980's Iran-Iraq war (NAS 1993). Some of the Iranian mustard agent casualties from that conflict were treated in European hospitals, and their medical status and treatments were well documented. In that example, casualties suffered from pulmonary, eye, and skin lesions at similar incidence levels as battlefield observed among mustard agent casualties from World War I. During World War I:

- 80% - 90% of sulfur mustard casualties suffered skin lesions;
- 86% suffered eye involvement; and
- 75% had pulmonary damage (NAS 1993).

Among the Iranian casualties:

- 83% suffered skin lesions;
- 92% had eye problems; and
- 95% had pulmonary damage (NAS 1993).

Long-Term Effects

Despite having only limited medical literature on long-term health effects from exposure to mustard agent and Lewisite, in their 1993 review, the NAS

committee concluded that there was some information linking exposure to these agents and certain long-term health effects. They broke down their findings based on the strength of the supporting evidence as:

1. Causal relationships
   a. The evidence found indicated a ***causal relationship*** between exposure to mustard and Lewisite chemical warfare agents and the following health conditions:
   - Respiratory cancers
     - nasopharyngeal
     - laryngeal
     - lung
   - Skin cancer
     - pigmentation abnormalities of the skin
     - chronic skin ulceration and scar formation
     - leukemia (typically acute non-lymphocytic type, nitrogen mustard)
   - Chronic respiratory diseases
     - asthma
     - chronic bronchitis
     - emphysema
     - chronic obstructive pulmonary disease
     - chronic laryngitis
   - Recurrent corneal ulcerative disease (includes corneal opacities; acute severe injuries to eye from Lewisite will also persist)
   - Delayed recurrent keratitis of the eye
   - Chronic conjunctivitis
   - Bone marrow depression and (resulting) immunosuppression (an acute effect that may result in greater susceptibility to serious infections with secondary permanent damage to vital organ systems)
   - Psychological disorders
     - mood disorders
     - anxiety disorders (including post-traumatic stress disorder)
     - other traumatic stress disorder responses (These may result from traumatic or stressful features of the exposure experience, not a toxic effect of the agents themselves)
   - Sexual dysfunction (scrotal and penile scarring may prevent or inhibit normal sexual performance or activity)
2. Suggested causal relationship
   a. The evidence found ***suggested a causal relationship*** between exposure and the following health conditions:
   - Leukemia (acute non-lymphocytic type, sulfur mustard)
   - Reproductive dysfunction (genotoxicity, mutagenicity, etc.; mustard agents)
3. Insufficient evidence of a causal relationship (NAS 1993)
   a. There was ***insufficient evidence found to demonstrate a causal relationship*** between exposure and the following health conditions:

- Gastrointestinal diseases
- Hematologic diseases
- Neurological diseases
- Reproductive dysfunction (Lewisite)
- Cardiovascular diseases (except for those that may result from serious infections shortly following exposure – heart disease resulting from rheumatic fever, for example)

Epidemiological studies of World War II Mustard Era Agents and Lewisite Experimental Subjects

The 1993 NAS committee's call for new high quality epidemiological research on these veterans was answered when in 2000 VA's Environmental Epidemiology Service reported a retrospective mortality study of 1,545 World War II Navy veterans experimentally exposed to low-levels of mustard agent at U.S. military facilities in Edgewood, MD. Previously, there had not been studies to evaluate possible long-term health affects among this group. Mortality among these subjects was compared to 2,663 similar Navy veterans who were not part of these experiments (Bullman & Kang 2000). These test participants were ideal for this study, because every one of them had been stationed at the same location in Bainbridge, MD, between 1943 and 1945, when these experiments had occurred. This feature made it relatively straightforward to locate participants years later.

The VA study reported no increased risk associated with mustard agent exposure, for any cause of death, and no increased risk in-cause specific mortality associated with level of mustard agent exposure among exposed veterans (Bullman & Kang 2000). In contrast, earlier studies of World War I veterans exposed to mustard agent during that war reported increased risk of death from lung cancers and respiratory related diseases. The 1984 NRC committee had reported that studies of those mustard agent exposed World War I veterans had determined that 10 years after their wartime exposure, veterans had residual disabilities including:

- chronic bronchitis (usually associated with emphysema);
- bronchial asthma;
- chronic conjunctivitis;
- blepharitis;
- keratitis; and
- corneal opacities (NRC 1984).

The VA researchers speculated that apparent differences between theirs and the earlier studies could reflect that veterans in the Edgewood Arsenal experiments that they studied, in contrast to many World War I veterans, wore protective clothing and were exposed for relatively short periods of time to relatively lower levels of agents (Bullman & Kang 2000).

Because of the large sample size available for this VA study, it had substantial statistical power, with a 95% power to detect a two or greater increase of risk of deaths due to respiratory cancers (Bullman & Kang

2000). Moreover, since exposures occurred over 40 years before this study, all possible long-term health effect would have had time to reveal themselves.

Health Effects amongst Post-World War II Experimental Subjects

The 1980s series of NRC reviews of the health consequences of participation in the DoD chemical warfare agent tests between 1955 to 1975 reported little evidence of long-term health concerns. The primary focus of the NRC reviews was to evaluate the possible long-term health consequences to subjects of DoD's chemical warfare agent experiments conducted at the Edgewood Arsenal. Based upon available mortality data for this group, and relevant toxicological data, experimental subjects were reported to be healthier in comparison to era controls, and both controls and subjects were healthier than the general population (NRC 1984).

However, the NRC committee was careful to point out certain weaknesses of the studies of these veteran-subjects, which served to limit conclusions about long-term health effects in subjects of these post-World War II experiments by DoD (NRC 1984).

The NRC committee did report certain long-term effects among these subjects. For example, follow-up data suggested that repeat CS (a riot control agent) exposure may lead to allergic contact dermatitis in some Edgewood Arsenal subjects, and possibly, repeat exposures might induce idiosyncratic hepatitis or allergic pneumonitis in some individuals (NRC 1984).

The committee found little evidence on the long-term health effects from tested psychochemicals.

- PCP
- LSD
- Synthetic cannabis analogs
- Other agents (NRC 1984)

For example, they found no case-reports for the subjects that indicated mental or cardiovascular effects immediately following exposures. However, with essentially no long-term follow-up data available for these subjects, the committee indicated that it was not possible to comprehensively evaluate possible long-term effects from low-level exposures to these agents (NRC 1984).

The 1982 NRC review of experiments involving exposure to acetylcholine esterase inhibitors including organophosphorus military nerve agents concluded that there was no firm evidence that any of the tested compounds examined produced long-term adverse human health effects at the exposures used in DoD's experiments at Edgewood, MD.

> "On the basis of available data, in the judgment of the panel, it is unlikely that administration of these anticholinergic compounds will have long-term toxicity effects or delayed sequelae" (NRC 1982). However, the committee also cautioned that "more intensive study is

required to confirm this conclusion" (NRC 1982).

Recent IOM Review on Long-Term Health Effects

In 2003, the IOM published a report on the health status of the individuals who had been previously assessed in the earlier 1980s NRC reports described above. The IOM follow-up survey reviewed 4,022 subjects out of the approximately 6,720 soldiers who were the original subjects of DoD's experiments between 1950 and 1975 at U.S. Army Laboratories at Edgewood Arsenal, MD (Page 2003). Among those subjects:

- 256 were exposed to sarin;
- 740 to VX;
- 571 to psychochemicals including LSD;
- 1,366 to irritants including CS; and
- 147 to vesicants including mustard agent.

Since participation in the original experiments involved rigorous inclusion and exclusion criteria, developing an external control group was not feasible. Instead, the IOM follow-up study was able to develop useable internal controls. This was made possible through comparison of those subjects:

1. who were exposed exclusively to organophosphorus (OP) military nerve agents;
2. exposed to either no active chemicals; or
3. exposed to two or more agents ***other*** than the OP nerve agents (Page 2003).

The IOM study reported only two statistically significant differences between these groups. Those subjects exposed ***only*** to OP nerve agents reported:

1. fewer attention problems in comparison to subjects exposed to ***other*** chemical agents; and
2. greater sleep disturbances in comparison to subjects exposed to ***no*** active agents.

Among subjects exposed ***only*** to OP nerve agents, neurological diseases including Parkinson's, and chronic multi-symptom illnesses such as CFS and FM, were reported to be not significantly different from either control group, and were generally very low among all three groups.

Strikingly, subjects reporting exposure to chemical agents in ***civilian*** or military work ***other*** than through their participation in DoD's Edgewood Arsenal experiments; reported many statistically significant adverse neurological and psychological effects, regardless of their experimental exposure.

Psychological Impact of Test Participation

Not surprisingly, the mere act of participation in experiments such as these can lead to long-term psychological effects. For example, the evaluation of veteran subjects of DoD's mustard agent experiments found significant rates of PTSD when compared to controls that did not participate in those experiments. For example, researchers at VA's National Center for PTSD used structured interviews to assess PTSD and other psychosocial outcomes among 24 subjects of World War II mustard agent experiments (Schnurr et al., 1996).

- 92% reported they had volunteered for the original mustard experiments
- 96% had participated in gas chamber exposure tests

During the mustard agent tests:

- 22% of the subjects reported that they understood the dangers involved
- 67% were ordered to not discuss their participation with anyone

Similar effects (described in Section 2 of this VHI) have also been reported among survivors of the 1995 terrorist attack with the chemical warfare agent sarin against civilians in the Tokyo subway system.

Most of these human subjects (83%) reported experiencing physical symptoms following the experimental mustard agent exposures. These same subjects were examined by researchers again nearly 5 decades later. In comparison with men of similar age, they were found to still be suffering effects including being less psychologically and physically healthy. Similarly, they were also found to suffer a remarkably high PTSD prevalence of 17 percent. The current prevalence of sub-diagnostic mustard-gas-related PTSD was 25 percent. Lifetime estimates for full and sub-diagnostic PTSD were reported to be 17 and 33 percent, respectively. Strikingly, the only mustard gas experience that predicted lifetime full or sub-diagnostic PTSD was the number of exposures to the gas (Schnurr et al., 1996).

A related study evaluated PTSD among 363 veterans randomly selected from a VA list of veterans who had been subjects in DoD's mustard agent experiments during World War II. Investigators reported:

- 32% of these veterans suffered from full PTSD
- 10% for partial PTSD

PTSD prevalence among these subjects was found to be a function of risk and protective factors, including:

- volunteering;
- physical symptoms during the tests; and
- the participants were forbidden from disclosing what happened to them.

Veterans with full PTSD reported:

- poorer physical health;
- a higher likelihood of several chronic illnesses;
- health-related disability;
- greater functional impairment;
- higher likelihood of health care use than those with no PTSD; and
- veterans with partial PTSD also had poorer outcomes than did veterans with no PTSD in some of these health areas (Schnurr et al., 2000).

Project SHAD and Project 112 Veterans and VA Health Care

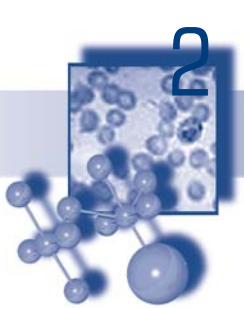
In April 2003, VA's Environmental Epidemiology Service (EES) reviewed the utilization of VA health care for 3,712 Project SHAD veterans. The review found that 31.9 percent of SHAD and Project 112 veterans had been seen at least once at a VAMC between 1970 and 2003. Their most frequent diagnoses are similar to those found in the general U.S. population for this age group. Further, no particular health care problem stood out among the SHAD/Project 112 veterans who had utilized VA health care. While this review was certainly not a substitute for a well-designed epidemiological study, it summarized the clinical experience of SHAD/Project 112 veterans who had received medical care from VA, and verified that there were no unusual health problems among this group.

This data obtained from VA inpatient and outpatient medical records does not allow for meaningful comparisons with other SHAD veterans who have not utilized VA health care, or to comparable military veterans who did not participate in Project SHAD. To obtain valid epidemiological data that could characterize the overall health status of all SHAD veterans in comparison with their military and civilian peers, VA contracted with the Institute of Medicine (IOM) to conduct a three-year, $3 million study to evaluate health risks among all veterans who participated in Project SHAD. The IOM held their first public meeting on March 21, 2003.

Epidemiological Study of SHAD Veterans

Unfortunately, there is no diagnostic test that can be performed now, decades after the SHAD tests, which will indicate which, if any, agents participants were exposed to, nor whether any specific medical problem might be related to such an exposure. The IOM study, however, will address the question whether SHAD veterans are experiencing greater morbidity or mortality compared to military veterans who served during the same era in the 1960's but who were not involved in Project SHAD.

Fortunately, accurate diagnosis of health problems is based primarily on a patient's symptoms and pathologic findings upon examination, and not by determining possible exposures. In fact, for many health problems, for example, most cancers, medical science does not know the cause of the disease, and treatment is the same regardless of etiology. As a result, high quality health care can be provided now for any SHAD veteran with a health problem seeking care from the VA before the results of the IOM study are complete.

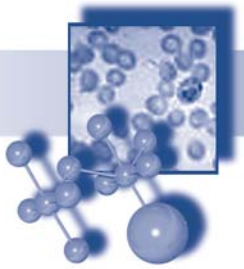


2 Health Effects From Chemical, Biological Agents and Radiological Weapons

Introduction

Part 1 of this VHI briefly covered the history of human experiments involving exposures of U.S. service members to chemical and biological agents, and radiological weapons. Also reviewed were studies that evaluated the long-term health of participants of those experiments. For the majority of veterans, these past experiments conducted by DoD will amount to their only military encounter with these warfare agents/weapons.

However, recent focus to the risk of terrorist actions within the U.S. brought attention to health effects for all U.S. citizens from these agents, including veterans, through a potential terrorist event. In principle, a terrorist attack with chemical, biological, or radiological weapons could involve a wide range of agents. Part 2 of this VHI reviews the health effects from well-known military warfare agents and weapons, which includes standard military nerve and blister agents such as sarin, VX, and mustard agents, and military biological agents such as anthrax. It also reviews some common non-military agents that could also be used by terrorists in an attack, such as readily available nerve agent pesticides. A section on the use of a “dirty bomb” and the effects of depleted uranium (DU) is presented.



