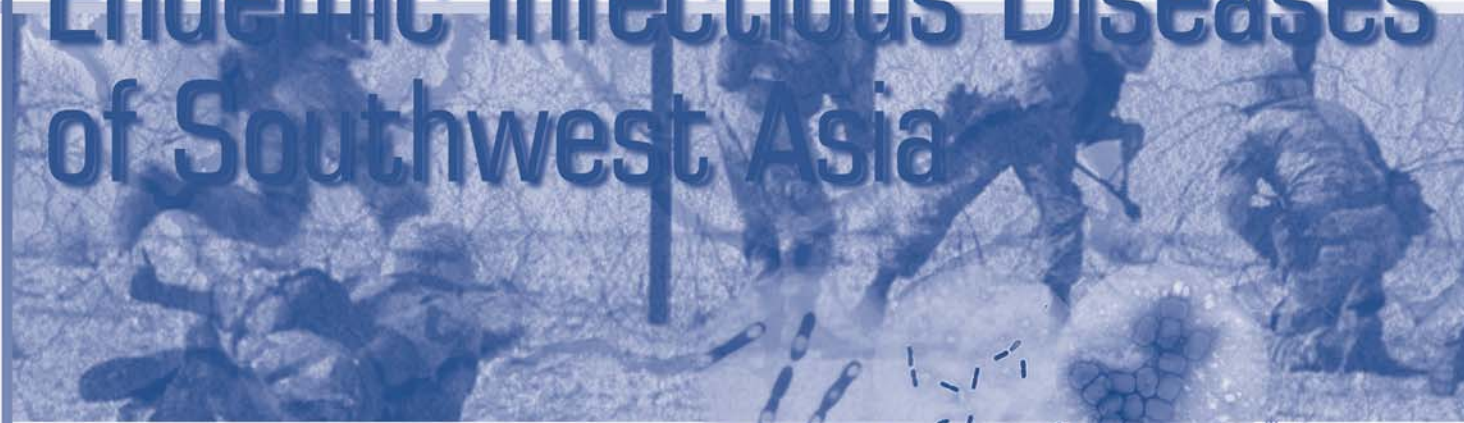




Veterans
Health
Initiative

Endemic Infectious Diseases of Southwest Asia



Independent Study Course Released: October 2003

Sponsored by
Department of Veterans Affairs
Employee Education System

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 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 pleased to present the enclosed Veterans Health Initiative (VHI) independent study guide on the "Endemic Infectious Diseases of Southwest Asia". Many of the Veterans who present to health care providers in the VA have deployed to areas where dangerous and difficult to diagnose diseases are present. This VHI was written by many recognized experts within VA and the Department of Defense (DoD). It has been designed and written for VA and DoD physicians and health care providers.

We need to ensure that our Veterans get the right care, at the right time, in the right place, and at the right cost. It is therefore important that all clinicians be aware of the specific conditions that may confront individuals who have deployed to Southwest Asia, particularly during military conflict in Afghanistan and Iraq. What may appear to be a relatively minor symptom or problem in the person may in fact be a major health care issue, if not a life-threatening problem for the individual. Greater general awareness of the specialized health issues facing persons who may have been exposed to infectious diseases is needed to assure therapeutically appropriate clinical responses.

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 who may have been exposed to infectious diseases during their deployment. This is one way that we can ensure provision of quality health care across the continuum of acute care, rehabilitative care, and extended care. VA sees veterans with infectious diseases in a variety of health care settings, and they are counting on you to provide the best care possible. We owe them nothing less.

A handwritten signature in blue ink, reading "Robert H. Roswell, M.D.", is positioned above the printed name.

Robert H. Roswell, M.D.

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Independent Study Outline

The recent crises in Afghanistan and then Iraq have resulted in an influx into Southwest Asia of Western military personnel, peacekeepers, humanitarian workers, and journalists. At the same time, unprecedented numbers of internally displaced persons and refugees have overwhelmed much of the already fragile infrastructure, setting the stage for outbreaks of infectious diseases among both foreigners and local populations.

Physicians, who travel to Afghanistan and Iraq as part of U.S., Canadian, and other Coalition military forces, or as participants in humanitarian programs, need to be familiar with the epidemiology, diagnosis, and treatment of the endemic infectious diseases of Southwest Asia. Western health care providers will also have to be alert for unusual infections among military personnel and veterans, travelers, relief workers, and others returning from this region.

This Veterans Health Initiative (VHI) provides essential information for health care providers about the infectious disease risks in Southwest Asia, particularly in Afghanistan and Iraq. Emphasis is placed on diseases not typically seen in North America.

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.

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

1. describe background data on Afghanistan and Iraq;
2. identify the endemic infectious diseases of Southwest Asia;
3. identify the infectious diseases of Afghanistan and Iraq of limited military importance;
4. explain the recent outbreak of Norovirus infection in Afghanistan;
5. describe long-term concerns related to endemic infectious diseases in Southwest Asia;
6. describe the historical background of infectious diseases in Afghanistan and Iraq;
7. identify the clinical findings associated with the infectious diseases of Southwest Asia;
8. describe the diagnosis of infectious diseases in Southwest Asia;
9. list the treatment regimens for infectious diseases found in Southwest Asia; and,
10. describe prevention measures effective for infectious diseases in Afghanistan and Iraq.

Purpose

Background

Objectives

Independent Study Outline

Outcome The expected outcomes of this independent study are to improve the quality of health care provided to Veterans and military personnel who served in Southwest Asia, including Afghanistan and Iraq. Drug treatments and dosages provided in this VHI should be double-checked prior to prescribing therapy.

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

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

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:

- Introduction
- Malaria
- Diarrheal Diseases
- Typhoid Fever
- Viral Hepatitis
- Leishmaniasis
- Arboviral Diseases
- Respiratory Diseases
- Tuberculosis
- Rickettsial Type Diseases
- Anthrax
- Leptospirosis
- Sexually Transmitted Diseases
- Plague
- Infectious Diseases of Limited Military Importance
- Recent Outbreaks: Norovirus (Norwalk-Like Virus) Infections
- Long-Term Health Concerns
- Conclusions
- References
- 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, (**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.**) 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.

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:

Bob Smith, EdD, MCP
205-731-1812, Ext. 317; E-mail - bob.smith@lrn.va.gov

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

Program Development

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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

Accreditation Council for Continuing Medical Education (ACCME)

The VA Employee Education System designates this educational activity for a maximum of 3.5 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 3.5 continuing education clock hours for participating in this course.

American Nurses Credentialing Education

VA Employee Education System designates this educational activity for 4.2 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.

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Mark R. Wallace, MD

Antimicrobials..... The newer uses of antimicrobials for treatment has not been approved by the FDA.

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Some Malaria Drugs..... Some of the Malaria drugs have not been approved by the FDA for pharmaceuticals.

Gregory C. Utz, MD

Antimalarials..... The use of antimalarials for the treatment and chemoprophylaxis has not been approved by the FDA.

Patrick Olson, MD, MPH, FACP, FACPM

Multiple medicines..... The use of multiple medicines for treatment has not been approved by the FDA.

AMA and ANCC Continuing Education Credits

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.

Acknowledgement

Much of the material included in this VHI was excerpted from an article published in a peer-reviewed medical journal on June 15, 2002:

“Endemic Infectious Diseases of Afghanistan,”

by Mark R. Wallace, Braden R. Hale, Gregory C. Utz, Patrick E. Olson, Kenneth C. Earhart, Scott A. Thornton, and Kenneth C. Hyams,

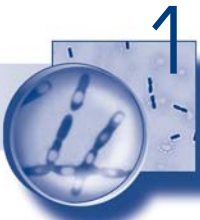
Clinical Infectious Diseases 2002:34 (Suppl 5), pages S171 to S228.

The Editors of this VHI wish to thank the University of Chicago Press for their generous support in the use of this journal article, which was written by U.S. government employees and is therefore in the public domain.

An extensive literature search also was conducted to assess the infectious disease threat for Coalition troops who were deployed to the Arabian Gulf beginning in late 2002 in preparation for “Operation Iraqi Freedom”. This information was included in this study guide to aid in the health care of this cohort of deployed veterans.

Disclaimer

The views expressed in this program do not necessarily reflect the official positions or policies of the VA, DoD, or the U.S. and Canadian government. Drug treatments and dosages provided in this study guide should be double-checked prior to prescribing therapy.



Introduction

The recent crises in Afghanistan and then Iraq have resulted in an influx into Southwest Asia of Western military personnel, peacekeepers, humanitarian workers, and journalists. At the same time, unprecedented numbers of internally displaced persons and refugees have overwhelmed much of the already fragile infrastructure, setting the stage for outbreaks of infectious diseases among both foreigners and local populations.

Physicians, who travel to Afghanistan and Iraq as part of U.S., Canadian, and other Coalition military forces, or as participants in humanitarian programs, will need to be familiar with the epidemiology, diagnosis, and treatment of the endemic infectious diseases of Southwest Asia. Western health care providers will also have to be alert for unusual infections among military personnel and veterans, travelers, relief workers, and others returning from this region.

Over 300,000 U.S. troops were deployed in combat operations in Afghanistan and Iraq from October 2001 to mid-2003. Like all hazardous deployments, some combat veterans will return from Iraq and Afghanistan with deployment-related health problems. Troops are especially at risk for traumatic injuries and infectious diseases. As in all wars, some returning troops will suffer from psychological effects related to surviving a life-threatening experience. Western troops subsequently engaged in hazardous peacekeeping activities in Iraq and Afghanistan will encounter similar health risks as combat troops.

As an indication of these health risks, recent military deployments elsewhere in the developing world have resulted in substantial infectious disease morbidity (1-4). The U.S. humanitarian effort in Somalia (1992–1993) was marked by outbreaks of malaria, dengue, and diarrheal illness; febrile diseases accounted for the majority of field hospital admissions in Somalia. During a later U.S. deployment to Haiti (1994), troops also experienced high rates of febrile illness, at least 30% of which was due to dengue (4). Canada's military experiences were similar, with several cases of malaria following their Somalia deployment. Dengue and malaria were predominant diseases experienced by the troops in Haiti and Honduras. Acute diarrheal disease has also been a common problem among deployed Canadian Forces.

This Veterans Health Initiative (VHI) provides essential information for health care providers about the infectious disease risks in Southwest Asia, particularly in Afghanistan and Iraq. Emphasis is placed on diseases not typically seen in North America. For the purposes of this study guide,

Central Asia refers to the countries of Afghanistan, Turkmenistan, Uzbekistan, Tajikistan, and Kyrgyzstan. South-Central Asia includes the above countries plus Pakistan. Iraq and Kuwait will be considered as part of western Asia.

Afghanistan

Located in South-Central Asia, much of Afghanistan is mountainous, with windswept high desert plains in the north and southwest (Figure 1). The total area of Afghanistan is about the size of Texas (647,500 square kilometers) and supports a population of approximately 26 million. Two decades of war and civil unrest have led to massive infrastructure destruction, resulting in both internal and external population displacements on a vast scale. Infant mortality is high (147 deaths/1000 live births) and life expectancy is short (46 years). Per capita income is estimated at \$800 per year (5).

The public health system has been severely disrupted by recent events, leaving ample opportunity for epidemics of infectious diseases. Available data suggest that the Afghan population is severely affected by infectious diseases, with reports of excess mortality from diarrheal disease (including cholera), respiratory tract infections, and measles (6, 7).

U.S., Canadian, and other Western troops began deploying to Afghanistan on October 7, 2001, in support of "Operation Enduring Freedom". The military troops and civilian humanitarian personnel deployed in and around Afghanistan will be at risk for a variety of infectious diseases. Although foreign workers will have greater access to safe drinking water, clean food, shelter, and appropriate immunizations, the risk for endemic infections are considerable. In the past, infectious diseases have produced major disruptions in both military campaigns and humanitarian efforts. The Soviet military had extraordinary annual attack rates of infectious diseases of 53%–69% during their occupancy of Afghanistan in the 1980's, the majority of which was caused by viral hepatitis, typhoid, dysentery, and respiratory tract infections (8, 9).

Iraq

Iraq is slightly more than twice the size of Idaho (Figure 2). It is located between Iran, Turkey, Syria, Jordan, Saudi Arabia, and Kuwait. The population of Iraq is approximately 24 million.

- 75%-80% is Arab
- 15%-20% Kurdish
- 5% Turkoman, Assyrian, or other

The religious affiliation of the country is mostly Muslim (97%).

- 60%-65% Shi'a
- 32%-37% Sunni
- 3% other

Iraq's climate is primarily desert. Winters are mild to cool, with dry, hot, cloudless summers. Northern mountainous regions along Iranian and Turkish borders experience cold winters with occasionally heavy snows.

Iraq's terrain is mostly broad plains. Reedy marshes are found along the Iranian border in the south and contain large flooded areas. Mountains are present along the borders with Iran and Turkey.

Formerly part of the Ottoman Empire, Iraq became an independent kingdom in 1932. A "republic" was proclaimed in 1958, but in actuality a series of military strongmen have ruled the country since then, the latest being Saddam Hussein. Territorial disputes with Iran led to a costly eight-year war between 1980 and 1988. In August 1990, Iraq seized Kuwait, but was expelled by United Nations (U.N.) Coalition forces during January-February 1991. As a result of Iraq's refusal to comply with U.N. mandates regarding weapons of mass destruction, the U.S. again began deploying troops to the Gulf region in late 2002. Coalition forces subsequently won a decisive victory over Saddam Hussein's regime during April 2003, in "Operation Iraqi Freedom".

Iraq's economy is dominated by the oil sector, which has traditionally provided about 95% of foreign exchange earnings. In the 1980's financial problems caused by massive expenditures in the eight-year war with Iran and damage to oil export facilities by Iran led the government to implement austerity measures. Iraq's seizure of Kuwait in August 1990, subsequent international economic sanctions, and damage from military action by an international Coalition beginning in January 1991, further reduced economic activity.