Chemical Warfare Agents

Introduction

This section provides a brief description of these agents, how people might be exposed to them, what health effects including reproductive health effects and psychological effects they may cause, and what various groups that have reviewed health effects have said about long-term health consequences from exposure to chemical agents.

Chemical warfare agents are synthetic organic chemicals that are designed to cause rapid lethal and debilitating effects in humans. Since World War II, the most common military chemical warfare agents of concern include the **O**rgano**P**hosphorus (OP) nerve agents such as sarin and VX; and the vesicant blister agents such as the mustard agents.

The OP military nerve agents have general chemical form and an anticholinergic mode-of-action that are essentially identical to commonly used OP pesticides, described in the next section. The main difference is that the military nerve agents are designed to be more toxic to humans, and to have certain physical properties desirable for military use. The blister agents have no particular analogs, although some agents in this class, the nitrogen mustard agents, have been used as chemotherapy agents.

How can humans be exposed?

As described in Section 1 of this VHI, the most likely source of clinical effects seen in veteran patients would be the result of certain human experiments involving exposure of U.S. service members to chemical warfare agents conducted by DoD before 1975. However, this could change if there were a terrorist attack in the U.S. involving such agents or if U.S. service members were attacked with chemical weapons while in combat or peacekeeping missions abroad.

During the Gulf War in 1991, Iraq was known to possess both chemical and biological weapons (which was later confirmed by U. N. inspection teams). DoD reported that neither chemical nor biological weapons were ***intentionally*** used by Iraqi forces during the Gulf War.

In perhaps the most well-known chemical warfare agent case of the Gulf War in 1991, U.S. service members in March 1991 used explosives to

destroy a large ammunition depot (known as Khamisiyah), following the Gulf War cease-fire. This site was later found to have contained chemical agent munitions that contained sarin and the closely related agent cyclosarin. Small amounts of these agents were released into the atmosphere during the demolition (DoD Khamisiyah Case Narrative 2002). Other munitions at that site contained mustard agent, but DoD has concluded that their destruction did not lead to any release of agent.

Based upon atmospheric transport modeling carried out by the CIA, in 1997 the DoD notified nearly 100,000 Gulf War veterans who had been in the vicinity of Khamisiyah at the time of the demolitions, that they may have been exposed to trace levels of military OP agents. This model suggested that some veterans could have been exposed to low-levels of sarin and cyclosarin; levels too low to cause any acute (immediate) cholinergic poison signs and symptoms (DoD Khamisiyah Case Narrative 2002). DoD clinically confirmed this conclusion with the observation that no cases of acute cholinergic poisoning symptoms related to exposure to OP nerve agents were reported during the Gulf War in 1991, i.e., that:

> "no evidence exists that any soldiers at Khamisiyah exhibited symptoms consistent with exposure to a chemical warfare agent" (DoD Khamisiyah Case Narrative 2002).

However, low-level (insufficient to cause any signs or symptoms) exposures from inhalation may have occurred to some U.S. service members in the Gulf War region in the days following the cease-fire in 1991.

How are chemical warfare agents absorbed and eliminated from the body?

Chemical warfare agents can be absorbed either by inhalation of vapors, or through dermal contact with liquid agent.

Sarin and cyclosarin are relatively volatile agents, and the primary exposure concern for these agents is via inhalation (OSAGWI Technical Report 2002). Some of the OP nerve agents such as VX have substantially lower vapor pressure, and are hazardous primarily via direct skin contact and absorption.

Mustard agents are also much less volatile, and the primary exposure is dermal contact, although inhalation of aerosolized mustard agent also can be an important route of exposure.

All of these chemical warfare agents are rapidly metabolized and excreted, primarily in the urine, regardless of route of exposure.

What are the signs and symptoms of exposure?

Exposure to OP chemical warfare nerve agents can lead to poisoning signs and symptoms that are virtually identical to those caused by their OP pesticide analogs. These agents can produce irreversible inhibition of the

enzyme acetylcholine esterase (AChE), which is crucial to normal central and peripheral nervous system and muscle function. Because inhibition is irreversible, complete recovery involves the body's production of new enzyme to replace the inhibited AChE, which can take days to weeks.

Acute cholinergic poisoning symptoms usually develop within minutes or hours of exposure, and include:

- miosis;
- rhinorrea;
- headache;
- nausea;
- dizziness;
- sweating;
- anxiety; and
- restlessness.

Life-threatening symptoms may include:

- muscle fasciculation;
- weakness;
- tremor;
- uncoordination;
- convulsions;
- vomiting;
- abdominal cramps; and
- diarrhea.
- death can occur through respiratory paralysis

Tokyo Subway Attack

Perhaps the most dramatic terrorist attack with chemical warfare agents in recent history was the March 20, 1995 attack against civilians in the Tokyo subway system with the OP military nerve agent sarin. That attack resulted in more than 5,000 persons requiring emergency medical evaluation following possible exposure in and around the subway system where the sarin was released (Okumura et al., 1996; Ohbu et al., 1997).

Of the approximately 5,000 persons seeking medical attention, 641 victims were treated within hours of the attack at a local hospital emergency room (Okumura et al., 1996; Ohnu et al., 1997).

1. Most of those victims (531 cases) exhibited only mild sarin poisoning signs and symptoms, including miosis, and measurable decrease in blood cholinesterase levels. Such casualties were treated as out patients and released following 6 hours of observation.
2. Those casualties with more severe poisoning (112 cases) exhibited more severe cholinergic signs and symptoms including weakness, difficulty breathing, fasciculation's, and convulsions. These patients had plasma cholinesterase levels depressed from 20 to greater than 80 percent of normal (Okumura et al., 1996).

3. In-patients were treated with atropine and pyraldoxime chloride (2-PAM), and patients exhibiting convulsions (8 cases) were treated with diazepam (Okumura et al., 1996).
4. Two patients died, and 5 required emergency respiratory support.
5. Within 4 days, 105 of these more severely poisoned casualties were discharged, although 70 still complained of eye symptoms.

It is virtually certain that a great many more civilians were exposed during this incident at concentration levels that caused little or no poisoning. The levels experienced by these individuals did not cause them to seek medical attention.

Mustard Agent Symptoms

The immediate signs and symptoms of mustard agent poisoning include severe irritation and tissue damage to eyes, skin, and respiratory and gastrointestinal (GI) tracts. Usually the onset of symptoms is delayed for some hours after exposure.

One report of Iraqi use of mustard agent against Iranian troops in 1984 documented health effects in more than 5,000 Iranian casualties.

- Affected individuals had first to third degree burns over 20 to 70 percent of the total skin surface.
- Eye exposure caused tearing, severe conjunctivitis, and temporary loss of vision.
- Corneal abrasion was nearly always present, and photophobia and blurred vision developed in some cases.
- Upper airway involvement due to chemical burning of the throat led to pharyngitis and tracheobronchitis.

These effects were quite severe, and this group suffered approximately 15 percent mortality

Those who survived the initial symptoms later experienced various GI complaints, including:

- nausea;
- vomiting; and
- diarrhea.

After five to seven days, hematological problems were the greatest health threat to survivors (Kadivar and Adams, 1991).

What is known about long-term health effects from military nerve and mustard agents?

OP Nerve Agents

Exposure to sarin and VX chemical warfare agents can lead to rapid intoxication, incapacitation, and even death. However, some patients who survive severe poisoning by these and other OP nerve agents such as pesticides have been shown to later develop subtle, chronic neurophysiological and

neuropsychological abnormalities. Such effects in a patient, while not necessarily immediately observable, nevertheless can be detected using standardized neurological test batteries. For example, subtle deficiencies have been reported for survivors of acute OP poisoning in tests for:

- intellectual functioning;
- academic skills;
- abstraction, and flexibility of thinking; and
- simple motor skills.

Such deficiencies can be caused by many other hazardous exposures or a disease, so establishing an exposure history is critical to linking such effects to exposure of OP agents.

Certain OP chemicals used in the past have also been known to cause delayed neuropathies (or polyneuropathies) among casualties who recover from severe acute cholinergic poisoning. However, OP chemical warfare agents such as sarin and VX as a class are not normally considered to cause such effects in humans.

In 1998, VA requested the National Academy of Sciences (NAS) to review possible long-term health effects from exposure to sarin. Although NAS focused on sarin, their findings are applicable to other related OP nerve agents such as VX.

In their 2000 report, the IOM committee came to three specific conclusions about long-term effects of sarin exposure based on whether the exposure was high, medium, or low (NAS 2000). They concluded that:

1. "there is sufficient evidence of a causal relationship between exposure to sarin and a dose-dependent acute cholinergic syndrome that is evident seconds to hours subsequent to sarin exposure and resolves in days to months."

Thus, humans suffering a large exposure to sarin show a well-characterized acute cholinergic syndrome as evidenced by acute cholinergic signs and symptoms. Such acute poisoning signs and symptoms are consistent with synaptic buildup of acetylcholine as a consequence of sarin exposure, resulting in widespread over-stimulation of muscles and the central and peripheral nervous system. Acute cholinergic signs and symptoms are evident in seconds to hours after exposure and usually resolve in days to months.

At high doses, convulsions and death can occur

The IOM committee further concluded that:

2. "there is limited and/or suggestive evidence of an association between exposure to sarin at doses sufficient to cause acute cholinergic signs and symptoms and subsequent long-term health effects." Subsequent to acute cholinergic poisoning, some individuals show persistent symptoms that include:

- fatigue;
- headache;
- visual disturbances such as asthenopia, blurred vision, and narrowing of the visual field;
- asthenia;
- shoulder stiffness;
- symptoms of post-traumatic stress disorder (PTSD); and
- abnormal test results, of unknown clinical significance, on the digit symbol test of psychomotor performance, electroencephalogram (EEG) records of sleep, event-related potential, visual evoked potential, and computerized posturography.

These conclusions were based in part on review of reports of industrial workers in the U.S accidentally exposed to sarin, and of civilians exposed during the terrorism episode in Japan, described earlier. Following a terrorist attack, civilian casualties might suffer from PTSD. It is not surprising, given the highly traumatic nature of the attack itself. Similarly, veterans exposed to mustard agent in experiments conducted during World War II showed similar effects.

Finally, the NAS committee also concluded that:

3. "there is inadequate or insufficient evidence to determine whether an association does or does not exist between exposure to sarin at low doses insufficient to cause acute cholinergic signs and symptoms and subsequent long-term adverse health effects."

In other words, there is not sufficient evidence to conclude that persistent symptoms will be observed ***in the absence*** of immediate signs and symptoms of acute cholinergic poisoning. However, it is important to note that there are no well-controlled studies of long-term health effects in humans exposed to sarin at doses that do not produce any acute signs and symptoms.

Mustard Agent

The mustard agents are considered to be likely human carcinogens, and humans exposed to mustard agent are at increased risk of respiratory and skin cancers in decades following exposure. Part 1 of this VHI provides the summary of long-term health effects associated with mustard agents by the IOM in their 1993 report, "Veterans at Risk: Health Effects of Mustard Gas and Lewisite" (NAS 1993). IOM concluded that several specific chronic diseases are causally associated with exposure to this compound, including:

- various respiratory cancers;
- skin cancer;
- chronic skin ulceration and scar formation;
- chronic respiratory disease including:
  - asthma;
  - chronic bronchitis; and
  - emphysema.
- chronic eye diseases; and
- various psychological disorders including PTSD.

The NAS committee also found suggestive evidence (weaker than the associations for the conditions just mentioned) that exposure to mustard agent was associated with leukemia.

How may exposure to these agents affect reproductive health?

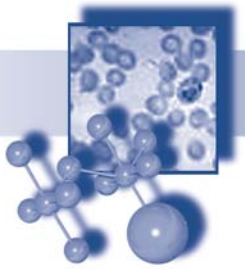
OP nerve agents, including pesticides and chemical warfare agents, are not considered as a class to be teratogenic agents. Mustard agents are considered to be likely human carcinogens. However, the 1993 NAS review, which examined studies on a possible link between mustard agent exposure and reproductive dysfunction, concluded that:

the data was inadequate to support conclusions about human reproductive health effects (NAS 1993)

Is there a test to verify exposure?

OP and mustard chemical weapon nerve and blister agents are rapidly metabolized and excreted from the body. Metabolites indicating exposure can be detected in urine within minutes to hours following exposure. However, metabolism and excretion of these compounds is generally complete within days of an exposure in cases where the individual survives the initial exposure.

Consequently, there is no test available today that can confirm exposure to these chemical warfare agents that may have occurred months or years in the past



Toxic Pesticide Agents

Introduction

Pesticides are products containing compounds that are intended to prevent, destroy, repel, or reduce pests. The majority of pesticides available in the U.S. have only low or moderate acute toxicity. Nevertheless, in the U.S. alone, there were about 18,000 hospital admissions for pesticide poisonings from 1971 to 1976. More than one-quarter of these were from **O**rgano**P**hosphorus (OP) pesticides, which are toxicologically and chemically related to the OP military nerve agents described previously (Save et al., 1988; Minton & Murray, 1988). Some examples of commonly used carbamate pesticides also have significant acute human toxicity. Thus, some commonly available pesticides probably possess sufficient acute toxicity to be potentially used in a terrorist attack.

In the U.S., pesticides are regulated primarily by the U.S. Environmental Protection Agency (EPA). The EPA is charged with evaluating the safety of pesticides before they can be marketed and used in the U.S.; with the goal of ensuring that they will not pose unreasonable adverse risks to human health and to the environment. The EPA grants those pesticides that meet their requirements a license or "registration," which permits their distribution, sale, and use. In general, pesticides are regulated and licensed for specific applications, such as on a specific crop. For example, the EPA may restrict the use of more toxic pesticides to specially licensed applicators. Some pesticides are considered sufficiently safe to be licensed for essentially unrestricted use in the U.S. for home and personal protection. These are the commonly available pesticides seen at garden stores and supermarkets.

Common OP pesticides such as Malathion and parathion, like their OP military agent counterparts such as sarin and VX, are anticholinergic poisons. Metabolism and elimination of OP pesticides are also similar as their military OP nerve agent counterparts. This means that signs and symptoms of poisoning are essentially the same for both classes. That is, OP pesticides also cause the irreversible inhibition of the enzyme acetylcholine esterase (AChE), which is crucial to normal nerve and muscle functioning.

Acute (immediate) cholinergic poisoning symptoms from OP pesticides usually develop within hours of exposure, and include:

- miosis;
- headache;

- nausea;
- dizziness;
- anxiety; and
- restlessness.

Life-threatening symptoms from acute cholinergic poisoning may include:

- muscle fasciculation;
- weakness;
- tremor;
- uncoordination;
- vomiting;
- abdominal cramps;
- diarrhea;
- sweating;
- salivation, and excessive tearing; and
- death can occur by respiratory paralysis.

Acute cholinergic poisoning by some of the more toxic, but also common OP pesticides is a serious public and occupational health issue. Recently, the EPA restricted the use of the OP pesticide Dursban® (chlorpyrifos), which used to be commonly available for home use, based primarily upon concerns about excessive acute toxicity risks.

Many common carbamate pesticides, which include household pesticides such as carbaryl, also act as anticholinergic agents, although their inhibition is reversible. Carbamate pesticides cause reversible inhibition of the enzyme AChE, and acute poisoning results in symptoms that are very similar to that seen with OP pesticides, but with shorter duration.

Long-Term Effects

Some patients who survive severe acute poisoning from OP pesticides show subtle, chronic neurological abnormalities, which can be detected using standardized neurological tests. Such effects can be detected for months or perhaps even years following the acute poisoning event. Although such effects in a patient might not be obvious to the clinician, nevertheless, subtle but measurable deficiencies have been reported for survivors of acute OP poisoning in tests for:

- intellectual functioning;
- academic skills;
- abstraction and flexibility of thinking; and
- simple motor skills (Brown and Brix 1998).

There are no treatments for these effects

Although a few OP pesticides are known to cause quite serious delayed neuropathies (or polyneuropathies) following recovery from severe acute cholinergic poisoning, OP pesticides in common use in the U.S. today are not considered normally to cause such effects.

Acute poisoning by carbamate pesticides can be quite serious and even cause death, but such poisonings have not been associated with chronic neurological effects as seen following acute poisoning by OP pesticides.

How may exposure to these pesticides affect reproductive health?

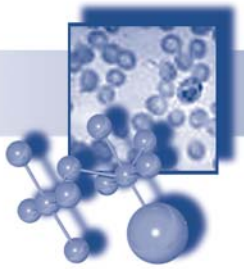
In general, the EPA requires animal and other data from manufacturers showing that a pesticide does not cause birth defects or other reproductive and developmental toxic effects before it can be licensed for use. As pesticide classes, the OP and carbamate pesticides are not considered to be teratogenic to laboratory animals.

Is there a test to determine exposure?

OP and carbamate pesticides are rapidly metabolized and eliminated primarily in the urine following exposure. Pesticide metabolites might be detected within hours to days following exposure to the typical pesticide.

There is no test available today that can detect an exposure to these pesticides that may have occurred in months to years in the past

Furthermore, these pesticides are widely used in within the U.S., and essentially all U.S. citizens are likely to have some more-or-less constant exposure to them in food and from other sources, which could compound any attempt to measure exposure.



Biological Warfare Agents

Introduction

Attacks with biological agents remain a concern for U.S. military planners. VA health care providers may be required to respond to casualties who have been exposed to biological warfare agents, perhaps even in cases where the initial injury is unrelated to that exposure. Furthermore, domestic terrorist attack with biological warfare agents could involve many casualties, as well as the "worried well", who may have been exposed or fear they have been exposed to the agents.

In the aftermath of a terrorist attack or responding to veterans returning from combat, the clinician might not know of an exposure to an infectious agent, which may have been unrecognized at the time of treatment rendered at the site of the attack. Casualties could be sent to VAMCs for injuries unrelated to an incidental exposure to a biological agent. Because of the relatively long incubation period of some biological warfare agents, symptoms might manifest only after transfer to a stateside hospital or a VAMC.

It is important that VA health care providers have

1. a high index of suspicion about biological agents;
2. be prepared to take appropriate action; and
3. provide appropriate health care in response to a biological warfare agent incident occurring either at home or abroad.

The following material was developed as background material for those who may be called upon to respond in such an emergency. It includes information on biological agents such as:

- anthrax;
- botulism;
- plague;
- smallpox;
- tularemia; and
- viral hemorrhagic fevers.

There is also information on biological agent simulants (agents with similar physical properties but without the lethality) that have been used in human experiments by DoD in the past, and which may be of concern to veterans potentially exposed to them.

Diagnostic and Treatment Continuum

Following an exposure to any biological infectious agent, medical personnel must be aware of the diagnostic and treatment continuum, which includes:

1. clinical presentation;
2. diagnosis;
3. treatment;
4. infection control; and
5. long-term issues.

Key issues to consider related to this continuum.

1. Mass exposures are possible in the battlefield or domestically.
2. Etiology may or may not be known upon admission to VA facilities.
3. Primary diagnostic work-up may not be considered initially, but signs and symptoms may present after admission due to longer incubation periods of some agents.
4. Possibility exists of organisms with altered toxic profile.

Categories of Biological Warfare Agents

The U.S. Department of Health and Human Services Center for Disease Control and Prevention (CDC) places biological agents into three categories, A, B, and C (Table 1). This VHI will focus on Category "A" agents, which are the greatest concern because they are easily disseminated, often easily transmitted, produce a high mortality rate and have a high social disruption potential. Category "A" agents include (Table 1):

Biological Warfare Agents		
Category A	Category B	Category C
Anthrax	Brucellosis	Hantavirus
Botulism	Food-borne/Water-borne (e.g., Salmonella)	Multidrug-resistant Tuberculosis
Plague	Q Fever	Nipah Virus
Smallpox	Staphylococcal Enterotoxin B	Tick-borne Hemorrhagic Fever
Tularemia	Viral Encephalitis	Yellow Fever
Viral Hemorrhagic Fever		

Table1

Since these agents have catastrophic potential, but are not often seen in everyday practice, it is important that all medical personnel understand the need for special preparations related to the treatment of patients who may be infected by them.

Anthrax

Introduction

Anthrax has always been considered a bacterium with high potential as a bacteriological weapon because its spores survive for so long. In 1979, an outbreak of largely inhalational anthrax occurred in Sverdlovsk, Russia. Sixty-six people died, while an additional 11 are known to have survived. It is assumed that other less severe cases were not documented and so the death rate was not really known. The cases occurred as the result of an accidental aerosol release from a biological research institute nearby, and it was concluded by investigators that this unusual epidemic was related to biological warfare studies. It is of interest that the longest incubation period recorded in that episode was 43 days, although the incubation period is usually said to be between 1 – 7 days for anthrax.

During October 2001 in the U.S., a case of inhalational anthrax was diagnosed by an astute infectious disease physician in Florida along with capable laboratory support. This led to the discovery that anthrax spores had been intentionally distributed through the U.S. mail system. There were 22 cases of anthrax, including 5 deaths, resulting from this biological attack.

Infectious Agent

Bacillus anthracis (B. anthracis) (Figures 1-3) is a gram-positive spore forming with rod, spore, and vegetative forms. It is found in soil or herding animals. Occupational exposure occurs from handling the hides, wool, or bones from infected animals and the disease is seen in veterinarians, agricultural works, and others who handle infected animals. The spores can be long-lived, but person-to-person transmission, if it exists, is rare.

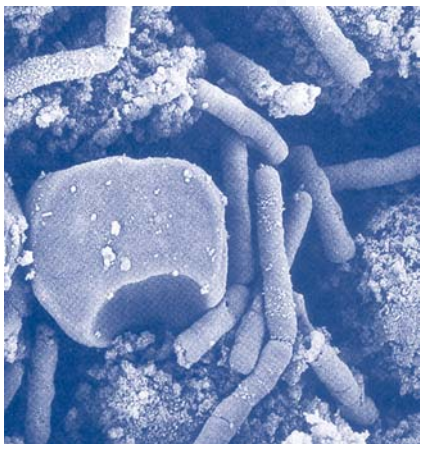


Figure 1

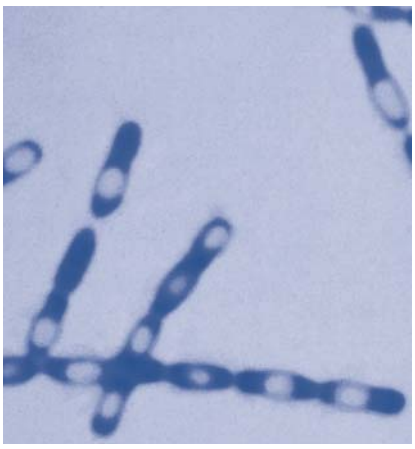


Figure 2

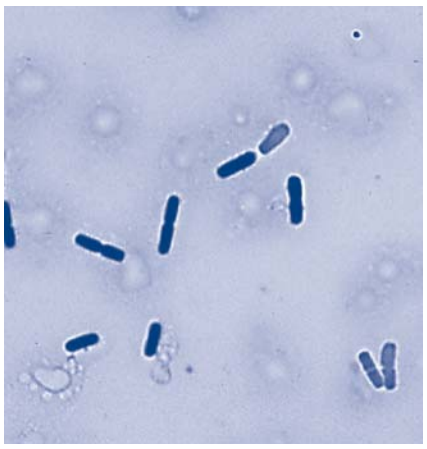


Figure 3

Figure 1 shows anthrax bacteria shown under an electron microscope.

Figures 2 and 3 are light microscopic views of the *B. anthracis* organism.

Anthrax presents in two major forms, and one minor form:

1. Skin (cutaneous - Major) - Cutaneous anthrax can occur when the anthrax bacteria enters the body through unintact or broken skin. Patients with cutaneous anthrax will develop a sore that progresses to a very classic black eschar (scab). A clinician seeing a patient with a skin wound that has a black eschar should assume that patient has skin anthrax until proven otherwise. Cutaneous anthrax is generally a less serious form of this disease.
2. Inhalational (Major) - Inhalational anthrax is far more serious and occurs when the anthrax bacteria is inhaled into the terminal bronchioles and alveoli. Patients with inhalational anthrax may present with fever, but rapidly progress and require rapid and intensive intervention if they are to survive.
3. Intestinal anthrax (Minor) - This has been described, but is rare and difficult to diagnose. It tends to occur in explosive outbreaks of food poisoning.

Cutaneous Anthrax

Clinical Findings

- *B. anthracis* enters through unintact skin
- Incubation in 1 to 12 days
- Small papule forms in 1-2 days that progresses to a vesicle (Figure 4)
- The vesicle progresses to a necrotic ulcer that forms with a black eschar (Figure 5)
- The lesion is painless with surrounding edema
- Fever, headache, malaise, and regional lymphadenopathy may be present

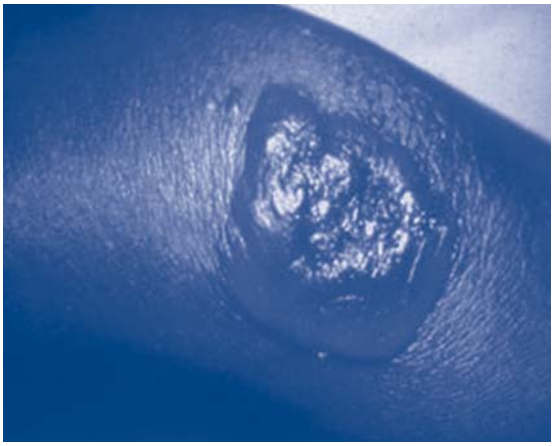


Figure 4

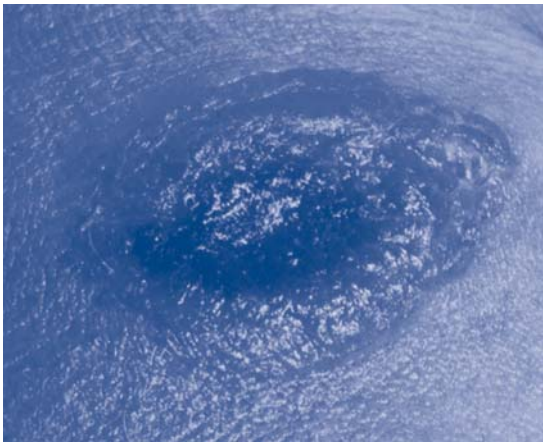


Figure 5

Figure 4 shows an early cutaneous anthrax lesion at the vesicular stage.
Figure 5 shows the surrounding edema and early diagnostic black eschar.

Figures 6 and 7 shows the progression of a lesion on the neck, again, note the diagnostic black eschar.

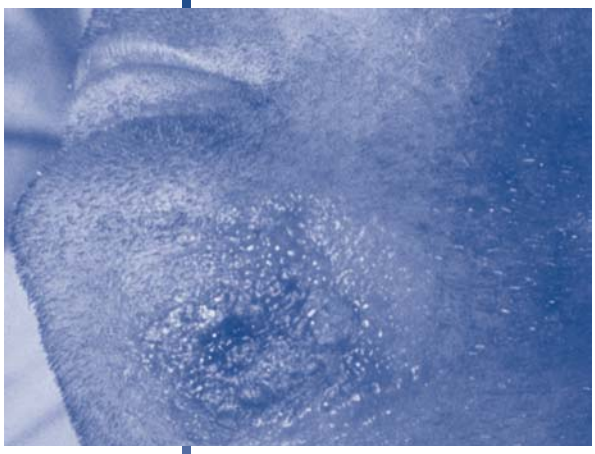


Figure 6

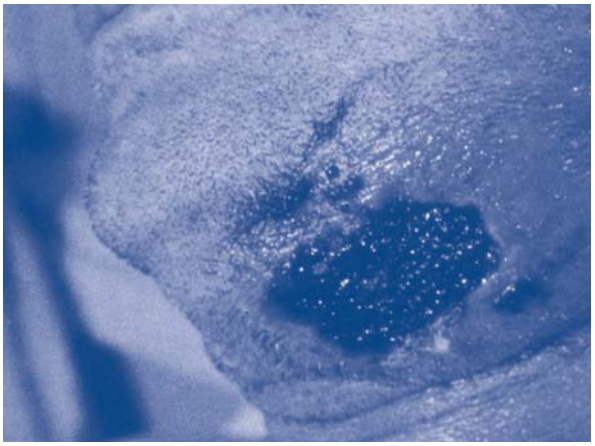


Figure 7

Figure 8 shows evidence of regional lymphadenopathy. Figure 9 shows the diagnostic black eschar.