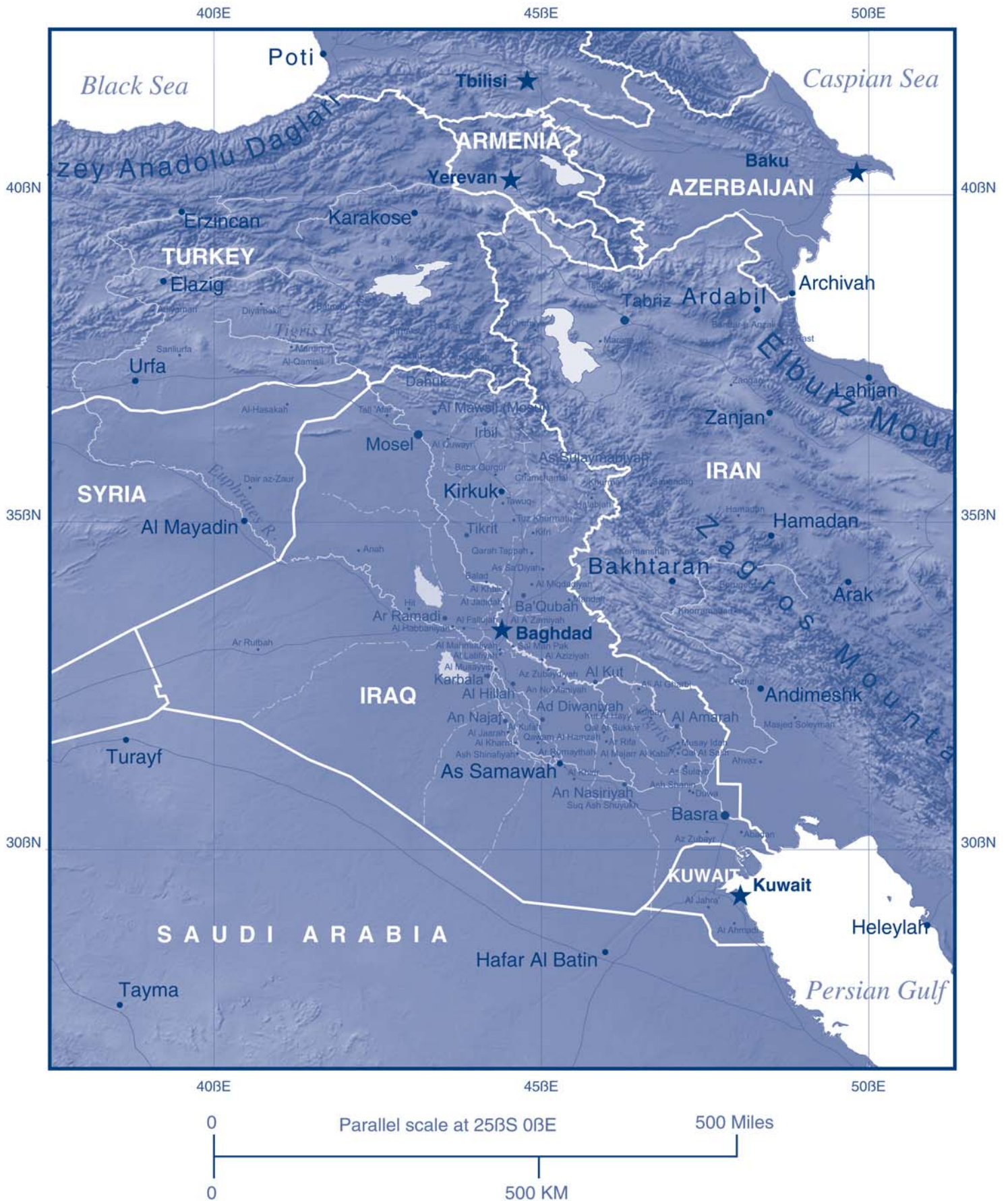
The effects of prolonged sanctions have been evident in almost every aspect of health care, with an exodus of health care professionals, loss of Iraqi hospital access to foreign journals, textbooks, and the Internet, and embargo restrictions on some essential medicines (10, 11). At the same time, communicable diseases have become a major cause of morbidity and mortality in the local population, particularly due to acute lower respiratory infection, diarrheal diseases, and measles (12).

Historically, infectious diseases also have been a major cause of morbidity among visitors to this region (13). Based in part upon U.S. experience with infectious diseases among Allied troops sent to Iraq in World War II, troops recently deployed to Iraq as part of "Operation Iraqi Freedom" may be at increased risk of sand fly fever, malaria, diarrheal diseases, typhoid fever, amoebic dysentery, giardiasis, viral hepatitis, and leishmaniasis (14).

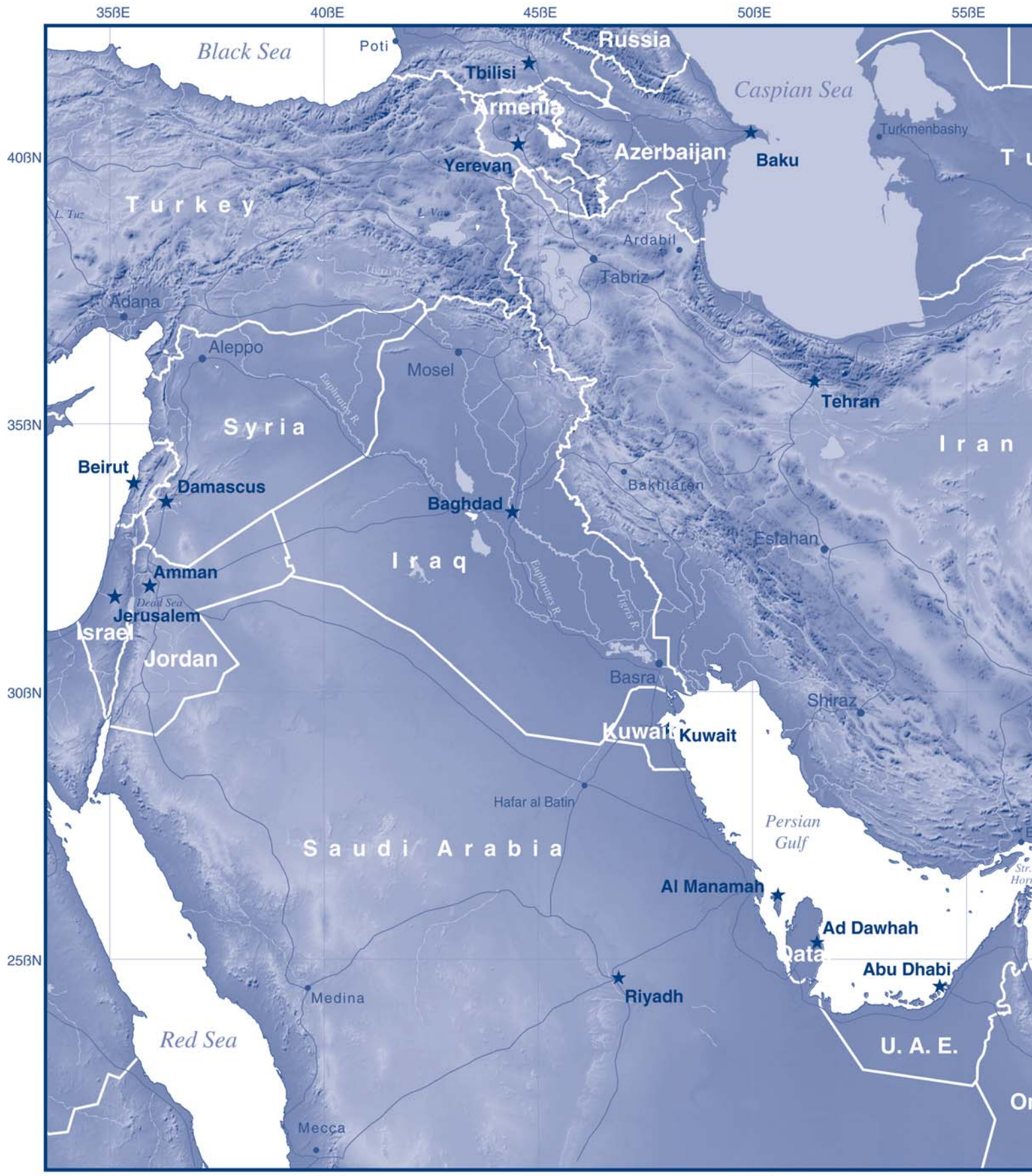
During the Gulf War in 1991, infectious diseases also were a concern for Coalition troops, which included 700,000 U.S., 45,000 British, and 5,000 Canadian military personnel (15). However, effective preventive medicine efforts, plus fortuitous weather, and geographic factors, kept infection rates among troops extremely low (16). Nearly all-infectious disease problems involved common traveler's type diarrhea and acute upper respiratory infections, which are frequent during crowded troop movements. There was only one known death among U.S. troops due to infection, meningococcal meningitis (17). Despite the paucity of infectious diseases during the Gulf War, there has been more than a decade of debate regarding the existence of unique "Gulf War Illnesses" (18-20).

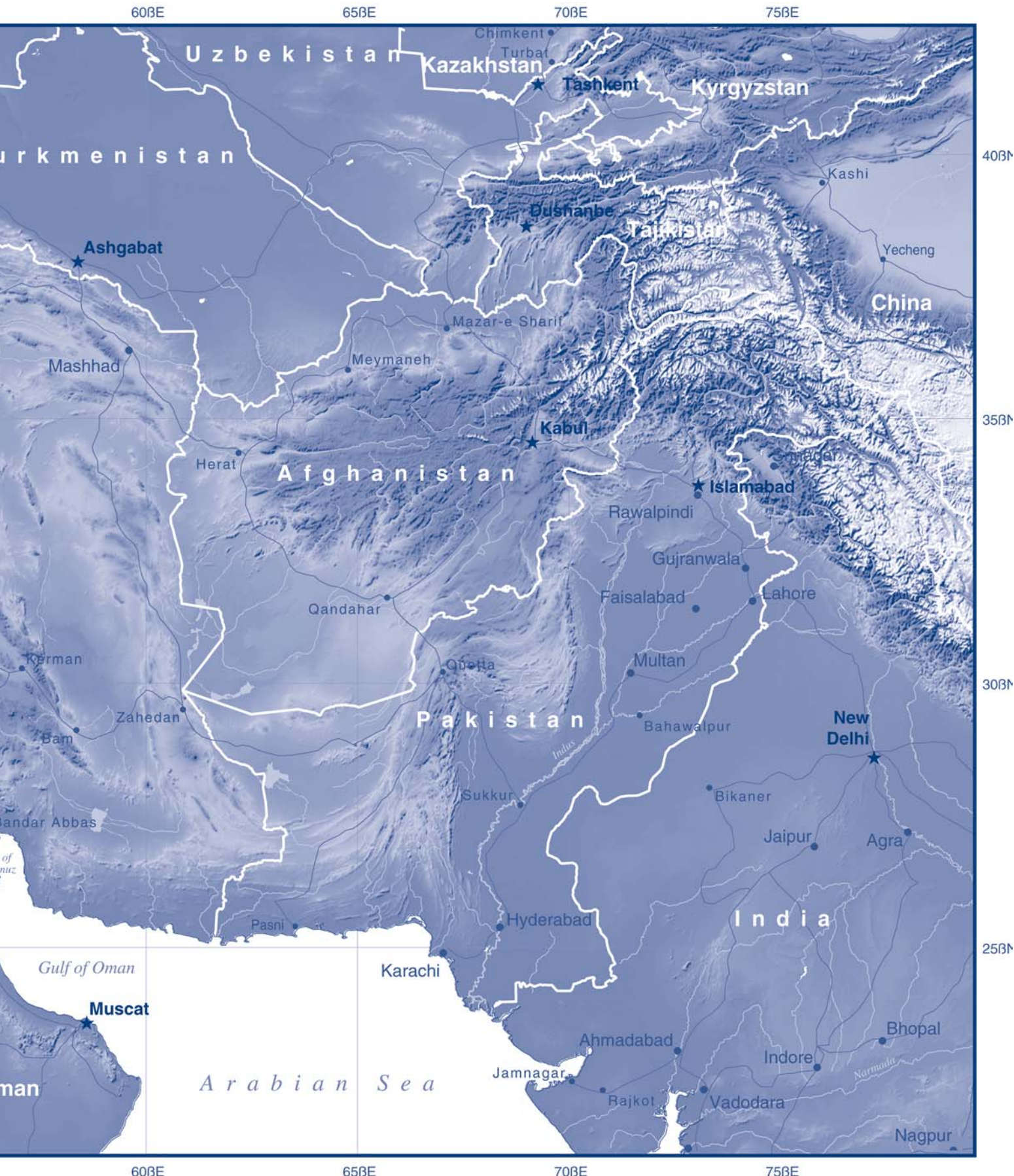
Map of Afghanistan and surrounding region





Western Asia







Malaria

Malaria remains the most important infectious cause of death worldwide, with forty percent of the world's population at risk (21).

The World Health Organization (WHO) estimates that there are 300–500 million cases of malaria and as many as 2–3 million deaths per year (22). In areas of civil unrest or governmental collapse, the risk of malaria increases (23).

Civilians are not the only population at risk. Throughout history, malaria has contributed to the success or failure of military campaigns (24, 25).

During World War II, U.S. Army forces lost about 9 million sick days to malaria. Sick days from malaria exceeded days lost to battle injuries. Malaria was also a major problem for Western troops during the Vietnam conflict and resulted in one million days lost from malaria and an additional 18,000 cases imported into the United States (26).

Afghanistan

Malaria is endemic throughout Afghanistan (27). A large proportion of the Afghan population fled to Pakistan after the Communist overthrow of the Kabul government in 1978 and after the Soviet invasion in December 1979. Up to 3 million refugees settled in Pakistan. Refugees began returning to Afghanistan after the success of “Operation Enduring Freedom” in the fall of 2001. During this resettlement, the incidence of malaria increased (28-30).

Multiple factors contributed to a higher risk of malaria in Afghanistan.

1. collapse of governmental vector control programs,
2. inadequate shelter,
3. crowding of displaced people,
4. increased pools of water from construction of shelters and sanitation efforts,
5. lack of available or affordable antimalarial medications,
6. increased resistance of *Plasmodium* species to antimalarials and of the vectors to pesticides, and
7. an influx of refugees into previously stable zones of malaria endemicity (28, 29).