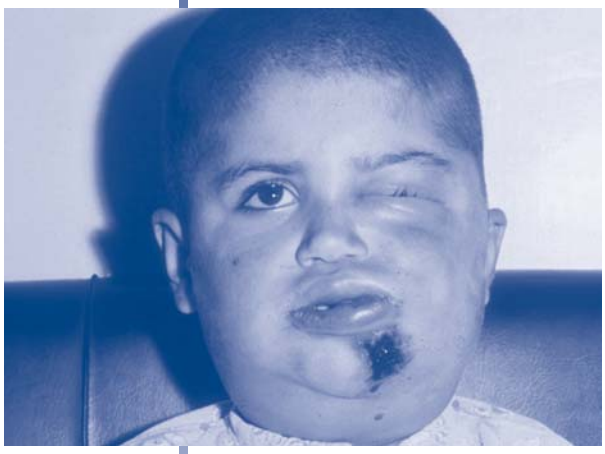


Figure 8

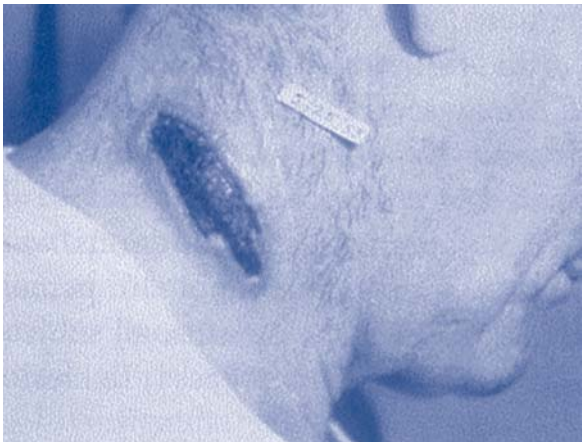


Figure 9

Inhalational anthrax

Pathogenesis

- *B. anthracis* spores are deposited in terminal bronchioles and alveoli
- Spores are ingested by macrophages that migrate to peribronchia/mediastinal lymph nodes
- Spores incubate, become vegetative in approximately 10 days
- The vegetative form of *B. anthracis* produces toxin that causes all the damage

Clinical Findings

- Fever
- Fatigue
- Chest pain
- Non-productive cough
- Hemorrhagic mediastinitis evident on CXR/CT/MRI after 1-3 days
- Abrupt onset of severe respiratory distress
- Septic shock and death 1-3 days later
- Meningitis and plural effusions are possible findings
- CXR/CT/MRI Findings (at this stage) include:
  - widened mediastinum, pleural effusion; and
  - pulmonary infiltrates possible, but maybe not.

According to Inglesby, et al., (2000) the following are the signs, symptoms, and findings associated with the terrorist mail attacks (10 cases) with anthrax in the U.S. in 2001.

- Fever/chills 10/10
- Non-productive cough 9/10
- Dyspnea 8/10
- Myalgia 6/10
- Abdominal pain 3/10
- Rhinorrea 1/10
- Fatigue/malaise 10/10
- Nausea/vomiting 9/10
- Chest pain 7/10
- Headache 5/10
- Sore throat 2/10

Lab and X-ray Findings in these 10 cases included:

- WBC normal to slight elevation with left shift frequent 10/10
- Transaminases >40 u/l 9/10
- CXR 10/10 abnormal
  - Pleural effusions 8/10
  - Pulmonary infiltrates/consolidation 7/10
  - Mediastinal widening 7/10
- CT 8/8 abnormal
  - Mediastinal widening 7/8
  - Pleural effusion 8/8

Prophylaxis and Treatment

In the event of another attack with anthrax, both prophylaxis and treatment will be required. ***Casualties with documented exposure*** (from proven source or shared environment with proven case), but without clinical symptoms consistent with the disease of anthrax should receive ***chemoprophylaxis*** to prevent development of disease as follows:

- Ciprofloxacin or doxycycline for 60 days

Prophylaxis is **NOT** indicated for those without exposure with a documented case or to a reservoir of *B. anthracis*.

The recommended treatment for ***documented infection*** with *B. anthrac*is consists of the following:

- ***Cutaneous:*** Oral Ciprofloxacin for 60 days
- ***Inhalational:*** Early Empiric Treatment (high index of suspicion, clinically compatible scenario):
  - Combination antibiotics – then based on ***in vitro*** activity using IV ciprofloxacin or doxycycline + 1 or 2 additional antibiotics (rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, clarithromycin).
  - Switch to oral ciprofloxacin or doxycycline when appropriate.
  - Total Treatment – 60 days.
  - Expect need for drainage of pleural effusions.

Infection Control

Neither cutaneous nor inhalation anthrax are transmitted person-to-person, so normal hospital infection control procedures are adequate. The following is the recommended control procedures:

1. No need for isolation – no person-to-person transmission
2. Use standard barrier precautions
3. Disinfect any potentially spore containing materials or equipment
4. High-efficiency particulate air filter masks are not indicated
5. No need to prophylax patient contacts (unless they had similar exposure as patient)

Anthrax Immunization

Immunization is recommended for high-risk persons, including laboratory workers who work with *B. anthracis.* Many military personnel have also received anthrax immunization against its possible use as a weapon.

Long Term Issues with Anthrax Infection

There are few long-term effects from cutaneous anthrax except scars. Inhalation anthrax involves a long recovery period due to extensive tissue damage by toxins and systemic disease. There may be subsequent respiratory disability. Naturally occurring anthrax poses difficulty in decontamination, thus there is a potential for prolonged exposure.

Botulism

Introduction

Botulism is not an infection, but is a disease caused by poisoning or intoxication with botulinum toxin, produced by *Clostridium botulinum (C. botulinum)*. There are three types:

1. classic food-borne;
2. wound; and
3. intestinal (sometimes called infant and adult)

It is also possible to cause poisoning through the inhalational route in experimental models. All routes result in a flaccid paralysis from the neurotoxin.

Infectious Agent

Food-borne botulism is caused by toxins produced by *C. botulinum*. Most naturally occurring cases result when the toxin is produced in improperly process canned, low acid, or alkaline food. However, botulinum toxin has high biological weapon potential.

C. botulinum is a spore-forming obligate anaerobic bacillus, which produces several types of toxin. A few nanograms of the toxin can cause illness. The toxin is attractive as a potential weapon for a number of reasons:

1. Easy to produce or acquire in large quantities.
2. Highly lethal via aerosol or food (5% mortality for food-borne).
3. Incubation of clinical manifestations:
   - 2 hrs – 8 days (food-borne)
   - 12 – 80 hrs (inhalation – experimental)
4. Action: Blocks cholinergic synapses.

Clinical Presentation

Botulism presents as:

- acute;
- afebrile;
- symmetric;
- descending flaccid paralysis;
- multiple cranial nerve palsies (ptosis, diplopia, blurred vision, enlarged/sluggish pupils, dysarthria, dysphonia, dysphagia);
- dry mouth/injected pharynx;
- progressive loss of gag reflex and respiratory muscle activity and;
- death occurs from respiratory failure.
  - artificial ventilatory support may be required for long periods; and
  - botulinum intoxication is primarily a clinical diagnosis, although an assay for the toxin may be done through a reference lab.

Prophylaxis and Treatment

Treatment for botulism is primarily supportive and ventilator support may be required for weeks to months. A licensed intravenous polyvalent botulinum antitoxin is available from CDC through local health departments and should be administered as early as possible to retard or arrest progression. (An investigational toxoid is available for laboratory workers, but is in limited supply and only provides coverage for a few months so this does not have widespread applicability.) There is no prophylaxis except to prevent progression once poisoning signs and symptoms develop.

Infection Control

1. No special requirements or isolation is required for patients with exposure to botulinum toxin.
2. Standard precautions need to be reviewed as a routine since this involves a biological agent.
3. Human-to-human transmission is not of concern, and decontamination is accomplished by removal of exposed materials or clothes and washing.
4. Contaminated food and utensils should be disinfected and disposed of properly.

Long-Term Effects

Survivors may have fatigue and shortness of breath for years.

Plague

Introduction

Plague is a zoonotic disease associated with rodents. Squirrels especially are a natural reservoir. However, it also may exist in rabbits and domestic cats. The disease is spread by flea bites to humans and various other animals. Plague can present in two main forms:

1. Bubonic
2. Pneumonic

Infectious Agent

Plague is caused by the bacillus, *Yersinia pestis (Y. pestis)*.

Clinical Presentation

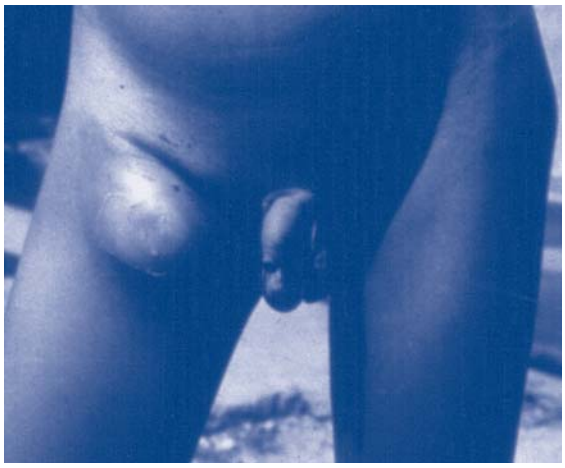


Figure 10

Bubonic plague

Presents with a regional infection manifested by a large swollen lymph node, called a bubo (Figure 10). The incubation period is 1 – 7 days and 1 – 4 days for primary plague pneumonia.

Pneumonic plague

The more serious form, where an individual inhales the organisms and presents with a non-specific febrile illness that progresses rapidly to:

- pneumonia;
- septic shock;
- disseminated intravascular coagulation; and
- death.

Pneumonic plague is a highly contagious

condition in the hospital setting, and would be the most likely type to occur in a terrorist attack.

Figure 11 is a micrograph of the *Y. pestis* organism.

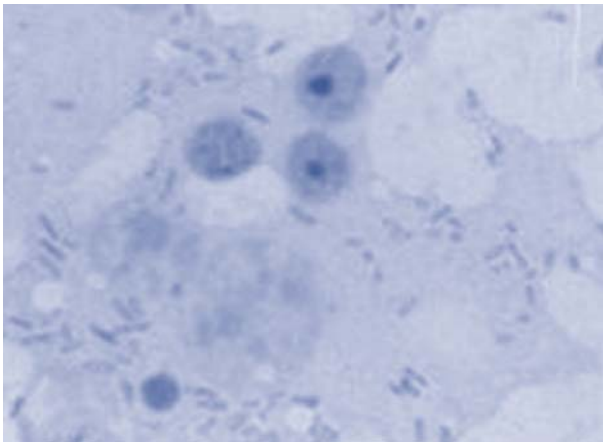


Figure 11

Treatment

Rapid initiation of antibiotic treatment is required.

- Streptomycin IM or Gentamicin IV/IM or Doxycycline, ciprofloxacin, chloramphenicol (all IV).
- Change to PO when indicated.

In a mass casualty settings.

- Doxycycline, ciprofloxacin, chloramphenicol PO.
- All therapy continued for 10 days.

Patients are also likely to need treatment for complications.

- Gram-negative sepsis
- ARDS
- DIC
- Shock
- Multi-organ failure

Prophylaxis

When exposure is confirmed:

- IV antibiotics for anyone with T >38.5C or cough, or
- PO antibiotics for symptoms after mass exposure.

For asymptomatic exposures or close contacts of proven cases:

- doxycycline, ciprofloxacin, chloramphenicol for 7 days PO.

Infection Control

Plague infection control issues are critical because this organism is readily transmitted via respiratory droplets.

- Standard respiratory droplet precautions are required of hospital workers using surgical masks, gowns, gloves, and eye protection.
- Patients should be isolated for up to 48 hours after antibiotics are administered for this infection.
- Inpatients who have been diagnosed with plague who are in the hospital and are being transferred around the hospital should also wear surgical masks to prevent infection of other hospital workers.
- Mortuary workers and other hospital personnel should be advised

of the diagnosis of plague.
- No spore formation – thus, no unusual environmental decontamination needed.

It is important to emphasize for those in whom exposure to aerosolized *Y. pestis* has been confirmed, prophylaxis should be instituted as soon as possible.

Anyone who has been exposed who has a fever or cough should be treated as if they have plague and get appropriate IV antibiotics and clinical monitoring. In addition, for close contacts of cases, they can also receive oral antibiotics for seven days.

Smallpox

Introduction

Smallpox is a viral disease, which is unique because the last naturally occurring case was in Somalia in 1977. In 1979, the WHO certified global eradication of the disease. All known variola stocks are held by CDC or the State Research Center in Russia. However, the possibility that one of these or other unknown supplies of variola might be used as a weapon exists, and therefore smallpox cannot be dismissed by clinicians.

- Smallpox is easily transmissible person-to-person.
- It presents as a non-specific viral syndrome that progresses to a characteristic rash.
- It is very highly contagious, particularly in the rash stage (Figures 12, 13, and 14).

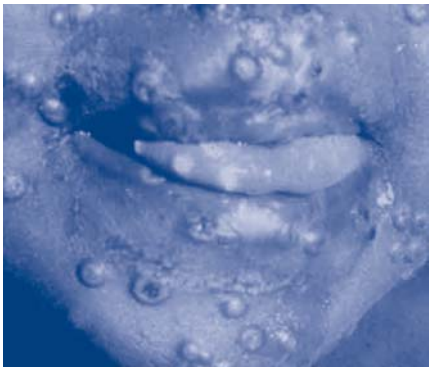


Figure 12

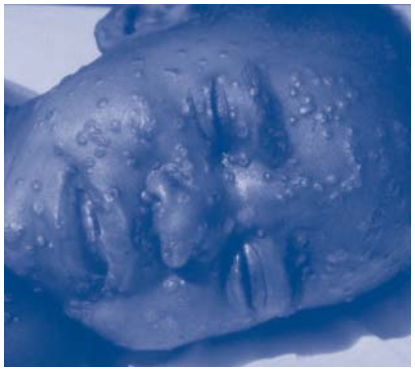


Figure 13

Figure 14

Clinical Findings and Infectious agent

Smallpox is caused by Variola, a species of othopoxvirus. Smallpox (variola) has some similarities and important differences with chickenpox (varicella) (Table 3 presents the similarities and differences between smallpox and chickenpox).