Malaria was a major problem for occupying Soviet troops during 1981-1989. Soviet military personnel stationed in Afghanistan imported a total of 7683 cases of *Plasmodium vivax* (*P. vivax*) malaria from Afghanistan into the

former Soviet Union. Malaria developed late in many of the troops returning home to the Soviet Union.

The signs and symptoms of malaria appeared in:

- 24% of cases within 1 month
- 23% after 1–3 months
- 20% after 4–6 months
- 3% after 1 year (31)

In Afghanistan, the epidemiology of malaria is seasonal and hypoendemic in most of the country and in neighboring Pakistan at elevations of < 1500–2000 meters. This also included the urban areas of Kabul and Jalalabad. In the rice-growing region of eastern Afghanistan, transmission is highest and is mesoendemic (7, 32). Malaria zones include the eastern provinces and large areas in a crescent shape encompassing the north, west, and south of the country and excluding the central highlands and high mountain ranges of the east (7, 32). The malaria season is from April through November, with very few cases reported in the winter months.

Until recently, *P. vivax* made up about 90% of cases and *P. falciparum* the remainder.

Up to 20% of recent cases are due to *P. falciparum*, and multiple outbreaks of *P. falciparum* malaria have been reported since 1999 (7). In all, it is estimated that 2–3 million cases of malaria occurred in Afghanistan in 1999 alone, with 300,000–450,000 being *P. falciparum* malaria (7). In Pakistan, both *P. vivax* and *P. falciparum* are found (34–36). Afghanistan's northern neighbors also have seen a surge in cases of malaria coinciding with the exodus of Afghan refugees (37, 38).

Note: Beginning in 1999, the proportion of malaria due to *P. falciparum* has been climbing in Afghanistan, probably because of the use of chloroquine as the first-line antimalarial (33).

Note: Western troops, peacekeepers, and humanitarian relief workers are at risk for both *P. vivax* and *P. falciparum* malaria while working in Afghanistan and surrounding countries.

Iraq

A somewhat similar situation prevails in Iraq, where following nearly half a century of malaria-free status, a significant outbreak of *P. vivax* malaria occurred in 1994–1995, with a peak of about 100,000 cases per year (11, 12 in pages 45–49, 27, 39). This epidemic was attributed to movement of people from endemic into malaria-free zones, delays in access to effective treatment, and lack of effective control measures following the Gulf War (11).

Subsequent implementation of vector control programs with the support of the WHO, including indoor residual spraying and distribution of pyrethroid-treated nets, led to a decline in malaria incidence (12). A total of 4134

malaria cases were recorded in the country in 1999 (39) and only 1120 malaria cases in 2001 (39). While there is a potential for introduction of *P. falciparum* into the southern region of Iraq, all malaria apparently is caused by *P. vivax* (12, 39, 40).

In Iraq, the epidemiology of malaria is seasonal and of low endemicity. There are two transmission peaks, May-June and August-October (40). Affected regions include Duhok, Erbil, Sileimanya, Ninewa, Tamin, Baghdad, and Basrah (40, 41) below 1500 meters. Eighty-four percent of all malaria in 2001 was reported from the three autonomous governates of Erbil, Duhok, and Suleimanya. Duhok alone accounted for 74% of all malaria reported in Iraq (40).

CAUTION

Among veterans of “Operation Iraqi Freedom”, P. vivax malaria should be considered in the differential diagnosis of patients presenting with a febrile illness. Although U.S. troops are provided malaria prophylaxis, breakthrough infections can occur. Because P. falciparum malaria was supposedly eradicated from Iraq in the 1980’s, it is not thought to be a problem for returning veterans (12 on page 45).

Resistance

Under the pressure of chloroquine therapy, resistance patterns in Southwest Asia have mirrored the world trend. Chloroquine resistance was first noted in Pakistan in 1984 (42) and in Afghanistan in 1986 (43) and is now widespread in eastern Afghanistan. Resistance is sub-categorized as RI, RII, or RIII, from least to most resistant.

- RI is defined as complete clearance but with recrudescence of parasitemia within 28 days.
- RII, there is a marked reduction in parasitemia, but incomplete clearance.
- RIII means no significant reduction in asexual parasitemia.

In Afghanistan, 55% of *P. falciparum* had RI resistance and 11% had RII or RIII resistance (33).

In the North West Frontier and Balochistan provinces of Pakistan, where high concentrations of Afghan refugees were located:

- RI resistance to chloroquine is very high for *P. falciparum*, ranging from 30% to 84%
- RII resistance variable, from 2% to 36% (28, 34)
- RIII resistance has not been reported (33)

Sulfadoxine-pyrimethamine (Fansidar®) is widely believed to be effective (7, 33), although published studies are lacking. In neighboring refugee camps in western Pakistan, resistance to sulfadoxine-pyrimethamine was found in all districts sampled, with a range of 4% to 25% (average, 12%) (44).

Treatment

Among residents of Afghanistan and neighboring countries, the WHO has recently published recommendations for treatment (7).

1. For uncomplicated *P. falciparum* malaria
 - a. sulfadoxine-pyrimethamine, 25 mg/kg (per the sulfa component), is recommended as a single oral dose.
 - b. For adults, 3 tablets taken as a single oral dose would be sufficient after a confirmed blood smear or dipstick test.
2. For *P. vivax* malaria
 - a. chloroquine can be given as a daily dose over 3 days as shown in Table 1:

Day	Recommended Dose
1	10 mg/kg
2	10 mg/kg
3	5 mg/kg, for a total of 25 mg/kg

Table 1

In Tajikistan, Uzbekistan, and Turkmenistan, the WHO suggests a 1-time dose of primaquine, 0.75 mg/kg, for gametocyte eradication after *P. falciparum* infection or primaquine, 0.25 mg/kg/day for 14 days, for terminal prophylaxis after *P. vivax* infection (7). Primaquine is not advocated for residents of Afghanistan, Pakistan, and Iran, given higher transmission rates and possible problems with compliance (7). Mixed *P. falciparum* and *P. vivax* infections, which are uncommonly reported, may be treated with chloroquine plus sulfadoxine-pyrimethamine. If primaquine is used, it must be used cautiously, given the high frequency of glucose-6-phosphate dehydrogenase (G-6-PD) deficiency in this region (45, 46).

Alternative therapy for uncomplicated *P. falciparum* malaria may include:

1. quinine plus either doxycycline, sulfadoxine-pyrimethamine, or clindamycin;
2. mefloquine;
3. artesunate plus mefloquine;
4. atovaquone-proguanil (Malarone); or
5. halofantrine (22, 47-50).

TREATMENT AND PROPHYLAXIS RECOMMENDATION

In Iraq, chloroquine resistant malaria is not currently known to be a problem. For this reason, chloroquine is still being advocated for chemoprophylaxis and treatment by the WHO and the CDC in Iraq, as well as the malaria risk regions of neighboring Syria and Turkey (12, 40, 41).

U.S. troops will likely use a quinine-based oral combination regimen. For complicated *P. falciparum* malaria:

- IV quinine,
- IV artesunate, or
- IM artemeter-based therapies are options (47-50).

Quinidine may be used when IV quinine dihydrochloride is not available, but requires close cardiac monitoring for potential QTc prolongation, QRS widening, and a proarrhythmic effect. Chloroquine-resistant *P. vivax* has not been reported in the area. Treatment for complicated *P. falciparum* malaria has been reviewed in depth (22, 47-52).

Theoretically, combination therapy, with two agents for which *P. falciparum* shows sensitivity, could be used to slow the development of resistance to individual antimalarials and potentially decrease malaria rates (53, 54). One

such scheme employs artesunate with mefloquine or sulfadoxine-pyrimethamine (Fansidar®). While not FDA approved or available in the U.S., artesunate eradicates asexual parasites more rapidly than other antimalarials and is gametocidal (54, 55). Consequently, there may be fewer resistant mutant parasites that survive treatment and could be transmitted (53-55).

TREATMENT RECOMMENDATION
For Iraq, the national recommended treatment for *P. vivax* infection, as per the WHO, is chloroquine 25 mg of base/kg over three days.

In Iraq, 150 mg tablets (base) are used for adults according to the schedule in Table 2:

Day	Recommended Dose (150 mg tablets)
1	4 tablets (600 mg) initially + 2 tablets (300 mg) after 6 hours
2	2 tablets (300 mg)
3	2 tablets (300 mg), plus Primaquine 0.25 mg/kg for 14 days

Table2

For adults, using 15 mg tablets (base), the schedule is for the 4th through 17th days: 1 tablet (15 mg) per day (for 14 days).

Note: U.S. service members routinely have G-6-PD determinations upon entry into the military, which facilitates the decision to use or avoid primaquine. Canadian Forces are also tested before deploying to a malaria endemic area.

Pregnancy or an age less than 1 year are considered contraindication for primaquine. G-6-PD deficiency must be ruled out prior to use of primaquine. G-6-PD deficiency is common in Iraq, Iran, Turkey, and other countries of the Middle East and may be of the severe Mediterranean variant (56-58). Empiric use of primaquine in indigenous people and in travelers should therefore be avoided until G-6-PD status can be determined.

Chemoprophylaxis

In Afghanistan, military troops and humanitarian workers may benefit from chemoprophylaxis during the malaria season. Oral mefloquine is the preferred agent (32, 59) and can be given as weekly dose of 250 mg of salt (1 tablet) beginning 1–2 weeks before entering the malaria zone and continuing for 4 weeks after leaving the area of risk. Children may be given prophylaxis with 5 mg/kg once weekly on the same schedule as adults. An alternative mefloquine dosage of 5 mg/kg daily for 3 days beginning 1 week before departure has been suggested by Boudreau et al., (60) to more rapidly achieve protective steady-state levels, but Canadian forces have reported more side-effects with this shortened course. When mefloquine cannot be taken, doxycycline can be substituted. Adults may take 100 mg by mouth daily beginning on the day before travel and continuing for 4 weeks after departure from the region of endemicity (59).

Opinion varies as to mefloquine use by aircraft pilots. Mefloquine may cause mild sleep disturbances, as well as affect fine motor and spatial discrimination functions (59). Schlagenhauf et al., (61) found no significant difference in performance by Swiss Air trainee airline pilots in a comparison of placebo with mefloquine. In the U.S. military, mefloquine is not allowed for those on flight status. The U.S. military has ruled out mefloquine malaria prophylaxis as a cause of domestic violence among veterans of the conflict in Afghanistan (62, 63).

DANGER
Contraindications to mefloquine include epilepsy, psychosis, depression, and cardiac arrhythmias.

Although not licensed in the U.S. for prophylaxis, primaquine may be a reasonable choice for prophylaxis if mefloquine or doxycycline cannot be used and the G-6-PD status is known to be normal. At least 4 studies have shown the agent to be safe and effective (64-67). When used as a prophylactic agent, it should be given as 30 mg of base/day for adults or 0.6 mg/kg/day for children (59, 68). Primaquine may be started on entry into a malaria zone or several days before travel to ensure tolerance; it may be stopped 1 week after departure.

Atovaquone-proguanil (Malarone®) has been recently licensed in the United States. It is highly effective for prophylaxis against *P. falciparum*. There is very little data on the effectiveness of this combination for prevention of *P. vivax* (69). Given that the majority of malaria in Afghanistan and Iraq is due to *P. vivax* and given the high cost of atovaquone-proguanil, it probably should be avoided as a first-choice prophylactic agent.

Because Iraq is a chloroquine-sensitive zone, chloroquine is the drug of choice for chemoprophylaxis (12, 40, 41, 55). The usual prophylactic dose is 5mg base/kg per week (300 mg base/wk for most adults) beginning one week prior to arrival in the malaria-endemic zone and continued for 4 weeks after leaving the area of endemicity. Additionally, gravid women can be administered the same weekly prophylactic dosing regimen to prevent relapse after primary treatment of a *P. vivax* infection. Following delivery,

primaquine can be given to G-6-PD normal women to assure radical cure (12, 55). Chloroquine allergic or intolerant patients may use alternative chemoprophylaxis with mefloquine, doxycycline, atovaquone-proguanil (Malarone®), or primaquine as described above for Afghanistan.

Prevention and control measures

The mosquitoes associated with malaria transmission in Afghanistan are *Anopheles* species (7, 29). Insecticide spraying with lambda-cyhalothrin and Malathion has been used extensively in a variety of experimental and public health measures in the Afghan refugee camps in Pakistan and in non-refugee sites in Pakistan. Highly effective control of *P. vivax* and *P. falciparum* can be achieved with spraying (70).

Residual spraying within tents and compounds has likewise been found to be effective (71). Permethrin impregnation of bed nets, *chadors* (Islamic cloth wraps used as veils and for sleeping), top sheets, cloth window screens, and other clothing have yielded excellent results (29, 30, 36, 71-74). Use of electric fans, pyrethrum coils, untreated curtains, pyrethroid-vaporizing mats, and permethrin-impregnated curtains has been shown to reduce the catches of blood-fed mosquitoes (72).

Insect repellants are widely used by individual travelers and military personnel, but are not practical for indigenous people, given the cost and need for reapplication after several hours (75). The U.S. military uses 35% diethyltoluamide (DEET), and this is currently recommended for travelers to areas of endemicity (75-77) during the hours between dusk and dawn. DEET can also be effectively used on clothing either alone or in combination with permethrin. Lesser-strength long-acting preparations are also available (78).

For prevention and control efforts in Iraq, *Anopheles* vectors are most important (12, 79). Given the expected disruption of vector control measures, shortage of insecticides, and displacement of populations within and outside Iraq due to "Operation Iraqi Freedom", the potential for a resurgence of malaria incidence rates is high (12, 80). The use of DEET and pyrethroid as a personal use measure is expected to be as effective in Iraq as in Afghanistan.



3

Diarrheal Diseases

Besides cholera, the most significant reported bacillary etiologies of enteric disease in Afghanistan are Salmonella and Shigella.

Diarrheal disease is one of the most important infectious disease problems in Southwest Asia. Historically, diarrheal diseases are also a major health threat for military populations. Soviet troops experienced high rates of enteric illnesses during their occupation of Afghanistan (9). During the

Gulf War in 1991, acute diarrhea was one of the major infectious disease problems for Western troops (16).

Afghanistan

Ongoing war and population displacement in Afghanistan have led to high morbidity and mortality from enteric disease (81). In many areas of Afghanistan, dilapidated water and sewage systems are frequently implicated as the cause of enteric outbreaks (82). In addition, economic downturn and upheaval after the breakup of the Soviet Union has led to plumbing and infrastructure neglect throughout Central Asia (83, 84).

During the occupation of Afghanistan in the 1980's, lack of potable water is cited as a primary reason Soviet soldiers had high enteric infectious disease rates. Fifty-eight percent of Soviet troops had major gastrointestinal infections (85). Bacillary and amoebic dysentery, and agents of other water-borne diseases (hepatitis A, typhoid) were major problems, because the Soviet personnel drank untreated local water (9).

Cholera is not typically the major cause of diarrhea among residents of South-Central Asia (86). However, cholera can cause epidemic diseases throughout the region. The 7th pandemic of cholera was caused by the El Tor biotype of *Vibrio cholerae* serogroup O1. It arose in Indonesia during 1961 and spread across Asia and Africa, reaching Pakistan, Afghanistan, and Uzbekistan in 1965 (87–89). El Tor replaced the classical cholera biotype in India and Bangladesh, but caused only sporadic small clusters of cases in South-Central Asia after 1970. Historically, cholera outbreaks in the region appear to originate in travel between Bangladesh and Pakistan, and then spread throughout South-Central Asia (87, 90, 91).

The only strain of *V. cholerae* now routinely isolated in South-Central Asia is O1, El Tor, serotype Ogawa (88, 92). Epidemic cholera re-emerged in Pakistan and Afghanistan in 1988 and has remained a significant cause of

morbidity and mortality ever since (93, 94). Also, the city of Samarkand, Uzbekistan, suffered outbreaks of El Tor cholera in 1985 and 1990 (95).

In 1993, a newly emerged *V. cholerae* serogroup, designated O139, reached Pakistan from the Bay of Bengal. It carries the same toxin cluster and causes symptoms identical to those caused by *V. cholerae* O1 El Tor, but has a different surface antigenic structure. After a few seasons of predominance, *V. cholerae* O139 virtually disappeared from the Karachi, Pakistan region by 1996, and this strain has probably not yet spread west of Pakistan (86, 93, 96).

Since 1998, better reporting methods indicate that cholera and cholera-like illness have been intermittently widespread in Afghanistan and the Pakistan-Afghan border areas (97–99). The Afghan cities of Mazar-e-Sharif, Bamiyan, Badakhstan, and Herat all have had significant outbreaks of serious diarrhea, but the largest was in Kabul (92). More than 14,000 cases of cholera-like illness were reported in 6 weeks of 1999, with greater than one-half in Kabul (100). Cholera continued to occur in 2000–2001 (7, 82, 101).

As stated in the beginning of this section, besides cholera, the most significant reported bacillary etiologies of enteric disease in Afghanistan are *Salmonella* and *Shigella*. In the vast majority of diarrheal cases, no etiologic agent is established. Soviet occupation troops in Afghanistan were greatly affected by *Shigella* (9). Some Soviet troops became extremely ill with combined cholera-shigellosis because of a severe lack of clean water (102). Not surprisingly, *Shigella* infections were also common in Uzbekistan and Tajikistan when Soviet troops were in Afghanistan (84, 103).

Note: Given the current upheaval in Afghanistan, cholera remains a major concern for the local population, humanitarian groups, and military personnel.

Although the etiologies of diarrhea in Afghanistan remain largely unknown, the causes of non-cholera diarrhea are well described in Pakistan (90, 104–107). Enterotoxigenic *Escherichia coli* (ETEC), *Shigella*, *Salmonella*, and *Campylobacter* species were typically isolated everywhere. More recently, *E. coli* O157: H7, a potent Shiga-like toxin producer, has been isolated (108). Shigellosis was usually caused by the more virulent *Shigella flexneri* and *Shigella dysenteriae* species (104, 109, 110). Rotavirus and enteric adenovirus were commonly found in Pakistani and nearby regions among children with diarrhea (105–107, 111, 112).

Iraq

The common diarrheal agents are found in Iraq and neighboring countries (12 at pages 14–19, 113). During “Operations Desert Shield and Desert Storm (Gulf War, 1990–1991), young Kuwaiti males were forcibly taken to camps in southern Iraq. Stool specimens from the earliest individuals to return to Kuwait were analyzed at the Mubarak Al Kabeer hospital (Thornton, unpublished data). Bacterial pathogens included *Shigella*,

Salmonella, *Campylobacter*, and six isolates of *V. cholerae* O1 biotype Ogawa. Importantly, common diarrheal pathogens have been found to be resistant to many types of antibiotics, but not quinolone drugs (113).

Western military personnel stationed in northern Saudi Arabia during the Gulf War buildup in late 1990, had large outbreaks of diarrhea due to ETEC and *Shigella sonnei*, both typical agents of travelers' type diarrhea in this region (114). The supplementation of the troops' diet with regionally acquired produce was at least partly responsible, and the number of cases fell when this was restricted. During the 1991 Kurdish refugee crisis in northern Iraq, diarrhea and malnutrition caused many deaths in young children (115). Even with better nutrition, the same enteropathogens probably accounted for many diarrheal cases afflicting British and Australian medical personnel assisting these refugees (116). Daily doxycycline prophylaxis and enforced hand-washing regimens in the Australians probably accounted for them having a lower incidence of diarrhea (36%) and lesser severity compared to the British contingent (69%).

Since the Gulf War, the few published reports in Iraq indicate an explosive increase in diarrheal disease due to the breakdown in sanitation, especially safe drinking water, which is available to only half the population served

before the war (11). The Iraqi Ministry of Health reported a 3-fold increase of bacterial dysentery, from 20,000 cases in 1989 to 63,000 cases in 1993 (12 at pages 10-19). In the same report, cholera cases were up from 1217 cases in 1991 to 2560 in 1998, with cases found in all governates (12 at pages 6 and 17).

Note: Outbreaks of cholera have been reported in Iraq following "Operation Iraqi Freedom" in early 2003, but only among local populations and not U.S. troops (11, 117, 118).

Treatment of diarrheal disease

Effective treatment of diarrheal disease has the potential to substantially lower morbidity and mortality. **Reduction of mortality from diarrheal disease is primarily related to effective management of dehydration (7).** Cholera is usually treated by oral or parenteral rehydration. Antibiotic therapy is a useful adjunct that may shorten the duration and volume of diarrhea (119, 120). However, in Pakistan, *V. cholerae* O1 strains have become resistant to tetracycline, ampicillin, and erythromycin, but not chloramphenicol or nalidixic acid (86, 96). Isolates of *V. cholerae* O139 have been resistant to trimethoprim-sulfamethoxazole, but susceptible to tetracycline (96). In Pakistan and Afghanistan, trimethoprim-sulfamethoxazole is the most commonly prescribed antimicrobial in cholera-like illnesses (121).

A fluoroquinolone is the medication of choice for *Shigella* dysentery in Afghanistan because resistance to most non-quinolone drugs is very high (109, 110).

If quinolone-resistant *Campylobacter* species is isolated, daily oral azithromycin (500 mg) might prove a useful alternative (122). Imodium may also be useful in controlling diarrheal symptoms.

Immunization

Two promising oral *V. cholerae* O1 vaccines are not yet licensed in the United States (123). Neither vaccine protects against the O139 strain.

Intestinal Parasites

Intestinal parasites have the potential to cause prolonged diarrhea, intestinal symptoms, and chronic health effects among military troops after their return to North America.

Afghanistan

A review of several studies in Pakistan dating from 1964 to 1985 found protozoan agents (especially *Entamoeba histolytica* and *Giardia lamblia*) to be more prevalent in the southern coastal part of the country, whereas helminthes (*Ascaris lumbricoides*, hookworms, *Taenia* species, *Hymenolepis nana*) dominated in the north (124, 125). *Cryptosporidium parvum* was reported in 10% of children in Rawalpindi, Pakistan (126), and has been found to be a major gastrointestinal pathogen in Turkmenistan as well (127). *Cyclospora* may also be present, because it was found in Irish travelers to Nepal and Pakistan (128).

Iraq

All common intestinal parasites are prevalent in Iraq (12 at pages 10-19, 129-131). *Giardia lamblia*, *Entamoeba histolytica*, *Hymenolepis nana*, *Strongyloides stercoralis* were the most often identified parasites in southern Iraq (129). In the case of Kuwaiti males held in southern Iraq during the Gulf War in 1991, stool samples commonly yielded parasites, with *Giardia*, *Entamoeba coli*, *Chilomastix*, and *Endolimax* often found together (Thorton, personal communication). *Cryptosporidium* infections have been found in certain occupational groups in Iraq (132).

TREATMENT RECOMMENDATION

Treatment with oral ciprofloxacin for 1–3 days or another fluoroquinolone would be the primary choice for cases of dysentery in military personnel or foreign aid workers who have served in Afghanistan or Iraq.

CAUTION

*In a recent review of cholera vaccines, the currently available parenteral vaccine against *V. cholerae* O1 is not recommended because of low protective efficacy and the high risk of adverse reactions (123).*

Note: Cholera is rare in Western travelers to areas of endemicity and has not been a problem for the U.S. military in recent deployments. U.S. military personnel do not receive cholera vaccine. No vaccine exists for other diarrheal agents, although several are in development.

Since the Gulf War in 1991, little has been published on parasites in Iraq, although Ministry of Health reports indicate both amoebiasis and giardiasis have increased 34-fold and 7-fold, respectively (12 at pages 10-19), and *Cyclospora* infection has been identified for the first time in 1999 (133). Fecal smears of animal handlers in Basra, Iraq, found 50% of 60 veterinarians, butchers, and animal breeders tested to be positive for *Cryptosporidium parvum*; 14% of non-animal handlers were also positive (132). As in other poor and developing countries, giardiasis and amebiasis are common causes of diarrhea (134).

Note: For veterans of the Afghanistan and Iraq conflict, giardiasis and amebiasis should be considered when evaluating patients for chronic diarrhea. Amoebic infections can also lead to liver abscesses (135).



Typhoid Fever

A major public health concern in Southwest Asia is caused by infection with the bacterium, Salmonella typhi, (S. typhi - Typhoid fever)

water supplies. Although typhoid fever has not been a significant problem for the U.S. military since the early 20th century (137), it was a huge burden for the Soviet military during its Afghanistan campaign, causing 130,000 hospitalizations and disrupting military operations (9).

Typhoid fever also is a major health problem in Iraq (12 at pages 74 and 75). The incidence of typhoid rose steeply from 11/100,000 of the population in 1990 to 142/100,000 in 1994 (11).

Note: Some travelers could return to the U.S. before symptoms of typhoid begin.

may occur, but many patients report no change in bowel habits. Cough may be the predominant symptom in some cases, and neuropsychiatric presentations also occur. Relative bradycardia and rose spots are classic physical findings, but are not usually present. Gastrointestinal bleeding, bowel perforation, or a profound debility may occur in advanced cases (138). If untreated, mortality is 10%–30%, whereas appropriate therapy lowers mortality to about 1%.

CAUTION

Typhoid fever can be difficult to distinguish from other infectious diseases in Southwest Asia. The differential diagnosis of typhoid includes tuberculosis, brucellosis, intra-abdominal abscess, Rickettsial infections, malaria and West Nile fever.

Outbreaks occur frequently in South-Central Asia, as exemplified by the 8900 cases (1% of the city's population) that occurred during the first 6 months of 1997 in Dushanbe, Tajikistan (136). The Tajikistan epidemic, like most others, was found to have been caused by contaminated public

Clinical findings

After a typical incubation period of 8–14 days, typhoid fever begins insidiously with malaise, fever, chills, headache, and myalgias. Either diarrhea or constipation

Diagnosis

Definitive diagnosis of typhoid fever depends on the isolation of *S. typhi* from blood, bone marrow, or biopsy of cutaneous rose spots. Culture of blood yields positive results for 80% to 90% of patients during the first week of illness, with diminishing yields as the disease progresses. Culture of bone marrow often

yields positive results when blood culture results are negative and in cases where antibiotic treatment was begun prior to collection of blood (139). Rose spot skin snips may be diagnostic, but only a minority of patients have these typical lesions. Stool culture yields positive results for about one-half of patients with typhoid fever (138).

Treatment

Traditional therapy for typhoid fever has relied on 3 inexpensive antimicrobials: ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole. Multiresistant strains (resistant to all 3 traditional agents) were first noted in the Middle East and South-Central Asia in the late 1980s and are now widespread. Ninety-three percent of tested strains for the Tajikistan outbreak were multiresistant (136).

Compared to cephalosporins, quinolones are associated with fewer clinical failures and a more rapid response (142). Complicating the use of quinolones for multidrug-resistant typhoid has been the recent emergence of quinolone-resistant *S. typhi*, which has been reported elsewhere (143-146).

The optimal treatment of quinolone-resistant or -unresponsive *S. typhi* infection is unclear. A parenteral third-generation cephalosporin, such as ceftriaxone, would be a reasonable choice. An oral third-generation cephalosporin, such as cefixime, may offer a convenient option for those that are not seriously ill (147). Azithromycin is a novel approach for multidrug-resistant typhoid and appears to have success rates comparable to ciprofloxacin and ceftriaxone (148, 149).

Pending susceptibility data, it would seem prudent to initiate therapy for typhoid with an oral quinolone, changing to either a third-generation cephalosporin or azithromycin if clinical failure occurs, or quinolone resistance is documented. Standard doses would be ciprofloxacin, 500 mg orally b.i.d. for 10 days, ceftriaxone, 2 g IV q.d. for 14 days, or azithromycin as a 1-g loading dose followed by 500 mg q.d. for 6 days; azithromycin may be given orally or IV. Dexamethasone may be a valuable adjunct for patients with severe typhoid, especially those with altered mental status or hypotension not responsive to rehydration (150).

Prevention

The prevention of typhoid depends primarily on the provision of uncontaminated water and effective sewage disposal. Vaccines lower the risk of infection by about 70%, but may be overwhelmed by large inocula (151). Two vaccines are in popular use in North America and Europe.