Similarities and differences between smallpox versus chickenpox		
	Variola (Smallpox)	**Varicella (Chickenpox)**
Incubation	7-17 days(~12 days)	14-21- days
Prodrome	2-4 days	Minimal/none
Distribution*	Centrifugal	Centripetal
Progression*	Synchronous	Asynchronous
Scab formation	10-14 d p rash	4-7 d rash
Scab separation	14-28 d p rash	<14 d rash

* Denotes important differences

Table1

Early symptoms are non-specific:

- fever;
- headache;
- backache;
- vomiting;
- malaise; and
- aches for 2-4 days.

A rash appears 2-3 days later in a centrifugal pattern with synchronous emergence and progression from maculopapules to vesicles to pustules scabs over in 1-2 weeks.

Mortality ~ 30% - due to toxemia often with massive bleeding

Laboratory diagnosis not required after index cases are confirmed (BL-4 Lab required for diagnostic studies).

Treatment

There is no known treatment for smallpox

Medical personnel will need to provide supportive measures, and isolate the patient to prevent further infections. This is important because transmission occurs primarily after rash appears. As part of this treatment, consider isolation at non-hospital facilities. Antivirals are under investigation as a treatment, and antibiotic prescriptions may be used for secondary bacterial infections.

Prophylaxis

Vaccination with vaccinia virus is effective in preventing disease if the vaccine is administered within 3 days of exposure.

Infection Control

Infection control for smallpox has to take immediate priority once it has been determined that there is a patient with smallpox

Infection control involves appropriate isolation and vaccination of contacts. The smallpox vaccine is likely effective in preventing appearance of smallpox if given within 3-4 days of exposure.

The following procedures make up this response:

1. **ACTIVATE FACILITY SMALLPOX HEALTH CARE RESPONSE TEAM**
2. Initiate smallpox vaccination of all hospital workers (include housekeeping, mortuary workers, etc)
3. Vaccinate all close contacts of index case(s)
4. Patients should be kept in respiratory isolation: aerosols and pustules are infectious
5. Keep isolated for 7-10 days after onset of rash
6. Bedding & equipment – autoclave, destroy or launder with hot water/bleach

Tularemia

Introduction

Tularemia (rabbit fever, deer fly fever, Ohara's disease) is a bacterial infection, which is most common in people who handle infected wild rabbits. Other infected animals, ticks, or contaminated food or water also transmits tularemia. The disease presents as a febrile illness with a wide array of clinical manifestations depending on where the bacteria enters the body. Tularemia can present as a(n):

- systemic infection;
- oral or mouth or throat infection;
- skin infection; or
- pulmonary infection.

It is considered to be a potential biowarfare/bioterrorism agent particularly when used as an aerosol. Like plague, it would present as a primary pneumonia, but can be slower to present than either plague or anthrax. Important features include:

- one of the most infectious pathogens known – inhalation of as few as 10 organisms can cause disease;
- occurs widely, recovered from soil/water and vegetation;
- vectors mostly small mammals (moles, mice, rats, rabbits);
- humans become infected naturally by bites from flees/ticks from infected animals or exposure to animal tissue, fluids or aerosols;
- between 1985-1992, 1409 cases reported in U.S. with 20 deaths; and
- no person-to-person transmission.

Infectious Agent

Tularemia is caused by *Francisella tularensis (F. tularensis)*, a small, non-motile, aerobic, gram-negative coccobacillus.

Clinical Presentation

Symptoms of tularemia include:

- fever;
- headache;
- muscle pains;
- arthralgia; and
- a dry, non-productive cough.

High fever and severe constitutional distress appear suddenly within approximately 10 days of exposure. One (or more) ulcerating lesion(s) develops at the infection site, usually the arm, eye, or mouth. The regional lymph nodes enlarge, suppurate, and drain. Pneumonia, meningitis, or perionitis may complicate this infection, which has a mortality rate of about 6 percent.

There are a number of forms of tularemia:

1. ulceroglandular;
2. glandular;
3. oculoglandular;
4. oropharyngeal;
5. pneumonic;
6. typhoidal; and
7. septic.

The symptoms of pneumonic tularemia include:

- pharyngitis;
- bronchiolitis;
- pneumonitis;
- pleuritis;
- hilar lymphadenitits are common, as is;
- pulse/temperature dissociation.

It is difficult to distinguish from Q fever without laboratory assistance

Diagnosis

There is no rapid diagnostic testing available. The diagnosis is suggested by gram stain or DFA on secretions or biopsy specimens. However, definitive diagnosis requires growth of *F. tularensis* from culture of pharyngeal washings/sputum or other infected fluids confirms diagnosis.

Treatment and Prophylaxis

1. Streptomycin IM or Gentamicin IM or IV or
2. ciprofloxacin IV (10d), doxycycline, chloramphenicol IV (14-21 d).

In a Mass Casualty Setting.

1. Doxycycline PO 100mg BID x 14 days.
2. Ciprofloxacin PO 500 mg BID x 14 days.

Vaccination

A live attenuated vaccine is under review by FDA.

Infection Control

Since there is no person-to-person transmission, only standard precautions for hospital, labs, linens, housekeeping, and mortuary workers are required.

Q Fever

Introduction

Q Fever is an acute febrile Rickettsial disease with considerable variation in the severity and duration of the symptoms. Domestic animals (sheep, cattle, and goats), cats, wild animals, and ticks usually host *Coxiella burnetii (C. burnetti)*. Humans become infected after contact with contaminated materials, such as:

- feces or blood;
- inhaling contaminated dust or droplets; and
- (rarely) ingesting contaminated food or unpasteurized milk.

Infectious agent

C. burnetti causes Q Fever in humans. It has two antigenic phases and has unusual stability. It can reach high concentrations in animal tissues and is resistant to many disinfectants.

Clinical presentation

Symptoms of Q Fever include:

- fever;
- headache;
- muscle pains;
- arthralgia; and
- a dry, non-productive cough.

Hepatitis or pneumonia also may develop during the early stages of disease. In rare occurrences, Q fever can cause endocarditis and subsequent aortic heart valve complications. Generally, infected and appropriately treated patients recover completely.

Diagnosis

Laboratory diagnosis is made by demonstrating a rise in specific antibodies in paired sera.

Treatment

Tetracyclines, particularly doxycycline, for 15 to 21 days are indicated for acute disease. Chronic disease (endocarditis) requires long-term antibiotics.

Infection Control

Only standard precautions are required.

Viral Hemorrhagic Fevers (VHF)

Introduction

Viral hemorrhagic fevers (VHF) are actually caused by a collection of several viruses, including Ebola (Figure 15), Lassa, Marburg, Rift Valley Fever (RVF), New World Crimean-Congo Hemorrhagic Fever virus, and New World Arenaviridae (NWA). All present as a severe febrile illness, where coagulation problems are the predominant clinical sequelae.

Because of frequent bleeding, the viral hemorrhagic fever viruses are also very contagious in the hospital setting.

1. **Strict blood and body fluid precautions are needed to maximize infection control**
2. **VHF's have an incubation period of 4-21 days, with a mortality rate that varies from 10-90%**

Clinical presentation

Diagnosis requires high index of suspicion when seeing the following symptom complex, which are the accepted clinical criteria for VHF:

- Temperature > 38.3C of < 3 wks
- Severe illness, - 2 symptoms:
  - epistaxis;
  - hemorrhagic rash;
  - hematemesis;
  - hemoptysis;
  - bloody stool; and
  - no predisposition for hemorrhagic disease.

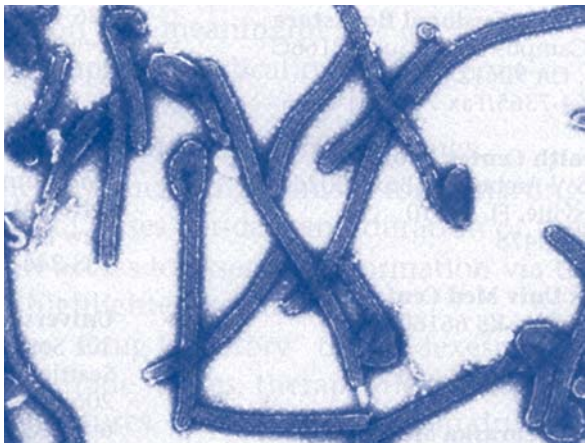


Figure 15

Treatment

1. There is no specific treatment except for Lassa, NWA, and Rift Valley where Ribavirin for 10 days is recommended.
2. Otherwise, the treatment is supportive.
3. Infection control is extremely important since the viruses are highly contagious.
4. There is no effective prophylaxis.

Infection Control

Infection control procedures for patients with the viral hemorrhagic fevers are critical

There are numerous infection control procedures that **MUST** be adhered to. A good infection control program will keep the infection level low, or non-existent.

1. VHFs are highly infectious via blood/bodily secretions
2. Isolation and barrier precautions required
3. Strict hand hygiene, double glove
4. Impermeable gowns, coverings
5. N-95 masks or PAPRs
6. Face shields/goggles
7. Required for health care workers and housekeeping, mortuary staff, etc
8. Patients in isolation rooms
9. Negative air pressure rooms thru HEPA filter
10. Restricted access by non-essential staff/visitors
11. Patients with same diagnosis can be roomed together
12. Patients with Ebola, Marburg, Lassa, NWA – no sexual activity for 90 days after recovery

Staphylococcal Enterotoxin B (SEB)

Introduction

Staphylococcal Enterotoxin B is one of seven enterotoxins produced by the bacterium *Staphylococcus aureus (S. aureus)*. The staphylococcal enterotoxins are the most frequent cause of common food poisoning, which presents with nausea, vomiting, and diarrhea shortly after exposure. Therefore, many people have been exposed to SEB.

In high doses, SEB may cause fatalities. SEB was developed for military use as an incapacitating agent to hinder combat effectiveness on an enemy on the battlefield. For use as a biological weapon, SEB is spread as an aerosol that can be inhaled.

After exposure to an aerosol of SEB, symptoms develop rapidly in 3 to 4 hours. The major symptoms include:

- acute fever;
- chills;
- non-productive cough;
- shortness of breath;
- headache; and
- nausea and vomiting.

There is no test for exposure to SEB after acute symptoms have resolved

In addition, there are no known long-term health effects from exposure to SEB, but follow-up studies of exposed populations have not been conducted.

Long-Term Health Impact from Infection by Biological Warfare Agents

The long-term sequelae following infection (and recovery) by biological warfare agents must also be considered. These include the psychological impacts including documented cases of PTSD (Hyams, et al., 2002).

Biological Warfare Agent Simulants

In addition to the biological warfare agents listed above, much less hazardous biological agent ***simulants*** have also been widely used in U.S. biological warfare agent experiments. These biological warfare agent simulants are used as relatively non-toxic stand-ins or substitutes for the actual biowarfare agents. Commonly used simulants include:

- *Bacillus globigii* (BG) (since renamed *B. licheniformis*);
- *E. coli;* and
- *Serratia marcscens*.

Such biological simulants have been considered safe. The VA understands today that they can be opportunistic pathogens under certain unusual circumstances. Those circumstances, such as severely compromised immune competency, are probably not relevant to active duty personnel, but they could be a concern for the general U.S. population.

Bacillus globigii (BG)

Bacillus globigii (B. globigii), long used as a biological warfare agent simulant, is commonly abbreviated as BG, although it sometimes appears in the literature as *B. licheniformis*. *B. licheniformis/globigii* is not generally considered to be pathogenic, but is recognized as a cause of such acute infections from intravascular catheter-acquired sepsis and from food poisoning.

In general, members of the genus *Bacillus* are aerobic or facultatively anaerobic gram-positive or gram-variable spore-forming bacteria that are found ubiquitously in decaying organic matter, dust, soil, vegetables, and water. A species related to *BG, Bacillus anthracis* is of course pathogenic for humans (see above entry) and is the basis of anthrax biological weapons (adapted from Principles and Practice of Infectious Diseases, ed, GL Mandell, JE Bennett and R Dolin, eds, 2000).

BG is not normally considered to be harmful. DoD selected BG as a less infectious biological warfare agent “simulant” in the Project SHAD tests, described earlier. However, BG is associated with a number of opportunistic

infections, particularly in a hospital setting with debilitated, immune-suppressed, or traumatized patients. Opportunistic infectious diseases would be expected to occur shortly after exposure to BG, and long-term infections are not expected among individuals exposed decades in the past.

Clinical Manifestations

Infection by some *Bacillus* species include:

- acute food poisoning; and
- localized infections related to trauma; for example:
  - ocular infections
  - deep-seated soft tissue infections; and
  - systemic infections like:
    - meningitis;
    - endocarditis;
    - osteomyelitis; and
    - recurrent bacteremia.

Risk factors associated with acquiring *Bacillus* infections include:

- intravenous drug use;
- sickle cell disease; and
- foreign bodies including:
  - intravenous catheters; and
  - immune-suppression from various causes, including:
    - infection with human immunodeficiency virus (HIV).

BG specifically has been clinically associated with intravenous catheter-acquired sepsis. BG has also been reported in acute food poisoning cases in which cooked meats and vegetables were most commonly implicated. The median period of incubation was about 8 hours, and the predominant symptom was diarrhea with vomiting.

Zinc cadmium sulfide

Zinc cadmium sulfide (ZnCdS) was used by DoD as a tracer material for studying potentially harmful particles dispersed in air. ZnCdS particles dispersed in air behave similarly to some biological agents, and because they fluoresce under ultraviolet light, the spread of ZnCdS particles can easily be detected.

DoD used ZnCdS in Project SHAD and in other tests conducted in the 1950s and 1960s in several urban and rural locations in the U.S. and Canada. In 1994, DoD asked the National Research Council (NRC) to review the potential human health risks of ZnCdS. In their 1997 report, the NRC committee reviewed the toxicokinetics, bioavailability, and toxicity of ZnCdS as related to the studies conducted in the 1950s and 1960s. The NRC previously concluded that the risks to civilian populations of non-cancer health effects and lung cancer from ZnCdS tests conducted by DoD appear to be low.