A major public health concern in Southwest Asia is caused by infection with the bacterium, Salmonella typhi, (S. typhi - Typhoid fever)

TREATMENT RECOMMENDATION
In view of the proliferation of multidrug-resistant typhoid, oral fluoroquinolones and parenteral third-generation cephalosporins have become the standard, initial therapies pending susceptibility testing.

1. Inactivated intramuscular Vi vaccine
2. Oral attenuated Ty21a strain.

Note: Because U.S. and Canadian military personnel in Southwest Asia will have received one of these typhoid vaccines and have access to safe drinking water, they are at low risk of typhoid fever.

Visitors to both Afghanistan and Iraq should consider obtaining a typhoid vaccination. Considerable data also support the use of typhoid vaccine in preventing or stemming typhoid epidemics (151, 152).



5

Viral Hepatitis

Viral hepatitis is a health risk for Western troops, coalition peacekeepers, and humanitarian workers deployed to Afghanistan, Iraq, and neighboring countries. Historically, hepatitis A and B have been major infectious disease threats for military forces (153, 154). More recently, there has been concern about hepatitis C, because a high prevalence of hepatitis C virus (HCV) infection has been found in some populations of U.S. military veterans (155, 156).

Afghanistan

Viral hepatitis was a serious problem for Russian troops during the Soviet Union's incursion into Afghanistan in the 1980s (8, 9, 157-159) and remains a major health threat to the local population. More than 115,000 cases of acute viral hepatitis were reported in a population of 620,000 Soviet troops who served in Afghanistan (8). Morbidity rates were so high that viral hepatitis was thought to have directly compromised Soviet military operations (8).

Hepatitis A is highly endemic in South-Central Asia where Coalition troops have been deployed (160). Hepatitis A virus

(HAV) is readily transmitted by the fecal-oral route, and is a universal infection among the resident population, with > 90% of 5-year-olds having been infected (160). The risk of HAV transmission among non-immune personnel is elevated during combat and humanitarian operations because of crowded living conditions and the difficulty of maintaining a high level of cleanliness while camping in the field. Ninety-five percent of cases of acute hepatitis among the Soviet troops deployed to Afghanistan were attributed to HAV infection, which was thought to have resulted from poor personal hygiene, a lack of clean drinking water, and the failure of cooks to wash their hands (8, 9, 157-159).

Hepatitis B is also endemic in Afghanistan and surrounding countries. In a study in nearby Pakistan, hepatitis B was the cause of 42% of cases of acute hepatitis (161). Among adults, hepatitis B virus (HBV) is transmitted by sexual and parenteral exposure. For military forces and peacekeepers, HBV infection could be contracted from the transfusion of contaminated blood that may have been inadequately screened in an emergency (162). Sexual contact and illicit drug use also are potential routes of HBV infection.

Like the other major types of viral hepatitis, hepatitis C is prevalent in South-Central Asia (163). Serological evidence of infection has been found in 16% to 24% of general populations surveyed in Pakistan (163). HCV infection is most readily transmitted by parenteral exposure to

contaminated blood. Sexual contact is not an efficient mode of transmission (164). HCV has been considered a potential health threat for military troops and veterans from illicit drug use, blood transfusions (before reliable screening of blood products became possible in 1993), and contact with the blood of battlefield casualties (155, 156). Injured troops could be infected with HCV if unscreened blood donors were used in an emergency (162).

Hepatitis E virus (HEV), which is transmitted via the fecal-oral route, is a potential infectious disease problem in developing countries from consumption of contaminated water and food. HEV infection is highly endemic in South-Central Asia, where one-third of the population may experience infection (165-167). Some of the largest epidemics of hepatitis E have occurred in Pakistan and India (168, 169), causing substantial morbidity and some mortality, especially during pregnancy. The general breakdown in sanitary measures in Afghanistan could potentially lead to HEV infections among Western personnel.

Iraq

As in the rest of the Middle East, viral hepatitis is relatively common in Iraq (170). Hepatitis A, B, C, delta, and E have all been reported.

Viral hepatitis in Western military populations

Given the diverse routes of transmission, the risk of viral hepatitis cannot be completely eliminated among deployed troops and peacekeepers. Nevertheless, in the near term, viral hepatitis probably will not be a major cause of morbidity for currently deployed U.S. military forces. Studies of U.S. military populations have shown that viral hepatitis has become much less of a problem. Analysis of DoD hospital records indicate that over the last 25 years there has been a steady decline in the incidence of viral hepatitis, whether transmitted by parenteral, sexual, or fecal-oral routes (173-176).

Hepatitis A is a concern now mainly during deployments to developing countries (177). The risk of hepatitis B is low except among patients with sexually transmitted diseases (177, 178). For hepatitis C, current military forces have been found to be at low risk of infection. In a recent study of 10,000 active duty U.S. troops, 0.5% had been infected with HCV, which is much lower than the 2.6% prevalence observed in the civilian adult population (179, 180).

Although HEV has the potential to cause epidemic disease in military populations (181), it has not been a problem for the U.S. military.

Note: Hepatitis E, a form of non-A, non-B hepatitis, is endemic in Iraq and a potential infectious diseases risk for Western troops serving in this region because there is no vaccine for this type of viral hepatitis (171, 172). The risk of hepatitis C appears to be low in Iraq (171).

Note: There has never been a documented outbreak of hepatitis E among U.S. forces. In addition, there has never been a documented outbreak of hepatitis E in Canadian Forces peacekeepers, despite their extensive deployments.

Hepatitis E also is relatively rare among Western travelers (182). One reason for the low risk of hepatitis E may be the fact that HEV infection requires a relatively large dose of infectious agent, usually from grossly contaminated drinking water (183).

Recent military deployments to Southwest Asia and Africa further illustrate the low risk of viral hepatitis for U.S. forces deployed abroad. Only a few cases of hepatitis A and

B were observed among the 700,000 U.S. troops deployed to Southwest Asia during the Gulf War in 1991 (16). Likewise, viral hepatitis was not a problem for U.S. troops sent to Somalia in 1992, even though hepatitis E virus was a common cause of acute sporadic hepatitis in the general population of Somalia during this period (184).

Several factors are responsible for the low risk of viral hepatitis among today's military forces. For one, the U.S. military places strong emphasis on both personal hygiene and camp sanitation, even during combat operations (185-187). In addition, the U.S. military can airlift bottled water and fresh food to combat troops, and can generate large quantities of potable water by use of portable reverse-osmosis units. Because of these preventive measures, diseases transmitted by the fecal-oral route, such as hepatitis A and E, should not be a major problem.

The U.S. military's emphasis on maintaining a drug-free environment also contributes to a reduced risk of viral hepatitis. During the last 20 years, illicit drug use has been nearly eliminated in the U.S. military by routine, random drug testing at induction and throughout military service (188, 189). As a result, hospitalizations for hepatitis B and C, which are efficiently transmitted by injection drug abuse, have decreased markedly (174, 175).

The risk of viral hepatitis has been diminished further by the development of the hepatitis B vaccine and, more recently, the hepatitis A vaccine. At present, military medical personnel, troops diagnosed with a sexually transmitted disease, and military members assigned for extended periods to countries with high rates of hepatitis B, are vaccinated against hepatitis B (190). The hepatitis B vaccine has not been given routinely to all incoming U.S. recruits, but young men and women are now entering military service with pre-existing immunity to hepatitis B because of national recommendations for adolescent immunization (191).

In 1995, the hepatitis A vaccine was introduced. This vaccine is given to incoming U.S. military recruits and to other troops before deployment to developing countries. Because of the effectiveness of the hepatitis A vaccine, immunoglobulin is no longer used on a routine basis for prophylaxis against hepatitis A (190). Both hepatitis A and hepatitis B vaccines can be recommended for anyone working in Afghanistan and Iraq for an extended period of time.

Although there is no vaccine, the risk of HCV infection has been substantially reduced because of the development of sensitive and specific serological tests. HCV is now virtually never transmitted from the routine transfusion of blood products (192).

In prior studies, HCV infection has not been associated with military deployments or the use of non-intravenous immunoglobulin (176, 177, 194). HCV infection has been found infrequently among recent military veterans or among military veterans randomly selected from the general population (180, 195, 196).

Note: HCV is not transmitted by casual contact, is not readily transmitted by sexual contact, and would not be transmitted from contact between infected blood and intact skin (193)

As is the case with hepatitis C, there is no commercially available vaccine for hepatitis E. Both hepatitis delta virus and hepatitis G virus infection are found in Southwest Asia (197, 198). The same measures that are effective in preventing hepatitis B are effective against delta hepatitis. Hepatitis G virus is similar in genomic structure to HCV, but has not been shown to be pathogenic (199).

Clinical Issues

Acute viral hepatitis presents with similar symptoms, principally:

- malaise,
- nausea,
- vomiting,
- abdominal pain,
- dark urine,
- light-colored stools, and
- jaundice.

The incubation period for acute viral hepatitis ranges between 3 and > 12 weeks. Therefore, symptoms can begin months after exposure. During diagnosis of acute cases of hepatitis among combat troops and peacekeepers, leptospirosis must be ruled out because this bacterial infection is a treatable cause of acute jaundice (200). There is no specific therapy for acute viral hepatitis, but there have been recent advances in the treatment of chronic hepatitis B and C (201).

Note: Viral hepatitis should not be a major problem for recently deployed Western troops. Only in the event of a major breakdown in sanitation would hepatitis E pose a threat for combat personnel.



Leishmaniasis

U.S. troops are at risk of leishmaniasis in Iraq.

Leishmaniasis is a zoonotic protozoan infection that is endemic throughout Southwest Asia (202). Currently, leishmaniasis is epidemic in Afghanistan, including the capital, Kabul. Leishmaniasis is also found in Iraq (11, 12 at pages 39-44). This parasitic infection results in a broad spectrum of clinical disease, with both visceral leishmaniasis (kala-azar) and cutaneous leishmaniasis occurring in this region.

Cutaneous leishmaniasis is the most common form in Southwest Asia. In contrast, visceral disease is rarely reported. Cutaneous leishmaniasis can cause significant morbidity when untreated (203).

Note: Cutaneous leishmaniasis affected 20 of 700,000 U.S. troops deployed in “Operation Desert Storm” to Saudi Arabia, Kuwait, and Iraq during 1990-1991 (15, 204).

Note: During “Operation Desert Shield” and “Operation Desert Storm” in 1990-1991, an unusual viscerotropic form of disease caused by Leishmania tropica was diagnosed in 12 U.S. soldiers, but no other Coalition military personnel (15, 204). There have been no additional cases of viscerotropic Leishmaniasis diagnosed among U.S. veterans of “Operation Desert Storm” in over 10 years.

Cutaneous leishmaniasis also affected Russian troops deployed to South-Central Asia in the 1980's (205). *Leishmania tropica* (*L. tropica*) and *Leishmania major* (*L. major*) are the etiologic agents of cutaneous disease in this region (202, 206).

Leishmania donovani (*L. donovani*) has been reported as the regional causative agent of visceral disease.

Sand flies of the genus *Phlebotomus* are the vectors that transmit both the *Leishmania* parasite among mammalian hosts and the sand fly fever virus. *Phlebotomus papatasi* is the vector species that transmits *L. major* throughout most of the Middle East and is present in South-Central Asia (202).

Phlebotomus sergenti has recently been identified as the vector for *L. tropica* in Afghanistan (207). Sand flies are small (2–3 mm long and < 1 mm wide) nocturnal biting

midges and may be associated with human habitation. Sand flies are weak and noiseless flyers that travel in short hops at low levels. They rarely travel > 100 meters from their resting and breeding places. The size of the *Phlebotomus* population strongly correlates with rainfall in the previous winter.

Afghanistan

Cutaneous leishmaniasis was first reported in Afghanistan in 1964, and the country has recently endured a severe and prolonged epidemic (208), including Kabul, the capital. In Kabul, only 31 cases were identified in 1964, but that number had swelled to 8500 cases by 1990. In 1996, it was estimated that 270,000 of Kabul's 2 million people were infected (209). Cutaneous leishmaniasis has been reported from most provinces of Afghanistan and can be presumed to be ubiquitous (210). Cutaneous leishmaniasis due to *L. tropica* infection has been defined as an emerging disease in parts of northeast Afghanistan and northwest Pakistan (203).

Outbreaks in refugee camps indicate that cutaneous leishmaniasis caused by *L. tropica* may be carried by refugees into areas previously unaffected by the disease (210). Cross-border movement is common and thought to enhance outbreaks around refugee camps. In one Afghan refugee camp in Pakistan, 38% of 9200 inhabitants had active lesions, and another 13% bore the scars of past infection (210).

Although the current epidemic is limited to cutaneous leishmaniasis, endemic foci of visceral leishmaniasis have been reported from Kabul and Badghis provinces (211, 212). Endemic foci of leishmaniasis have also been reported in Uzbekistan, Turkmenistan, and Tajikistan (205, 213).

In general, the age distribution of *Leishmania*-infected individuals reflects that of the Afghan population (208). Sand flies exist both inside and outside the home (210), but most transmission takes place in the home (209). Research suggests that living in the lower 2 stories of 5-story apartment buildings carried the greatest risk, suggesting limited vertical movement of the vector (209). High household occupancy is also a risk factor, with cases clustered in households (208).

Iraq

Both visceral and cutaneous leishmaniasis have been reported in Iraq due to *L. donovani* and *L. major*, respectively (214, 12 at page 42). *L. tropica* also is transmitted in Iraq (12 at page 39). ***As stated at the beginning of this section, U.S. troops are at risk of leishmaniasis in Iraq.*** The number of cases of leishmaniasis increased in the early 1990's in Iraq due to a shortage of proper insecticides, spraying machines, and other supplies and equipment (11, 12 at pages 39-44).

Clinical findings of cutaneous leishmaniasis

The incubation period is 2–8 weeks, although rarely it can be as long as 12–18 months. The lesion begins as an erythematous nodule at the site of the bite and slowly enlarges over several months. It eventually ulcerates, having a firm raised border with a crusted center (204).

- 80% of those infected have one or two lesions present
 - 45%, with most lesions occurring on the head,

- 26%, the hand or wrist, or
- 19% the lower arm, ankle, or foot.

Clustering of lesions is due to multiple bites from a single infected sand fly.

The mean size of the lesions is 2–3 cm (202). Dissemination is rare. The mean duration of active lesions is about 5 months and usually not longer than 12 months (204). Healing results in scar formation and generally gives life-long immunity (204). One report suggests that cutaneous leishmaniasis can be more frequent and severe in travelers from areas where the disease is not endemic (206).

Clinical findings of visceral leishmaniasis

Visceral leishmaniasis (kala-azar) is a chronic systemic disease with a prolonged incubation period of 2–8 months; rare patients have an incubation period of up to 2 years.

- Onset is gradual and consists of
 - fever,
 - weakness,
 - weight loss,
 - lymphadenopathy,
 - pancytopenia, and
 - hepatosplenomegaly.

Untreated, visceral leishmaniasis progresses to severe pancytopenia and may lead to death from hemorrhage or superinfection (215).

As noted, a less severe, viscerotropic form of leishmaniasis caused by *L. tropica* was found in 12 U.S. service members deployed during “Operation Desert Storm”. Clinical findings in these patients included fever, fatigue, abdominal pain, mild splenomegaly, adenopathy, and mild anemia. No skin lesions were found, and one patient was asymptomatic. Diagnoses were made on culture of bone marrow (204). No subsequent cases have been identified in the Middle East, and no cases have been noted in Central Asia.

Diagnosis

Leishmaniasis, especially if atypical or visceral, can present a diagnostic challenge; the likelihood of a successful diagnosis is inversely related to the duration of disease. Diagnostic tests include microscopic examination of a smear from the cutaneous lesion (to identify amastigotes), histological punch biopsy, and culture on special media (such as Novy, MacNeal, Nicolle). A smear from the nodular margin of the most active lesions should be obtained with scalpel or syringe, fixed in methanol, and stained with Giemsa. PCR is being increasingly used to aid in diagnosis (210). Serological and skin tests are available, but are not helpful in diagnosing acute cutaneous disease.

Treatment

Untreated, cutaneous lesions usually heal with some scarring.

Traditional therapy consists of a pentavalent antimonial agent (meglumine antimoniate or sodium stibogluconate) at a dose of 20 mg/kg/day for 20–28 days by slow IV infusion, but the antimonials are extremely toxic (216). Considerable data support the use of amphotericin compounds. Liposomal amphotericin has been approved for use in visceral leishmaniasis by the U.S. Food and Drug Administration (FDA), but has limited use because of high costs (217-219). Amphotericin B deoxycholate might be effective in complicated cutaneous leishmaniasis, although supporting data are limited (219).

Other potential second-line therapies for visceral disease include:

- pentamidine,
- miltefosine, and
- paromomycin (220).

Promising oral options for cutaneous disease include:

- ketoconazole,
- fluconazole,
- miltefosine,
- itraconazole, and
- dapsone (219, 220).

Before ulceration of cutaneous lesions, treatment can be attempted with intralesional injections with sodium stibogluconate or with cryotherapy. Optimal treatment of complex or visceral disease usually requires care in a tertiary medical care facility, because available therapies have substantial toxicity.

Prevention

Prevention measures include personal protection to limit sand fly bites, rodent control, and residual insecticide spraying. Sand flies can penetrate the mesh of mosquito nets, but application of permethrin enhances efficacy of nets. Fans can also reduce the ability of sand flies to bite. Flies cannot bite through cloth; thus, permethrin-treated, military uniforms should prove efficacious. DEET should be applied to all exposed skin surfaces, particularly about the face and ears, and especially at night. Indoor spraying is also effective (209).

DANGER

Drug therapy is toxic and should be limited to visceral disease or large, multiple, or mobility limiting cutaneous lesions.

CAUTION

These oral options are neither widely used in the region nor FDA approved for this indication.



Arboviral Diseases

Crimean-Congo Hemorrhagic Fever

CCHF is distributed widely throughout Asia, Europe, and Africa, and recent outbreaks of CCHF have occurred in Afghanistan and Pakistan (221).

The mortality rate from CCHF is about 30% (range, 15% to 50%), with deaths occurring between days 5 and 14 from onset of symptoms (234).

Crimean-Congo hemorrhagic fever (CCHF) is a zoonotic hemorrhagic fever caused by a virus of the bunyavirus family, which also includes Hantavirus and sand fly fever virus. The disease is transmitted by ticks, body fluids, and tissues from infected animals. Individuals with significant outdoor exposure, as well as butchers, abattoir workers, and veterinarians, are at increased risk of infection. Secondary human cases may occur among household members as a result of contact with infected body fluids from ill patients. Because nosocomial transmission is well described, health care personnel should use appropriate contact isolation.

Epidemiology

CCHF was first described in the Crimea in 1944. A virus later isolated from the Congo was found to be the same pathogen, resulting in the name Crimean-Congo hemorrhagic fever virus. Ixodid ticks may become infected with the CCHF virus either through transovarial transmission or through taking a blood meal from an infected animal (222). Many animal species are infected, but apparently, only humans develop illness (223). The illness has a predictable seasonality in some locations as a result of seasonal tick activity (224). It appears that most humans are infected as a result of tick bite, although direct contact with infected animals or people can occasionally result in infection. Except for one study conducted in Russia, it has been assumed that the number of asymptomatic cases is low (223).

Regional information

Recent Outbreaks

1. Forty-seven cases of CCHF were identified in the frontier area on the Afghan-Pakistani border in October 2001 (225).
2. Pakistan in late February of 2002 killed at least 3 people.
3. The U.N. reported in March 2002 that an outbreak of unknown hemorrhagic fever killed 28 people in eastern Afghanistan (226).

4. An outbreak in May-July 2000 in Gulran District, Afghanistan caused 15 deaths (227).
5. Quetta, Pakistan, had nosocomial transmission during a 1994 cluster (228).

CCHF has been reported in Iran (82, 229), Turkmenistan, Russia, the Middle East, Africa, and Eastern Europe. *CCHF has been reported sporadically in Iraq* (12 at page 20, 230-232).

Clinical findings

The incubation period following direct contact with infected blood or tissue is usually 3–6 days, with a maximum of 13 days (223, 233). The incubation period after the bite of an infected tick is 2–12 days.

Symptoms are sudden in onset include:

- fever,
- chills,
- headache,
- myalgia,
- dizziness,
- neck pain and stiffness, and
- photophobia.

Other symptoms include:

- back or leg pain may be severe,
- nausea and abdominal pain, possibly with diarrhea, may be present, and
- behavioral changes may occur.

Patients may also present with:

- flushed facies,
- conjunctival injection,
- pharyngeal hyperemia, or
- palatal petechiae (234).

Hepatomegaly occurs in about 50%. Fever is intermittent, and patients may be febrile on presentation (233).

Within 3–6 days:

- patients may develop hemorrhagic signs.

By the end of the first week, most patients are severely ill, with multiple organ involvement.

- Encephalopathy
- hepatic insufficiency
- renal failure
- pulmonary edema and capillary leak syndrome are common in severe cases

As stated at the beginning of this section, the mortality rate from CCHF is about 30% (range, 15% to 50%), with deaths occurring between days 5 and 14 from onset of symptoms (234).

Laboratory findings and diagnosis

Abnormal laboratory test results include elevated hepatic transaminase levels, thrombocytopenia, lymphopenia, evidence of disseminated intravascular coagulation (DIC), and elevated creatinine level. Diagnosis may be obtained by isolation of virus in blood or tissue samples, either by cell culture or by inoculation of a specimen into suckling mouse brain. PCR-based methods have recently been used successfully in diagnosis as well. Pathological specimens can be tested by fluorescent antibody staining.

Note: Serological assays are available for diagnosis of CCHF and were used in the field in both U.S. Desert Storm and Somalia deployments, but no cases were found.

ELISA seems to be the most sensitive serological method, followed by reversed passive hemagglutination-inhibition, immunofluorescent antibody assay, and complement fixation (235).

Treatment

Supportive therapy is the mainstay of therapy for CCHF. Most patients require monitoring in an intensive care unit for respiratory and hemodynamic support. The antiviral drug ribavirin has been used in treatment of established CCHF, with some published data supporting its use (236). The appropriate dosage of ribavirin is not well defined, The Centers for Disease Control and Prevention (CDC) recommends:

- Ribavirin IV
 - 50–100 mL infused over 30–40 minutes with a loading dose of 30 mg/kg (maximum dose, 2.64 g),
 - followed by 16 mg/kg (maximum dose, 1.28 g) IV q 6 hours for 4 days and
 - then 8 mg/kg (maximum dose, 0.64 g) IV q 8 hours for 6 days (for 10-day treatment) (236).
- Ribavirin oral dose (if the IV formulation is unavailable)
 - 2 g loading dose,
 - followed by 1 g orally q 6 hours for 4 days, and
 - then 500 mg q 6 hours for 6 days (total of 10 days).

CAUTION

Ribavirin therapy commonly causes hemolytic anemia and it is teratogenic (237).

Convalescent immune serum from previously infected patients has been used for treatment (238), but may not be available. The advisability of heparin therapy is controversial (234). Treatment of exposed health care workers with ribavirin should be considered (237). The CDC recommends a post-exposure prophylactic dose of 500 mg q6h for 7 days.

Prevention

For the individual:

- use of effective personal protective measures against tick bites and limiting animal exposure are the best ways to avoid infection,
- use of permethrin impregnated clothing and gear,
- tucking trousers into boots or socks,
- wearing light-colored clothing to facilitate tick identification,
- use of effective DEET insect repellants on exposed skin, and
- daily skin inspection for ticks (“buddy checks”) are mainstays of prevention.

Health care setting:

Nosocomial spread setting is possible, and appropriate universal precautions should be observed in the patient care areas and the laboratory.

- suspected patient should be placed in a private room,
- negative-pressure respiratory isolation should be considered,
- anyone entering the patient’s room should wear gloves and gowns, and
- those approaching within 1 meter should wear face shields or surgical masks and eye protection to prevent contact with blood or other body fluids (239).

The risk of nosocomial spread is greater with severely ill patients.

West Nile Virus Infection

West Nile virus is a member of the Japanese encephalitis group of flaviviruses and is found throughout Asia, Europe, the Middle East, and Africa.

Epidemiology

West Nile virus was first isolated in the West Nile District of Uganda in 1937. It is transmitted principally by culicine mosquitoes, but can be transmitted by other genera. A wide variety of animals can be infected. The virus typically infects young children in areas of endemicity. In temperate climates, the summertime is the peak of transmission because of increased activity of the mosquito vector.

There is no specific treatment for West Nile virus infection. Supportive care is the mainstay of medical intervention. The primary preventive measure is avoidance of mosquito bites. There is no available vaccine. The tempo of new outbreaks seems to be increasing worldwide.

Regional information

West Nile virus transmission almost certainly occurs in Afghanistan. The illness is well described in Pakistan (241, 242), Iran (243), and other neighboring countries. Antibodies to West Nile virus have been detected in the human population in Kunduz, Herat, Bamian, and Helmand provinces of Afghanistan (244). There are no current reports of West Nile virus infection in Iraq. One case of West Nile virus infection was diagnosed among Western troops during the Gulf War in 1991 (16).

Note: The West Nile virus has recently become established in the eastern United States, where it has spread rapidly, and has re-emerged in places like France (240).

Clinical findings

The infection is usually asymptomatic or, at most, causes a mild febrile syndrome. Only rarely are children affected with a more serious illness. Morbidity and mortality are generally confined to the elderly. Like many other flavivirus encephalitis agents, the ratio of encephalitic to non-encephalitic infection is very low (< 1%). Life-long immunity is conferred by infection.

The incubation period for West Nile virus infection is 3–6 days. Symptomatic disease is usually a febrile, flu-like illness with abrupt onset and moderate or high fever. Typical symptoms (in roughly descending order of frequency) consist of:

- headache,
- myalgias,
- arthralgias,
- maculopapular rash (in some outbreaks the rash is infrequent),
- facial flushing,
- sore throat,
- lymphadenopathy (also of variable frequency),
- conjunctivitis,
- ocular pain, and/or
- gastrointestinal symptoms (245).

In a small number of cases, acute aseptic meningitis or encephalitis can occur, which is associated with:

- neck stiffness,
- vomiting,
- confusion,
- somnolence,
- tremor of extremities,
- abnormal reflexes,
- convulsions,
- pareses, and
- coma.

Recovery is generally complete in non-fatal cases, but less rapid in adults than in children, and is often accompanied by long-term myalgias and weakness. Most fatal cases have been recorded in patients 50 years of age or older. Some authors have noted that the most recent outbreaks appear to have greater virulence than past reports (240, 245).

Laboratory findings and diagnosis

There are no pathognomonic laboratory findings of West Nile fever. Blood analysis may reveal mild leukocytosis. In patients with meningitis or encephalitis, the cerebrospinal fluid (CSF) may show moderate lymphocytic pleocytosis and elevated protein levels (245). MRI can also suggest acute infection (246). The virus can be isolated from the blood during the early phases of the infection, usually by inoculation into cell culture or suckling mouse brain. The virus can be recovered from the blood of immunocompetent febrile patients for up to 10 days and from blood of immunocompromised patients as late as 22–28 days after infection. Peak viremia occurs 4–8 days after infection.

Serological diagnosis is also available, although cross-reactivity with other flaviviruses is a problem. The most commonly used test is the IgM capture ELISA, but the reference standard is the plaque reduction neutralization test with acute and convalescent serum (247). CSF should be sent for IgM ELISA and PCR testing, although PCR yields positive results for only 50%–60% of confirmed cases (248). The American Red Cross began screening donated blood for West Nile virus infection in July 2003.

Sand Fly Fever

Sand fly fever viruses are in the *Bunyaviridae* family, as are CCHF virus and Hantavirus. The sand fly fever virus complex comprises a large number of species. In the Old World, three species are notable:

1. Toscana,
2. Naples, and
3. Sicily viruses.

A disease of military relevance, debilitating outbreaks have occurred among foreign troops in areas of endemicity, including U.S. and British troops stationed in the Middle East during WWII (249). Up to 20% of some Allied military units were briefly incapacitated by sand fly fever during WWII (250).