The NRC committee reported that animal data indicate that ZnCdS is not acutely toxic when given orally, consistent with its low solubility and apparent lack of bioavailability. The committee found that the particle size used in these tests could have been inhaled and deposited in the deep lung. Given the lack of reports of toxicity of inhaled ZnCdS, the committee instead reviewed related toxicity data on cadmium as the most toxic component of ZnCdS.

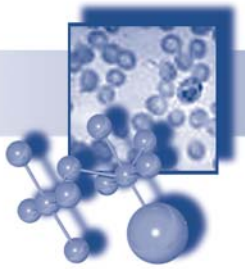
The NRC Committee concluded that:

> "inhaled cadmium has been shown in occupational studies and laboratory studies of animals to cause lung cancer, but not cancer at other body sites."

Further:

> "cadmium inhalation exposures associated with increased lung-cancer risk in animal studies involved higher concentrations (100 - 1,000 times higher), longer periods (lifetime exposures), and more-soluble compounds than the exposures to cadmium from ZnCdS in the Army's testing program."

The estimated upper bound, lung-cancer risks ranged from less than 0.01 X 10-6 to 24.0 X 10-6 (less than one per million to twenty-four per million).



Radiological Weapons

Introduction

With the end of the Cold War, the possibility of battlefield use of nuclear weapons appears diminished, although not eliminated. The possibility of terrorists obtaining nuclear weapons is disturbing, but probably unlikely given the enormous difficulty of obtaining the necessary components and underlying critical technology required to make a nuclear weapon. However, a much simpler radiological dispersant device or "dirty bomb" is an all too plausible terrorist scenario.

The radiological dispersant device or "dirty bomb" combines a radioactive material with a conventional explosive to disperse it. The radioactive material could potentially come from many sources, such as radioactive waste, or hospital or engineering radiation sources. The "dirty" term refers to the potential widespread radiological contamination that would follow exploding the bomb and the resultant dispersal of radioactive material. Although few nations possess the materials to make a nuclear bomb, radioactive sources suitable for a dirty bomb are generally much more available.

Ionizing radiation, like heat and light, is a form of energy. It can take the form of particles and rays given off by sources such as radioactive isotopes, stars, or high-voltage equipment. Most radiation occurs naturally, but some is produced by human activities.

VA has produced a comprehensive VHI specifically on radiation, which can be accessed at: http://www.va.gov/vhi.

How can Humans be exposed? — Radiation Exposure versus Contamination

A key distinction in considering human exposure to radiation is the difference between ***radiation exposure*** compared to ***radioactive contamination.*** The victim of a radiological incident may be internally or externally contaminated. Thus, an individual who encounters an external source of radiation will experience radiation ***exposure,*** which would cease the moment they removed themselves from the presence of the source. On the other hand, an individual who becomes physically ***contaminated*** with radioactive materials will have retained radioactive material in or on their body. In that case, the radioactive material may become internalized and exposure may continue for a long period of time.

For example, if a person were near an exploded "dirty bomb," radioactive material could enter their body via ingestion, swallowing, or inhalation of the radioactive material. Thus, although the physical explosion may leave them unharmed, and they might have received no significant external radiation exposure, the victim of such an attack could nevertheless become contaminated with residual radioactive materials. Obviously, such retained radioactive contamination could represent a radioactive exposure hazard to the victim, and possibly also to anyone coming into subsequent contact with that victim, including health care providers. However, the radiation risk to others probably would not be severe and life-threatening injuries should always be treated before a patient is decontaminated.

Internal contamination has three different ways to enter the body:

1. Ingestion
2. Inhalation
3. Direct exposure with entry through the wound

Regardless of entry point, the radioactive contamination may need to be treated. The treatment is discussed in a later portion of this section.

In the case of external exposure to radiation, evaluating the exposure level after the fact can be difficult, since the exposed individual is now ***removed*** from the direct source of radiation. That is, when a person is directly exposed to radiation they do not themselves become radioactive, even if the exposure leads to serious subsequent health consequences including death.

What are the short- and long-term health consequences of radiation exposure?

High exposures to ionizing radiation can cause acute illness or death. The immediate injuries caused by radiation exposure range from mild burns to death. Figure 16 shows radiation burns on the hands of an individual who was exposed to a high level of radioactivity.

There is no way to tell the difference between a radiation burn and a thermal burn, other than through history, e.g., known exposure to a heat. Therefore, health care providers must consider the history when symptoms present as shown in Figure 16.

Figure 16

Following a radiological event including a terrorist attack with a "dirty bomb," casualties may experience different types of radiological exposure including radiation from external sources (Figure 17), external radiological contamination (Figure 18), and internal radiological contamination (Figure 19)(top of the next page). The levels and type of exposure will determine the decontamination and treatment required for the victim.

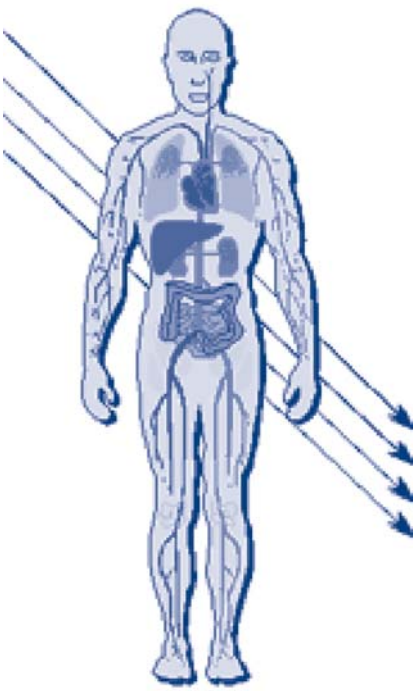


Figure 17

Figure 18

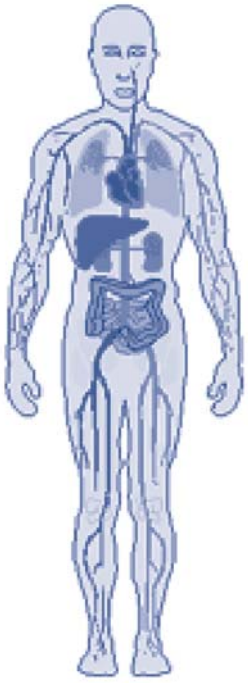


Figure 19

Acute Radiation Syndrome

Figure 20 depicts the levels of exposure, the phases of acute radiation syndrome in a highly exposed victim, and the potential damage. Figure 21 lists conventional units of measurement for radiation.

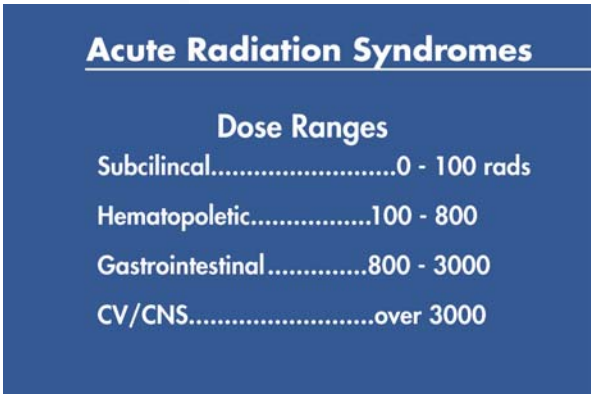


Figure 20

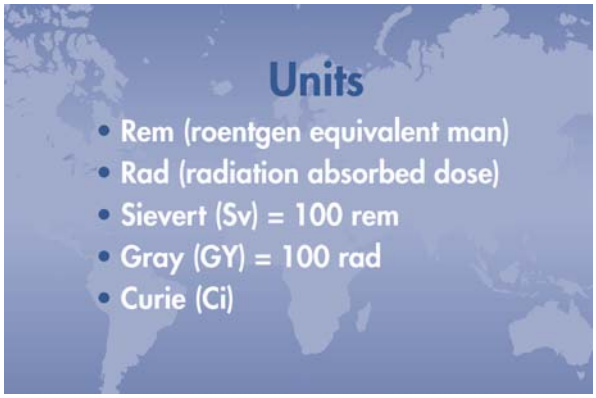


Figure 21

For example, if a casualty received a radiation exposure of 200 or 300 rads (2 to 3 Grays), then they would suffer the ***hematological phase*** of radiation syndrome. That is, 30 days following the exposure, white cells would fall to very dangerous levels. Such a case would then certainly experience infection, and could have bleeding disorders. If such victims were admitted to a VA medical center, then all of these radiation symptoms might be expected to be observed.

Long-Term Health Effects of Ionizing Radiation

Most information about the health effects to humans from ionizing radiation has been obtained by studying Japanese atomic bomb survivors and their offspring.

The principal long-term health concern is an increased risk for the development of malignancies. The risk for almost all types of malignancies has been shown to be increased by radiation exposure, although radiation is not as strong a carcinogen as is commonly feared. The risk increases with the radiation dose received and also may be influenced by other factors such as age at exposure and time since exposure.

Studies of Japanese survivors' children conceived after the atomic bombing of Hiroshima and Nagasaki have not found increases in birth defects or childhood cancers.

Several epidemiological studies of U.S. atmospheric nuclear weapons test participants have been performed, some of which have found increases in mortality. The VHI module "Veterans and Radiation" provides more information about these studies. No studies specifically limited to Atomic Veterans who participated in research projects are available.

Any radiation exposure level might in principle lead to cancer after a latency of years or even decades. In general, it usually is difficult or impossible to determine with certainty if a particular cancer in an individual is the result of a specific radiation exposure incident, although the likelihood often can be estimated based on epidemiological and other relevant data. Thus, according to the National Toxicology Program, the probability that a U.S. citizen will develop cancer in their lifetime is 30 percent to 50 percent.

> "The probability of developing cancer depends on many things, including the intensity, route, and duration of exposure to a carcinogen or carcinogens. Individuals may respond differently to similar exposures, depending on personal factors such as age, sex, nutritional status, overall health, and inherited characteristics. Only in a few instances, where studies of long-term human exposures and cancer incidence in restricted environments are available, can risk be estimated with confidence."

VA Medical Programs for Atomic Veterans

Atomic Veterans, including those who participated in research associated with nuclear tests described in Part One of this VHI, are eligible to participate in the VA's Ionizing Radiation Registry (IRR) Examination program. These veterans have special eligibility for treatment of conditions that the VA recognizes as possibly due to radiation. They also can receive compensation on a "presumptive" basis for 21 types of malignancies.

The presumptive malignancies include:

1. Cancer of the bile ducts
2. Cancer of the bone
3. Cancer of the brain
4. Cancer of the breast
5. Cancer of the colon
6. Cancer of the esophagus
7. Cancer of the gall bladder
8. Cancer of the small intestine
9. All forms of leukemia except chronic lymphocytic leukemia
10. Primary liver cancer
11. Cancer of the lung
12. Lymphomas (except Hodgkin's disease)
13. Multiple myeloma
14. Cancer of the ovary
14. Cancer of the pancreas
16. Cancer of the pharynx
17. Cancer of the salivary gland
18. Cancer of the stomach
19. Cancer of the thyroid
20. Cancer of the urinary tract (kidneys, renal pelvis, ureter, urinary bladder and urethra)
21. Bronchio-alveolar carcinoma (a rare lung cancer)

Additional Information

The VHI "Veterans and Radiation" may be obtained from the VAMC library or accessed from the Internet at http://www.va.gov/vhi.

The VHI also provides further informationon compensation eligibility rules and presumptive service-connection for veterans exposed to radiation.

Special Concerns for VAMC Health Care Providers

The most important thing clinicians should be aware of concerning radiological weapons or "dirty bombs" is that they are in principle easier to deal with than chemical or biological weapons because the radioactive contamination is so much easier to detect. Although potential radiation can be a source of tremendous concerns for victims, in some ways it is easier to deal with than chemical or biological contaminations because it may be measured more readily. Every VAMC should have radiation detection equipment and staff trained to evaluate casualties with possible external contamination, and the capability to provide appropriate decontamination.

Radiological Decontamination

The key to decontaminating an individual who has ***external*** radiological contamination is removal of the clothing followed by thorough washing of their body. These simple steps will remove 95 percent of the external contamination.

Following a radiological incident, casualties may present to the VA within minutes, hours, or days following their initial exposure. Their level of contamination may initially be unknown. This means that VA medical personnel will need to be aware of the decontamination and care that the victim has already received, if any. Ideally, any casualty seen at VA, whether veteran or civilian, has been decontaminated and treated for all of their acute injuries, and any kind of radiological injury. As in any emergency medical situation, the important thing is to take care of any life-threatening emergency first and worry about radiological effects second.

However, after being stabilized, if the victim still has small amounts of embedded material inside a surgical wound, which is now being dressed or closed, the patient may have to be returned to the operating room. A surgeon, a nuclear medical physician, and a health physicist (who will be there with a meter to measure the radioactivity, while the surgeon debrides the wound), will determine if the radioactive material has been removed. Such a scenario for a veteran patient recovering from a wound involving a radioisotope is a possibility at a VAMC.

Another more immediate special treatment situation that could occur in the aftermath of a terrorist attack with a radiological weapon might be if a victim ingested or inhaled a radioisotope. For example, radioisotopes that could be present following an attack with a “dirty bomb” could include radioactive forms of cesium or iodine. There are a number of methods available to speed the elimination of specific radioisotopes in the event they are retained in the body. The publication “NCRP Report Number 65” lists all isotopes and how to treat a victim who has ingested or inhaled them. For example, radioactive cesium that is ingested (not inhaled) can be treated with the agent Prussian Blue, an oral medication. Prussian Blue is not commercially available without calling Oak Ridge Reactor Facility in Oak Ridge, TN. Similarly, potassium iodine as an oral medication can be used to block uptake by the thyroid of radioactive forms of iodine.

It is critical to note that these approaches, blocking uptake following exposure to specific radioisotopes, must be done at or shortly after the time of exposure if they are to be effective.

Depleted Uranium (DU) – What Is It?

DU is a relatively recent radiological exposure concern for U.S. military veterans. DU is the residual portion of natural uranium that remains after some of the more fissionable uranium isotope is extracted for use in power plants and weapons. DU was first used in the Gulf War in 1991. It was used in armor penetrating munitions because of its high density and superior mechanical properties. DU contains about half of the radioactivity of natural uranium, and is a very low-level radioactive material. Heavy metal toxicity is a concern for individuals internally exposed to DU, especially potential toxicity to the kidneys and other organs.

How can humans be exposed to DU?

During the 1991 and 2003 Gulf Wars, U.S. troops were exposed to DU in several ways. A few were injured by "friendly fire" incidents. A greater number were crewmembers that were in relatively close contact with DU munitions in tanks or other vehicles. U.S. soldiers also may have been exposed to smoke or particulate containing DU while fighting an ammunition fire at Doha Depot during the Gulf War in 1991, or by entering or salvaging vehicles or bunkers that were hit by DU projectiles. During the Gulf War in 2003, some U.S. service members were also injured by DU munitions in "friendly fire" incidents. DU armor penetrating munitions were also used during the deployments to Bosnia and Kosovo. In fact, it seems likely that DU munitions and armor will be used in many future combat missions.

How can DU affect health?

Information on the possible health effects of DU exposure in military settings is limited. However, health effects from DU are presumably similar or identical to health effects from natural undepleted uranium. A significant amount of information about possible effects on humans from uranium exposure is available from occupational studies of uranium miners and millers and other uranium-associated occupations. The mode of exposure in those studies may not be in all ways comparable to wartime exposures with DU munitions. For example, uranium miners were exposed to radon gas and other toxic substances present in mines. Further, miners were exposed primarily via respiratory and dermal contact; friendly-fire survivors often have DU metal shrapnel embedding in their bodies. Other significant differences relate to the length and intensity of exposures; miners were typically exposed over years while veterans who were exposed only to DU typically had exposures lasting minutes to hours.

Studies of miners suggest that uranium can affect the kidneys and the respiratory system. Long-term exposure to uranium is thought to affect the kidneys and long-term inhalation of uranium (in the form of uranium oxide particles found in mines) may cause lung problems. Uranium miners who inhaled uranium dust for extended periods showed increased risks of lung cancer. However, exposure to radon accounts for virtually all of that increase in lung cancer risk. Animal studies have not conclusively demonstrated that natural uranium causes lung cancer in animals. The Baltimore VAMC has a program to monitor the health of Gulf War veterans with retained DU shrapnel. Currently, no clinically important health effects have been identified. However, this group is being followed by the Baltimore DU program, and surveillance of these veterans is continuing.

Is there a test to verify DU exposure?

VA has established a DU screening program for Gulf War veterans who are concerned about the possible long-term health effects of DU exposure. Gulf

War veterans who are concerned about potential DU exposure are invited to contact the Gulf War Health Registry Coordinator at their nearest VAMC. Interested veterans may request a DU protocol examination that includes:

1. a complete Gulf War Registry examination (if not already done);
2. a DU exposure questionnaire; and
3. if needed, a 24-hour urine collection for total uranium.

The 24-hour urine test measures total uranium, not DU specifically. However, this urine test would include any DU that is present. It is important to note that any possible health effects are due to total uranium concentration, not DU alone.

As noted previously, uranium is a naturally occurring element. Uranium occurs at some background level in the entire environment, and can be detected in pretty much all of the food and water we consume. Therefore, a certain background concentration of uranium is to be expected in urine. The amount expected would depend on how much uranium is consumed in the daily diet. At present, there is no valid technology that is sensitive enough to accurately measure DU in a urine sample where the total uranium is low enough to be considered "normal." (Normal means that the amount of uranium would be expected based on food and water consumption.) If an individual's sample falls above the normal limits, isotopic analysis can be performed to specifically determine the amount of DU as distinct from the "un-depleted" natural uranium that is present.

Baltimore DU Follow-Up Program

In 1993, the VA established the Depleted Uranium (DU) Follow-up Program at the Baltimore VAMC.

The clinical surveillance program was designed for:

- identifying;
- characterizing; and
- following individuals exposed to DU during the Gulf War in 1991.

The goal of the follow-up project is to – **"provide an on-going clinical surveillance of Gulf War veterans who have known or suspected imbedded DU fragments, DU contaminated wounds, or significant amounts of inhaled DU".**

The clinical surveillance is designed to:

1. detect the health effects, if any, of DU containing shrapnel or inhalation exposure; and
2. to provide recommendations for treatment to participating veterans and the physicians caring for them.

The Baltimore medical surveillance and follow-up program is also involved in the coordination and distribution of urine analysis materials for the DU screening program. The staff assists with processing specimens, coordinating specialized tests and analysis, and reporting results to patients, physicians, and the Gulf War database.

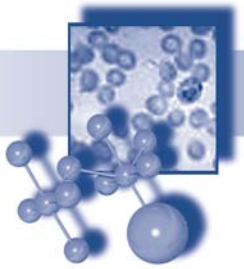
Most of the people participating in the DU follow-up program were exposed to DU when their U.S. Army vehicle was struck by DU-containing munitions. Veterans of friendly-fire incidents during both Gulf Wars are being invited to participate in the scheduled clinical evaluations as their exposure histories and current locations are confirmed.

In addition to helping individual veterans, the information gained through the DU screening and medical follow-up programs will improve our understanding of the potential health effects of DU and expand our knowledge about fragment removal, uranium absorption and distribution, and how uranium is eliminated from the body. Program officials hope that the program will also improve methods of the evaluation of uranium dose and the detection of health effects.

The evaluation of the toxicological and radiological effects of DU are intended to improve the scientific basis for providing advice about:

1. fragment removal;
2. understanding uranium absorption in the body;
3. uranium distribution in human tissue; and
4. how uranium is excreted.

Improved methods to assess uranium dose in humans may also result from these efforts. In addition, the DU program hopes to improve ways to detect toxic effects from low dose uranium exposure.



VA Programs to Prepare for Casualties from Attacks with Chemical, Biological, and Radiological (CBR) Weapons

Introduction

In the aftermath of the 9/11/2001 terrorist attacks, VA has taken a number of important steps to increase emergency preparedness and capabilities to respond to domestic attacks with weapons of mass destruction (WMD). VA has always had a responsibility to provide local and national assistance during all types of emergencies. Following the 9/11/2001 attack, VA has augmented these existing programs to be better prepared to respond specifically to emergencies due to terrorist attacks.

This section covers some basic information about new VA programs for:

1. emergency mass-casualty decontamination at VAMCs;
2. the emergency VA pharmaceutical caches;
3. existing VA emergency programs; and
4. materials designed specifically to inform VA staff about steps they can take to protect themselves, their fellow workers, and their families in the event of a terrorist attack.

All VA health care provides should be aware of these programs, and specifically, of the status of these programs at the facility where they work. They are all designed to protect and save lives, but for them to function as we want requires that VA staff be aware of the programs, and of their role in them.

VA Medical Center Emergency Mass-Casualty Decontamination Initiative

All U.S. citizens are concerned about the potential threat of a terrorist event in their community involving WMD. Such an event could produce an overwhelming number of casualties, and all nearby hospitals including VAMCs are likely to be called upon to help manage both physical and psychological victims. The ability to provide effective hospital decontamination in the event of such a mass-casualty incident is essential for continuation of operations of VHA facilities, including:

1. providing services to veterans in the community in the event of terrorist attack in the area;
2. protect VAMC staff and patients; and
3. protect capital infrastructure.

The VHA emergency mass-casualty decontamination initiative, begun in 2002, is intended to help VAMCs in competently responding to possible terrorist event that involves chemical, biological, or radiological weapons in their community. Taking these steps is seen as a basic requirement for maintaining VHA medical operation in the event of a terrorist emergency. As stated by VA Under Secretary for Health Dr. Robert Roswell,

> "following the 9/11 terrorist attacks, an effective hospital decontamination program has become a part of the cost of doing business for VHA."

The main two goals of the emergency mass-casualty decontamination initiative are:

1. to protect medical center facilities, staff, and patients; and
2. to provide necessary care to self-referring casualties in the event that local acute care facilities become overwhelmed following the attack in their community.

The initiative began in 2002 with an internal review process that identified 78 VAMCs with the greatest vulnerabilities. During 2003, staff from these facilities are being provided with a one-week decontamination-training course at one of VA's two decon training centers at the Bay Pines, FL and Little Rock, AR VAMCs. The plan is to continue implementing this program at remaining VAMCs when this initial phase is completed.

A critical part of the overall program was the in-house development of high quality training for the VA staff who will be responsible for conducting emergency mass-casualty decontamination activities at their medical center. Fortunately, VA had already established significant recognized expertise in such training at the Bay Pines and Little Rock VAMCs. With the assistance of VA's Employee Education System and other experts, VA has established a unified national decontamination-training center at these two facilities; a truly unique program and national asset. The Bay Pines and Little Rock decontamination training centers will meet both initial and ongoing medical center decontamination staff training requirements.

Following basic training, these medical centers are being provided with high-quality portable decontamination shelter/shower systems, and personal protective equipment required to complete the emergency mass-casualty decontamination program at their facility.

Finally, each facility will be required to conduct regular training and drilling exercises, and to report on the success of these exercises to Veterans Health Administration Central Office. Drilling and reporting are critical; VA must be able to publicly certify that our emergency capabilities are truly functional.

VA Pharmaceutical Cache Program

The VA Emergency Pharmacy Service in VA's Pharmacy Benefits Management Strategic Healthcare Group developed and maintains VA's emergency stockpile of critical medical supplies and equipment, known as "pharmaceutical caches."

These caches were established by the May 2002 VHA Directive 2002-026, "Pharmaceutical Caches in a Weapons of Mass Destruction Event." The Directive establishes policies for the configuration, maintenance, and deployment of pharmaceutical caches to be used in response to a potential terrorist attack with chemical, biological, or radiological agents/weapons. These caches are put in place at VAMCs to be ready to treat VA staff and other individuals seeking treatment at a VA facility in the aftermath of a domestic terrorist event.

The regular pharmaceutical inventory at each medical center is, of course, always available. In the event of a terrorist attack with chemical, biological, or radiological agents/weapons, VA's "just-in-time" inventory management system for equipment and pharmaceuticals could be overwhelmed. The pharmaceutical caches were developed:

1. to provide necessary pharmaceuticals and equipment;
2. to fill the gap between conventional hospital inventories; and
3. for potential emergency requirements.

Their availability will help to ensure the short-term preservation of the VA health care infrastructure until other resources can be brought in, and to support the medical center's involvement in the local community disaster plan.

There are two basic forms of pharmaceutical caches:

1. small caches intended for treating 1,000 casualties for two days; and
2. large caches for treating 2,000 casualties over two days.

Stocks will be maintained by regular rotation with existing hospital pharmacy stocks, replacing older products in cache with new ones. As of July 2003, there were 108 VA internal caches deployed and 143 caches scheduled for deployment.

References and additional reading on the Cache Program

http://www.usamriid.army.mil

http://www.ncrp.com/rpt65.html (NCRP Report #65)

http://www.va.gov/emshg

VA's Emergency Management Strategic Healthcare Group (EMSHG)

VA's Emergency Management Strategic Healthcare Group (EMSHG) has responsibility for the management, coordination, and implementation of the emergency management mission for VHA within the VA, as defined through relevant federal laws and regulations.

EMSHG provides:

1. comprehensive emergency management services to VA;
2. coordinates medical back up to DoD; and
3. assists the public via the National Disaster Medical System and the National Response Plan.

In addition to out-based headquarters staff, EMSHG has field staff that includes:

- District Managers;
- Area Emergency Managers; and
- Management Assistants located at offices throughout the Nation.

Collectively, these activities support the VA strategic goal to ***contribute to the public health and socioeconomic well being of the Nation and the VHA strategic goal to build healthy communities.*** More information about this program is available at: http://www.va.gov/emshg.

EMSHG Program Responsibilities

EMSHG and its national network of Area Emergency Managers coordinate VHA's role in a wide range of emergency management activities that include key interactions with other federal agencies at the regional and local levels.

VA/DoD Contingency Hospital System

EMSHG develops national plans and training programs to ensure back-up support to DoD of Defense medical systems during war or national emergency.

VA Contingencies

EMSHG provides guidance and consultation to VISNs to ensure that all VAMCs develop a comprehensive emergency management program with an all-hazards focus to include weapons of mass destruction.

National Disaster Medical System (NDMS)

EMSHG supports Federal Coordinating Center functions at designated VAMCs. EMSHG develops and coordinates national plans to assist in the implementation of the NDMS's support to state and local medical resources in the event of major domestic disasters, or the DoD medical care system when needed during military contingencies.

Federal Response Plan (Public Law 93-288)

EMSHG takes appropriate actions related to mitigation, preparedness, response, and recovery strategies for disaster threats. EMSHG coordinates VHA's participation in federal disaster response as specified in the provisions of the National Response Plan.

Continuity of Government

EMSHG executes assigned actions for VHA in support of the continuity of government plan in addition to responsibilities related to maintenance of specific sites.

Federal Radiological Emergency Response Plan

EMSHG provides response capability to supplement other federal, state, and local government efforts in response to accidents at fixed nuclear facilities or during transportation of radioactive materials. **The FRERP will soon be absorbed under the NRP**.

EMSHG also assists VA in responding to requests through the National Response Plan to support individual states and communities in times of emergency with:

1. Providing direct medical care to victims of disasters.
2. Augmenting staff of community hospitals, nursing homes, and other medical treatment facilities.
3. Providing stress counseling to disaster victims and responders.
4. Furnishing critically needed supplies, pharmaceuticals, equipment, facilities, and other resources.
5. Supporting both the national and VA caches for providing pharmaceuticals for use to treat casualties in a national or local emergency, including coordination with DHS (Strategic National Stockpile and National Medical Response Team) pharmacy caches.

VA Guides on Personal Preparedness for a Terrorist Attack

In addition to the programs developed to better prepare VA to respond to domestic terrorist attacks described earlier, VA has also prepared materials to inform and prepare VA employees on how to better protect themselves, their fellow workers and their families. These materials are primarily brochures available in hard copies, as well as being available on the Web at: http://www.vethealth.cio.med.va.gov/Pubs/Index.htm

The available brochures include:

"You can prepare for disasters"

Information on preparing for disasters.