TREATMENT and PREVENTION

As stated in the beginning of this section, there is no specific treatment for West Nile virus infection. Supportive care is the mainstay of medical intervention. The primary preventive measure is avoidance of mosquito bites. There is no available vaccine.

Sand fly fever viruses are health threats in Afghanistan, Iraq, and surrounding regions.

Natural history

The sand fly viruses are transmitted via the *Plebotomus* sand fly. In Central Asia, the sand fly is frequently found in association with burrowing rodents and is a poor flier. Consequently, the illness tends to be focally distributed (251). The epidemiology is similar to that of leishmaniasis, which is transmitted by the same sand fly vector. Solid immunity is conferred by infection. Most inhabitants of regions of endemicity are infected during childhood with this self-limited illness. However, the introduction of large numbers of naive hosts — like military personnel — into areas of endemicity may result in outbreaks of sand fly fever.

Regional information

In Afghanistan, the Sicily and Naples viruses are both prevalent (244). Iran, Pakistan, and the former Soviet republics of Central Asia have also documented transmission of these viruses as well (252, 253). Much of what is known of their epidemiology was elucidated during the Soviet occupation, when both Sicilian and Neapolitan sand fly fever were common causes of febrile illness among deployed troops (254, 255). In Iraq, there have been no reported outbreaks of sand fly fever, but this infectious disease was a major problem for Allied troops stationed in this region in WWII. However, no cases of sand fly fever were diagnosed amongst U.S. or Canadian troops during the Gulf War (15).

Clinical findings

The illness caused by sand fly fever virus is largely a non-specific flu-like illness, with an incubation period of approximately 3–6 days. In 17 experimentally infected volunteers, all experienced fever of about 3 days duration. Headache, myalgias, and low back pain were common, and photophobia, chills, nausea, and vomiting were noted in some patients (256). The Soviet literature describes a dengue-like presentation that was sometimes incapacitating for a few days (254, 255).

Laboratory findings and diagnosis

Serological testing is the most practical means of making the diagnosis (257). The virus can be cultured from blood of acutely ill patients. Leukopenia is a common laboratory abnormality (256).

Note: There is no antiviral treatment for sand fly fever, and supportive care is all that is required for this self-limited illness.

Treatment and prevention

Sand fly control measures will protect against infection. Because sand flies are not strong fliers, they will land on walls and other surfaces near their blood meals; therefore, contact insecticides can be

effective. Personal protective measures, such as wearing long-sleeved clothing impregnated with permethrin and using DEET-containing repellent on exposed skin, will assist in preventing exposure. Mosquito netting must be of fine mesh to be effective. Local fogging with insecticide may assist in controlling sand flies in fixed-area housing, such as encampments.

Traditional sand fly control measures in Central Asia have involved control of the rodent host (251).

Possible Regional Arboviral Diseases

Tick-borne Encephalitis

Tick-borne encephalitis (TBE) has not been specifically reported in Afghanistan, although it could occur there. Historically, the illness has been present in Central Russia and many of the former Soviet republics. TBE is not thought to be present in Iraq. The flavivirus of TBE is transmitted in Central Asia by the *Ixodes persulcatus* complex ticks. The virus circulates between the tick vector and rodent and insectivore hosts. People can be infected by tick bite, oral ingestion of virus, or aerosol (258).

The clinical course of TBE is frequently noted to be biphasic. Symptoms begin after 3–7 days of incubation, with fever, headache, myalgias, and malaise up to 1 week in duration. There are no specific symptoms in this first phase of illness to suggest TBE, and most persons recover. However, a significant percentage relapse with meningitis or meningoencephalitis in the second phase. Serological methods, particularly ELISA, are the most practical and widely used method of diagnosis. No specific treatment is available for TBE. There is an effective vaccine; however, it is not licensed in the United States.

Hantavirus Syndromes

Korean hemorrhagic fever first gained the attention of the Western world during the Korean War, when 13,000 cases were reported (259). The causative agent was identified in 1976 and named Hantaan for the river along the 38th parallel between North and South Korea. Since that time, further study has revealed a number of Hantaviruses causing renal or pulmonary syndromes around the world. The agent is transmitted to humans through inhalation of rodent excreta (259).

Antibodies to Hantaan virus have been demonstrated in India and Iran (259). The central Asian former Soviet republics are likely to harbor Puumala and Hantaan viruses. The Hantaviruses are not known to occur in Afghanistan or Iraq.

The clinical presentation of Hantavirus infection is variable and difficult to recognize (260). The infection is diagnosed by serological testing (259). Treatment involves both supportive care (including dialysis if needed) and ribavirin (261). The best means of prevention is avoidance of rodent habitats and protection against inhalation of contaminated dust or aerosols.

Sindbis Fever

Sindbis fever, or Okelbo fever, has a very wide geographic distribution, including Africa, the Middle East, Europe, Asia, and Australia. Clinical disease has not been identified in Afghanistan, but seroconversion has been demonstrated in Kunduz and Helmand provinces of Afghanistan (244).

There are no reports of Sindbis fever in Iraq, and very little Sindbis virus seroconversion was detected in one large serosurvey in Iran (243). The ecology of the Sindbis virus is similar to that of West Nile virus. Sindbis virus infection causes a maculopapular rash, a multi-articular arthritis, and constitutional symptoms.

Chikungunya Virus Infection

This viral infection may occur sporadically in both Iraq and Afghanistan, but has not been demonstrated in either location. Seroconversion to this virus has been noted in Helmand Province of Afghanistan, but there are no reports from Iraq (244). The virus causes a dengue-like illness with prominent arthralgias.

Bhanja Virus Illness

This tick-borne Bunyavirus is found in India, Pakistan, Central Asia, and also Eastern Europe and Africa (262). The presence of Bhanja virus in countries both immediately north and south of Afghanistan implies its presence within this country. However, the medical significance of this infection is not great. The illness is a self-limited febrile syndrome.

Issyk-Kul Virus Infection

This virus causes a non-specific viral syndrome and is found in the former Soviet republics north of Afghanistan (263). It has not been documented in Afghanistan. It seems to be associated with bats. Like Bhanja virus, it does not have a high rate of transmission to humans and should not be a significant medical concern if present.

Syr-Darya Virus Infection

This virus has been identified in Kazakhstan and has been associated with a summertime febrile syndrome (264). The geographic distribution of this virus is not clear, but it is unlikely to be a significant medical concern.

Other Arbovirus Infections

A large number of arthropod-borne viruses, including Isfahan, Wad Medani, Dera Ghazi Khan, Wanowrie, and other viruses, have been isolated in areas near Afghanistan (265). To date, the clinical significance of these viruses is unclear, but they are unlikely to have great clinical impact. Rift Valley fever is not known to occur in Afghanistan. Likewise, Kyasanur Forest virus, Omsk hemorrhagic fever virus, and Japanese encephalitis virus are not thought to be present, despite nearby areas of endemicity (244). Last, dengue is not clinically observed in Afghanistan, but the illness is present in both India and Pakistan (244). There are no published reports of any of these viral infections in Iraq.



8 Respiratory Diseases

Acute respiratory disease is a major cause of morbidity and mortality in Afghanistan and Iraq.

Typhoid fever often presented as a pneumonia among Soviet troops and should be considered in the local differential diagnosis of cough and fever.

Overcrowding, mass population movements and a collapse of vaccination programs all enhance the spread of respiratory tract infections throughout these countries. Recent data from Afghanistan have established lower respiratory tract infections as one of the leading causes of death in children < 5 years old (6, 82). Similarly, lower respiratory tract infections are the leading cause of death among young children in Iraq (12 at pages 6 and 8).

Outbreaks of pertussis and other common childhood diseases (12 at page 58) occurred in the 1990's in Iraq in association with deterioration of economic conditions (266).

Currently, laboratory facilities and disease reporting remain inadequate to define most respiratory infections in Southwest Asia. Given low immunization rates and limited public health capabilities, vaccine-preventable diseases, such as measles, influenza, pertussis, and diphtheria, are common. In Iraq, the number of cases of diphtheria increased substantially during the 1990's (12 at page 28). Influenza has been a major problem in Afghanistan (267, 268).

Respiratory diseases have long been recognized as major military health threats, capable of disrupting military operations (269). Adenoviruses, influenza virus, *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, and *Bordetella pertussis* have traditionally been the major agents. Recent U.S. military outbreaks of influenza (270), pertussis (271), and pneumococcal disease (272) demonstrate the power of these pathogens to alter military training and deployments. During the Gulf War in 1991, acute respiratory infections were one of the two most prevalent causes of medical problems among Coalition troops (16).

The Soviet army during its Afghan campaign had extraordinary high rates of pneumonia and bronchitis. Novozhenov and Gembitskii (273) reported that 43% of personnel deployed to Afghanistan contracted acute pneumonia during their first year. Although pulmonary illness affected Soviet personnel year-round, most respiratory disease occurred during the fall and winter seasons. As stated at the beginning of this section, typhoid fever often

presented as a pneumonia among Soviet troops and should be considered in the local differential diagnosis of cough and fever.

Prevention of respiratory tract infections in the military setting hinges on vaccination against influenza virus and, in some circumstances, pneumococci, and adenovirus (270). A recent U.S. Marine Corps outbreak of pneumococcal pneumonia was interrupted by the use of vaccination and azithromycin prophylaxis (272). Short-term antibiotic prophylaxis with azithromycin has also been shown to be effective in preventing respiratory infections in selected high-risk situations (274). Anti-influenza drugs may be useful if antigen drift renders the influenza vaccine less effective and outbreaks occur (270).



Tuberculosis

Although the U.S. military does extensive screening of troops for TB, this is one chronic disease that could manifest itself among veterans long after the conflict in Afghanistan and Iraq. Therefore, TB should be considered in the differential diagnosis of veterans returning from Southwest Asia who present with pulmonary disease or fever.

Note: Military personnel, peacekeepers, and humanitarian workers should avoid local milk and cheese products, which can also transmit brucellosis and Q fever.

The incidence of *Mycobacterium tuberculosis* (*M. tuberculosis*) transmission has always been one of the best mirrors of the socioeconomic conditions of a society (275). Tuberculosis is highly endemic in Southwest Asia and should be considered a serious threat to relief workers and others who are in close contact with the local population. Disease associated with infection by the closely related *Mycobacterium bovis* are commonly attributed to consumption of unpasteurized milk products.

As of 1997, the overall prevalence of tuberculosis in Afghanistan was 753 cases per 100,000 population, with 35% of the population latently infected. The estimated annual incidence of active tuberculosis in 2001 was 325 per 100,000, about 50 times the year 2000 U.S. tuberculosis incidence of 6/100,000 (82). WHO described the

tuberculosis situation in Pakistan in 1997 as "one of the worst in the world." Of note, a 1995–1998 study in Rawalpindi found that 52% of isolates were resistant to > 1 standard therapeutic agent, including ethambutol, isoniazid, and rifampin (276, 277).

In Tajikistan, the poorest of the former Soviet republics, the incidence of reported tuberculosis increased from 30 per 100,000 in 1995 to 105 per 100,000 in 2001 (278). The tuberculosis crisis in the Aral Sea area — bordered by Kazakhstan, Uzbekistan, and Turkmenistan — is considered by WHO to be the worst in the former Soviet Union (279). In Kazakhstan, studies in 1993 found 66% of isolates resistant to streptomycin. In Uzbekistan, after a declining period in the mid-1980s, morbidity and mortality rates from tuberculosis increased dramatically beginning in the mid 1990's (280, 281). Rates of multidrug-resistant tuberculosis are currently undefined for lack of capable regional laboratory facilities (282).

Kyrgyzstan's officially reported incidence of 119 cases per 100,000 population in 1997, ranked as the highest among countries of the former Soviet Union (283). Tests performed between 1985 and 1987 showed high levels of initial and acquired drug resistance in both urban and rural areas. Patients are frequently not treated with standard regimens, and isoniazid and rifampicin are often alternated to make scarce drugs go further (284).

Tuberculosis also is known to be widespread in Iraq (12 at pages 70-73). While less than some other Southwest Asian nations, Iraq has also seen critical increases in tuberculosis rates in the last decade due to a deterioration of the socioeconomic status of the population (12 at page 6). Cases increased in Iraq from 46 new cases in 1989 to 132 in 2000 per 100,000 population (12 at page 71). In Baghdad, over the last 50 years numerous cases of sudden death were attributed at autopsy to bilateral cavitary tuberculosis (285). The number of new cases nearly tripled from 46 per 100,000 in 1989 to an estimated 132 per 100,000 in 2000. One cause of the increase was thought to be interruption in supply of medications used for directly observed therapy (12).

Regimens of 5, 6, or 7 drugs may be indicated in patients with a history of prior treatment for TB, but multi-drug-resistant TB (MDRTB) is best treated by clinicians experienced with this medical problem. Anticipated medication course is 18 to 24 months or 12 months after culture-negative. Empiric therapy for suspected MDRTB includes:

- isoniazid,
- rifampin,
- ethambutol,
- pyrazinamide,
- an aminoglycoside or capreomycin,
- a fluoroquinolone, and
- either cycloserine, PAS or ethionamide (286).

Bacille Calmette-Gue ´rin vaccination may be effective in preventing severe manifestations of tuberculosis in children, such as tuberculosis meningitis. U.S. military personnel do not receive bacilli Calmette-Gue ´rin vaccination.

TREATMENT RECOMMENDATION

Given the high rates of resistance to isoniazid and streptomycin among M. tuberculosis strains in Southwest Asia, treatment of tuberculosis cases in this region should include isoniazid and rifampin, plus at least one other drug, all to be given as directly observed therapy.

Common choices for the additional drug include pyrazinamide or ethambutol. A 4-drug regimen containing isoniazid, rifampin, ethambutol, and pyrazinamide is optimal pending results of mycobacterial susceptibility testing.



10

Rickettsial Type Diseases

Coalition troops are at risk of Q fever in both Afghanistan and Iraq.