- Some basic items to purchase or have on hand over a 4-month schedule
- Preparedness activities you may want to take

"Decontamination in Washington, DC for Chemical, Biological and Nuclear Agents" (May 2002)

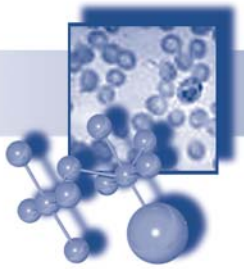
Provides directions to emergency decontamination facilities located near VA Central Office in Washington, DC, in the event VA employees are potentially exposed to toxic agents.

"Employee Awareness of the Potential Hazards of Weapons of Mass Destruction"

Provides a general introduction and basic awareness on hazardous biological, chemical, and nuclear materials for VA employees.

"Personal Emergency Preparedness"

Intended to raise awareness of VA employees and their families of the need to plan for potential incidents and enhance their capacity to effectively manage potential risks to their environments.



References

A fifty-year mortality follow-up study of veterans exposed to low-level chemical warfare agent, mustard gas. Bullman, T, Kang, H Ann. Epidemiol 2000;10:333-338.

Advisory Committee on Human Radiation Experiments (ACHRE), October 1995. U.S. Government Printing Office; Pittsburgh, PA.

Amon, SS; Schechter, R; Inglesby, TV; et al., for the Working Group on Civilian Biodefense. Botulinum toxin as a biological weapon. *JAMA*. 2001;285:1059-1070.

Borio, L; Inglesby, T; Peters, CJ; Schamaljohn, AL; et al., for the Working Group on Civilian Biodefense. Hemorrhagic Fever Viruses as a biological weapon. *JAMA* 2002;287:2391-2305.

Brown, MA; & Brix, KA, 1998. Review of health consequences from high-, intermediate-, and low-level exposure to organophosphorus nerve agents. Journ. Applied Toxicol, 18(6), 393-408.

Buchanan, A. Judging the past: The case of the human radiation experiments, *Hastings Center Report* 26, no. 3 (1996): 25-30.

Chin, J. Editor, Control of Communicable Diseases Manual, 17th Edition, APHA, Washington DC, 2000.

Crigger, BJ. Yes, they knew better (invited editorial), *Bulletin of the Atomic Sciences* 50(2) (1994): 29.

Dennis, DT; Inglesby, TV; Henderson, DA; et al., for the Working Group on Civilian Biodefense. Tularemia as a biological weapon. *JAMA*. 2001; 285:2763-2773.

Department of Defense. Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research. Directive No. 3216.2, March 25, 2002.

Gulf War and Health, Volume 1, Depleted Uranium, Sarin, Pyridostigmine Bromide, Vaccines, Institute of Medicine, National Academy of Sciences, 2000.

Health Consequences of Service During the Persian Gulf War: Recommendations for Research and Information Systems. Committee to Review the Health Consequences of Service During the Persian Gulf War, Medical Follow-Up Agency, Institute of Medicine, National Academy Press, Washington, DC, 1996, 193 pp.

Henderson, DA; Inglesby, TV; Bartlett, JG; et al., for the Working Group on Civilian Biodefense. Smallpox as a biological weapon. *JAMA*. 1999; 281:2127-2137.

Howe, EG; & Martin, ED. Treating the troops, Hastings Center Report, 21 (2) (1991): 21-24. Commentary by Annas, GJ; & Grodin, MA, pp. 24-27; and Commentary by Levine, RJ. pp. 27-28.

Inglesby, TV; Dennis, DT; Henderson, DA; et al., for the Working Group on Civilian Biodefense. Plague as a biological weapon. *JAMA*. 2000; 283:2281-2290.

Inglesby, TV; Henderson, DA; Bartlett, JG; et al., for the Working Group on Civilian Biodefense. Anthrax as a biological weapon. *JAMA*. 1999; 281:1735-1745.

Inglesby, et al. JAMA, May 1, 2002.

Kadivar, H; and Adams, SC, "Treatment of Chemical and Biological Warfare Injuries: Insights.

Derived from the 1984 Iraqi Attack on Majoon Island, *"Military Medicine* 156:171-172, 1991.

Long-term health effects of exposure to sarin and other anticholinesterase chemical warfare agents. Page, WF. Military Medicine, 2003;168:239-245.

Makhijani, Arjun. Energy enters guilty plea, *Bulletin of the Atomic Sciences* 50(2) (1994): 18-29.

Minton, NA; and Murray, VSG. A Review of Organophosphate Poisoning. Med. Toxicol. 3; 350-375, 1988.

Ohbu, S; Yamashina, A; Takasu, N; Yamaguchi, T; Murai, T; Nakano, K; Matsui, Y; Mikami, R; Sakurai, K; and Hinohara, S. Sarin Poisoning on Tokyo Subway. South. Med. J. 90, June 1997.

Okumura, T; Takasu, N; Ishimatsu, S; Miyanoki, S; Kumada, K; Tanaka, K; and Hinohara, S. Report on 640 victims of the Tokyo Subway Sarin Attack. Ann. Emerg. Med., 28; 129-136, 1996.

Possible Long-Term Health Effects of Short-Term Exposure to Chemical Agents, Vol. 1, Anticholinesterases, and Anticholinergics. Committee on Toxicology, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy Press, Washington, DC, 1982, 290 pp.

Possible Long-Term Health Effects of Short-Term Exposure to Chemical Agents, Vol. 2, Cholinesterase Reactivators, Psychochemicals, and Irritants and Vesicants. Committee on Toxicology, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy Press, Washington, DC 1984, 333 pp.

Possible Long-Term Health Effects of Short-Term Exposure to Chemical Agents, Vol. 3. Final Report: Current Health Status of Test Subjects. Committee on Toxicology, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy Press, Washington, DC, 1985,102 pp.

Presidential Advisory Committee on Gulf War Veterans Illnesses, Final Report. Washington, DC: U.S. Government Printing Office, December 1996, 174 pp.

Principles and Practice of Infectious Diseases, ed, Mandell, GL; Bennett JE; and Dolin, R; eds, 2000.

Report of the Defense Science Board Task Force on Persian Gulf War Health Effects, June 1994. Office of the Under Secretary of Defense for Acquisition and Technology, Washington, DC, 67 pp.

Savage, EP; Keefe, TJ; Mounce, LM; Heaton, RK; Lewis, JA; and Burcar, PJ. Chronic neurologic sequelae of acute organophosphate poisoning. Arch. Environ Health, 43; 38-45, 1988.

Schnurr, PP; Ford, JD; Friedman, MJ; Green, BL; Dain, BJ; and Sengupta, A. Predictors and outcomes of posttraumatic stress disorder in World War II veterans exposed to mustard gas. J Consult Clin Psychol 2000 Apr;68(2):258-68.

Schnurr, PP; Friedman, MJ; and Green, BL. Post-traumatic stress disorder among World War II mustard gas test participants, Mil Med 1996 Mar;161(3):131-6.

Technical Report, "Modeling and Risk Characterization of US Demolition Operations at the Khamisiyah Pit," April 16, 2002, Office of the Special Assistant for Gulf War Illnesses, U.S. Department of Defense. Available at: http://www.gulflink.osd.mil/khamisiyah_tech.

"The Front Lines of Biowarfare," by David Snyder. The Washington Post, May 6, 2003, page B03.

The Persian Gulf Experience and Health, National Institutes of Health Technology Assessment Workshop Statement, April 27-29, 1994, 28 pp.

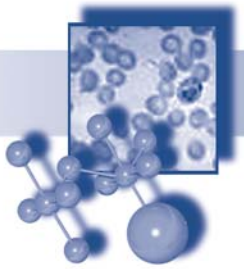
Toxicologic Assessment of the Army's Zinc Cadmium Sulfide Dispersion Tests, Commission on Life Sciences, Subcommittee on Zinc Cadmium Sulfide, National Research Council, 1997. 380 pp.

"US Demolition Operations at Khamisiyah," Case Narrative, Final Report, April 16, 2002. Office of the Special Assistant for Gulf War Illnesses: U.S. Department of Defense. Available at: http://www.gulflink.osd.mil/khamisiyah_iii.

Veterans at Risk: Health Effects of Mustard Gas and Lewisite. Committee to Survey the Health Effects of Mustard Gas and Lewisite, National Academy of Sciences, Institute of Medicine, National Academy Press, Washington, DC, 1993, 427 pp.

Veterans at Risk: Health Effects of Mustard Gas and Lewisite. National Academy of Sciences, Institute of Medicine, National Academy Press, Washington, DC, 1993, 427 pp.

Veterans Health Administration. "Requirements for the Protection of Human Subjects." Ch 9, in Manual M-3, Part I, Research and Development in Medicine, Oct. 30, 1992.



Additional Readings

1. Gulf War and Health: Volume 2. Insecticides and Solvents, Institute of Medicine, National Academy Press, Washington, DC, 2003, 650 pp (approximate).

2. Health Consequences of Service During the Persian Gulf War: Recommendations for Research and Information Systems. Committee to Review the Health Consequences of Service During the Persian Gulf War, Medical Follow-Up Agency, Institute of Medicine, National Academy Press, Washington, DC, 1996, 193 pp.

3. Medical and toxicology texts may be consulted for more information on the agents; however, the following summarize the currently accepted information on the risks of exposure for selected agents:

   Mitretek Systems Web site: http://www.mitretek.org/mission/envene/biological/agents/rickettsia.htm.

   University of Maryland School of Medicine Web site: http://www.umm.drkoop.com/conditions/ency/article/001337.htm.

   Colorado State University, Environmental Health Services Web site: http://www.chemdat1.ehs.colostate.edu/LARmanual/tular.htm.

   The Columbia Encyclopedia, 6th ed., New York: Columbia University Press, 2001, Web site: http://www.bartleby.com/65.

4. Presidential Advisory Committee on Gulf War Veterans Illnesses, Final Report. Washington, DC: U.S. Government Printing Office, December 1996, 174 pp.

5. Report of the Defense Science Board Task Force on Persian Gulf War Health Effects, June 1994. Office of the Under Secretary of Defense for Acquisition and Technology, Washington, DC, 67 pp.

6. The Persian Gulf Experience and Health, National Institutes of Health Technology Assessment Workshop Statement, April 27-29, 1994, 28 pp.

12 CME Exam

1. The Khamisiyah ammunition depot was found to contain which of the following chemical agents, following it's demolition by U.S. forces after the Gulf War cease-fire?

    a. Sarin and Mustard agent

    b. Sarin and Soman

    c. Soman and VX

    d. Sarin, Cyclosarin and Mustard agent

2. Which of the following agents is a likely carcinogen?

    a. Cyclosarin

    b. Mustard agent

    c. Soman

    d. VX

3. Which of the following is **NOT** considered to be a life-threatening symptom of chemical agents?

    a. Abdominal cramps

    b. Diarrhea

    c. Miosis

    d. Vomiting

4. Which of the following pesticides was removed by the EPA for home use in June 2000 because of acute toxicity concerns?

    a. Baygon (Propoxur)

    b. Cutters®

    c. Dursban® (Chlorpyrifos)

    d. Vapona

5. Which of the following is **NOT** a measurable deficiency following acute poisoning by an organophosphorus pesticide?

    a. Intellectual functioning

    b. Academic skills

    c. Simple motor skills

    d. Respiratory function

6. Which pesticide type causes reversible inhibition of the enzyme AChE?

    a. Methyl Carbamate

    b. Organochlorine

    c. Organophosphorus

    d. Pyrethroids

7. Which Biological Warfare Agent category has agents that have catastrophic potential?

    a. Category A

    b. Category B

    c. Category C

    d. Category D

8. Which Biological Warfare agent was used in the attacks in the U.S. after 9/11/01?

    a. Botulinum toxoid

    b. Anthrax

    c. Tularemia

    d. Smallpox

9. How many days after an individual received 200-300 rads (2-3 grays) of radiation will it take to drop their white cells to a very dangerous level?

    a. 10 days

    b. 20 days

    c. 30 days

    d. 40 days

10. What type of radioactive emissions does Depleted Uranium emit?

    a. Very weak Alpha

    b. Strong Alpha

    c. Beta

    d. Gamma

11. The Emergency Management Strategic Health Group's mission include all of the following, **EXCEPT**:

    a. Education

    b. Emergency Management

    c. Medical Care

    d. Research

12. The Federal Response Plan was established by:

    a. Executive Order 12656

    b. Public Law 93-288

    c. Public Law 97-174

    d. Presidential Executive Order 67

13. Without new federal legislation, authority to provide medical care without requiring copayments regardless if a veteran can prove service-connection will expire ___ year(s) after a veteran returns from a combat zone.

    a. 1 year

    b. 2 years

    c. 3 years

    d. 4 years

14. What year did President Nixon order the ceasing of the offensive biological warfare program?

    a. 1967

    b. 1968

    c. 1969

    d. 1970

15. Which of the following was **NOT** an incapacitating agent used in post-World War II human experiments?

    a. Heroin

    b. LSD

    c. PCP

    d. Tear gas

16. Which of the following is the annual whole-body occupational dose limit of radiation mandated by the U.S. Nuclear Regulatory Commission?

    a. .6 Rem

    b. 3 Rem

    c. 5 Rem

    d. 15 Rem

17. Which of the following reports break their findings down into the following categories: **Causal Relationships; Suggested Causal Relationships;** and **Insufficient Evidence of a Causal Relationship?**

    a. Advisory Committee on Human Radiation Experiments Report 1995

    b. Institute of Medicine, National Academy of Sciences Report 1993

    c. Institute of Medicine, National Academy of Sciences Report 2000

    d. National Research Council Report 1997

18. Which of the following is a **Suggested Causal Relationship** concerning long-term health effects of veterans who were exposed to mustard agents as experiment participants?

    a. Gastrointestinal diseases

    b. Hematologic diseases

    c. Leukemia diseases

    d. Neurological diseases

19. What percentage of veterans who participated in the DoD's mustard gas experiments suffer from full PTSD?

    a. 12%

    b. 22%

    c. 32%

    d. 42%

20. Which of the following is **NOT** a risk or protective factor of full PTSD?

    a. Higher likelihood of health care use than those with no PTSD

    b. Participants were forbidden from disclosing what happened to them

    c. Physical symptoms were **NOT** experienced during the tests

    d. Volunteering