Q Fever

Coxiella burnetii (*C. burnetii*) is the causative pathogen of Q fever. Q fever is a worldwide zoonosis consisting of

pneumonia, hepatitis, and occasionally meningoencephalitis or endocarditis. Many animal species can be infected, but sheep, goats, and cattle are the principal reservoirs. Urine, feces, milk, and especially placental tissues are potentially infectious. Humans are most frequently infected by inhalation of aerosolized body fluids from infected animals. The infectious dose of *C. burnetii* is exceptionally low—a single organism can cause illness (287).

Epidemiology

Q fever is not commonly diagnosed, but outbreaks of disease are regularly reported. Parturient animals shedding *C. burnetii* may be associated with outbreaks, but patients ingesting raw milk products are also at risk. It should be noted, however, that the pattern of clinical illness varies regionally, with a non-specific febrile syndrome, pneumonia, or hepatitis reported to be the most common presenting features of Q fever (288). A significant number of cases are presumably sub-clinical (289).

Note: Three possible cases of Q fever occurred among the 700,000 U.S. troops participating in the 1991 Gulf War (16, 290).

Regional information

A serosurvey in domestic animals revealed antibodies to *C. burnetii* in Balkh, Kunduz, and Baghlan provinces of Afghanistan (244). Q fever undoubtedly occurs in Iraq but there are no recent reports about the

incidence of this infectious disease. ***As stated at the beginning of this section Coalition troops are at risk of Q fever in both Afghanistan and Iraq.***

Clinical findings

Clinical Q fever can be divided into acute and chronic syndromes. The acute illness may be a non-specific febrile illness, pneumonia, hepatitis, or a combination thereof. The febrile syndrome has no particular identifying features. Rash, the usual hallmark of Rickettsial illness is generally absent. The pneumonia is variable and can present as an "atypical pneumonia," or

as a classic picture of multiple round, segmental opacities. Pleural-based opacities are common. Q fever hepatitis may present as a typical mild acute infectious hepatitis. Liver function testing yields abnormal results for a majority of Q fever patients, however. In rare cases, Q fever may present as acute or chronic meningitis or encephalitis (288, 291). Chronic Q fever generally manifests as endocarditis, granulomatous hepatitis, or vertebral osteomyelitis (292).

Treatment

The treatment of acute and chronic Q fever is significantly different. For acute forms, single-agent therapy with doxycycline is usually effective and is preferred to tetracycline (293). Treatment is generally given for 14 days. Alternative treatments are rifampin or fluoroquinolones. Chronic Q fever requires prolonged antibiotic courses, and valve replacement may be needed for endocarditis.

Diagnosis

Isolation of the pathogen is not advised except in specialized laboratories. Acute Q fever is usually diagnosed by demonstration of a 4-fold rise in antibody titer between acute and convalescent serum. Complement fixation, microimmunofluorescent antibody assay, and ELISA are all used for this purpose (288).

Prevention

Avoidance of unpasteurized milk and cheese and protection against ticks are effective prevention strategies, but prevention against the aerosolized pathogen is difficult. An inactivated vaccine is used for laboratory personnel working with *C. burnetii*, but is not licensed for general use.

Note: Foreigners in Afghanistan and Iraq should not consume unpasteurized milk products because of the risk of Q fever, brucellosis, and M. bovis infection.

Scrub Typhus

Scrub typhus gained attention in Western medicine during World War II and the Vietnam War when it impacted troops operating in Southeast Asia. The pathogen, *Orientia tsutsugamushi* (*O. tsutsugamushi*), is endemic from Japan, Korea, and nearby Russia through China and Southeast Asia and westward to India and Pakistan (294). The distribution of the pathogen within this area is notably focal, where it circulates between the various rodent species and *Leptotrombidium* mites. Humans are infected on entering this cycle and develop a typical Rickettsial-type illness, with the exception that lymphadenopathy is more prominent and rash is less common than for most other Rickettsial diseases.

Natural history

O. tsutsugamushi is transmitted to humans from the larval stage of the mite. The mite is infected transovarially by feeding on an infected host. The mites

have a large number of potential hosts, but are frequently found in association with rats and related rodents. The geographic nidus of risk can be very small, but may be very densely populated with infected vectors — a phenomenon known as “mite islands” (251, 295). The nature of the “mite island” is highly variable, depending on the behavior of local vector. For example, in West Pakistan the vector can be found in semidesert, plains, and high alpine areas up to 3050 meters (296-298).

Epidemiology

The scrub typhus pathogen is transmitted year-round in tropical climates and seasonally in temperate areas. Those with outdoor exposure are at greater risk of infection. Palm plantations and “edge ecozones,” such as that created by clear-cutting a forest section; provide a good habitat for the rodents and mites. Transmission has been noted to occur as well within urban areas, like Bangkok (299). The mites are extremely small and frequently are not noticed by the host.

Regional information

Serological evidence of scrub typhus has been reported from Kunduz and Badakhshan provinces of Afghanistan, but no clinical cases have been identified (244). The illness is well described in West Pakistan in ecozones similar to those of Afghanistan (296-298). Altogether, it is reasonable to expect the disease to exist in Afghanistan, although it is undoubtedly limited in distribution. Scrub typhus is not reported from Iraq and is unlikely to be present there.

Clinical findings

After an incubation period of 6–18 days, the patient may present with sudden onset of fever, headache, myalgias, and arthralgias. Patients may have a wide variety of respiratory, gastrointestinal, or neurological complaints as well. Signs may include:

- an inoculation eschar (50%–60%),
- regional lymphadenopathy (85%–90%),
- hepatomegaly, splenomegaly, conjunctival injection (30%), and
- macular rash (34%–71%).

It is most important in suspected cases to find an eschar, which is located at the site of the mite attachment. The eschar may be located virtually anywhere on the body, appearing as an ulcer, usually with a blackened center and surrounding erythema (295). The rash is present on a minority of patients; it begins as a truncal, macular rash late in the first week of illness and spreads to the extremities.

Laboratory findings and diagnosis

Elevated hepatic transaminase levels, thrombocytopenia, and hyponatremia are possible findings, with evidence of disseminated intravascular coagulation (DIC) in severe cases. The diagnosis is generally made serologically, by indirect immunofluorescence assay, immunoperoxidase assay, or ELISA. The traditional Weil-Felix test has been largely supplanted in

most laboratories, but is still used in some countries (295). About one-half of patients will react to the OX-K antigen by 10–14 days after onset. It should be noted that the Weil-Felix test could yield false-positive results from cross-reactivity with leptospirosis, relapsing fever, or urinary tract infections caused by *Proteus* species.

Treatment

The treatment of choice is tetracycline (500 mg q.i.d.) or doxycycline (100 mg b.i.d.) for 7 days (295). If a therapeutic response has not occurred within 72 hours, another diagnosis should be entertained, except in doxycycline-resistant locations. Chloramphenicol has been a traditional therapy and is also effective. Azithromycin and fluoroquinolones have *in vitro* activity and have been successfully used for treatment. Of note, some cases of doxycycline- and chloramphenicol-resistant scrub typhus have been identified over the past decade in northern Thailand. A recent study shows that rifampin at 600–900 mg/day was effective (300).

Prevention

The use of doxycycline at doses of 200 mg once a week will prevent scrub typhus infection. Post-exposure prophylaxis at the same dose is also effective, but should be continued for 6 weeks. Doxycycline in dosages (100 mg/day) used for malaria prophylaxis is also effective. Avoidance of mite-infected areas is the best means of prevention. Personal protective measures, such as permethrin-sprayed clothing and application of DEET, will lower attack rates.

Spotted Fever Rickettsial Diseases

Two spotted fever illnesses are recognized in Afghanistan: Siberian tick typhus and Mediterranean spotted fever. Two other pathogens, *Rickettsia mongolotimonae* (*R. mongolotimonae*) and Astrakhan fever rickettsia, have unclear distribution (301).

Another rickettsia, labeled JC 880, has been isolated from Pakistan, but its pathogenic status is not fully known (302).

Siberian tick typhus and Mediterranean spotted fever occur within Afghanistan. Mediterranean spotted fever is thought to be present in Iraq.

Geographic information

Rickettsia conorii (*R. conorii*), the agent of Mediterranean spotted fever, is widespread, and is found in Africa, the Mediterranean basin, India, Pakistan, and eastern Russia. The pathogen is transmitted by ixodid ticks of various species, depending on the location. As with scrub typhus and most other spotted fever rickettsiae, the pathogenic lesion is a vasculitis. Siberian tick typhus (*R. sibirica*) is found in Central Russia, Pakistan, and China. Astrakhan fever has been recognized as a clinical entity since 1983, but only recently found to be caused by a rickettsia similar to *R. conorii*. The region of known transmission borders the Caspian Sea.

Siberian tick typhus and *Mediterranean spotted fever* pathogens have been isolated near the Pakistani-Afghan border (302), and significant numbers of Afghans have seroconverted to a spotted fever rickettsia in a number of locations in the country (244). *Mediterranean spotted fever is thought to be present in Iraq*. The other rickettsiae mentioned have not been isolated in or near Afghanistan or Iraq, but are included as possibilities.

Clinical findings

Mediterranean spotted fever is the more serious of the spotted fever illnesses found in the region. The symptoms are typical of a spotted fever illness, with sudden onset of headache, fever, and myalgias. An eschar is frequently present, and a petechial rash may appear. Siberian tick typhus has a similar presentation, but is milder and not thought to be fatal. Mediterranean spotted fever can be fatal in 2% to 3% of those infected, particularly the elderly, or those with underlying illness (301).

Laboratory findings and diagnosis

Transaminitis, thrombocytopenia, and hyponatremia are possible findings on routine laboratory tests. Evidence for DIC may be seen in more severe cases. The diagnosis is usually made by detection of spotted fever group antibodies. Routine spotted fever serology does not generally distinguish between spotted fever group rickettsiae, although some research laboratories may have this capacity. Likewise, PCR testing or culture for the acutely ill patient or the tick vector may not be available except in a research setting.

Treatment and Prevention

Doxycycline is the treatment of choice for these pathogens. It is likely most patients could be cured with a single dose of doxycycline, but patients should be treated until symptoms resolve. The use of personal protection measures and other means to avoid tick attachment should suffice to prevent exposure to these pathogens (301).

Epidemic typhus is a historically important disease of populations compromised by war or famine, conditions currently present within Afghanistan and Iraq. It is caused by *Rickettsia prowazekii*.

Epidemic Typhus

The bacterial pathogen is transmitted by the bite of the common body louse. Lice are predictably present in conditions of poor hygiene, overcrowding, and poverty. The spread of typhus is enabled by wintertime conditions, which favor close contact and less-frequent clothing changes. Man is the

primary reservoir, but other animal reservoirs, including flying squirrels, have been identified.

Regional information

The disease is probably present in Afghanistan, with anecdotal reports of cases and documented seroconversion to typhus antigens among the population (244). There are no current reports of epidemic typhus in Iraq.

Clinical findings

After an incubation period of about one week, illness begins abruptly with fever, chills, headache, and myalgias. The illness becomes more severe, and the patient may be confined to bed, with unremitting fever and rash starting toward the end of the first week. The rash classically begins on the trunk and spreads to the extremities, at first macular, then becoming petechial. A decreased level of consciousness is common. The range of potential complications is large, with CNS, gastrointestinal, and pulmonary complications described. The reported case fatality rate in compromised hosts is as high as 40% (303). Brill-Zinsser disease or recurrent typhus may result from inadequately treated, stressed patients with co-existent illnesses or poor nutrition.

Laboratory findings and diagnosis

The diagnosis is confirmed by serological techniques. Immunofluorescent antibody assay or latex agglutination tests are considered reliable and will yield positive results for nearly all patients after day 15 of illness. Culture of the organism and PCR of the blood in acutely ill patients may be available from specialized laboratories. Weil-Felix testing is neither specific nor sensitive and is not recommended. Immunohistochemical staining of tissue (skin biopsy) can provide a rapid diagnosis if reagents are available (303).

Treatment and Prevention

Active agents include tetracycline, doxycycline, and chloramphenicol.

- A single dose of doxycycline is curative in most cases.

Note: The best means of prevention of epidemic typhus is elimination of the louse vector in the population at risk. Delousing with an agent such as DDT, lindane, or Malathion has been shown to be effective.

Endemic Typhus

Endemic, flea-borne, or murine typhus is significantly milder than epidemic (louse-borne) typhus and only occasionally results in death. It is caused by *Rickettsia typhi*. The classic cycle of transmission is between rats and the oriental rat flea. The cycle may involve the cat flea and opossums in some locations. Humans are a dead-end host, as with most other Rickettsial infections, exclusive of *Rickettsia prowazekii*.

The illness begins after 1–2 weeks of incubation, with:

- fever,
- chills, headache, and
- myalgias.

Rash may eventually be present in up to 50% of cases and is usually macular

Endemic typhus has a worldwide distribution, with seroconversion noted in such diverse countries as Iran, Nepal, and Ethiopia (304), and also reported within the Afghan population (244). The disease is thought to be present in Iraq as well.

or maculopapular. Symptoms and signs similar to epidemic typhus are reported, but are generally less severe.

- The illness is typically mild, with case fatality rates of 1 to 4% (305).

The antimicrobial agents listed for epidemic typhus are effective for murine typhus. The patient should be treated until 3 days after resolution of fever. Prevention efforts should focus on elimination of the rodent host and flea vector.

Relapsing fever is not a Rickettsial illness; however, the clinical presentation is similar. It is present in Afghanistan and neighboring countries to the north. Relapsing fever has not been reported in Iraq.

Relapsing Fever

Relapsing fever is very widespread throughout Africa, Europe, Asia, and North and South America. Soviet physicians diagnosed cases in Kabul and Mazar-e-Sharif in Afghanistan (244).

Tick-borne relapsing fever is caused by *Borrelia* species and transmitted by soft ticks (*Ornithodoros*), which are present in a variety of locations in Afghanistan. The feeding behavior of these ticks is different from that of ixodid ticks. They tend to live in nests or bedding and feed on victims while they sleep. The transmission of disease tends to be very focal because the ticks remain in the same area. The severity of disease is quite variable. In West Pakistan, severe illness has been reported, but mild illness has been noted in the central Asian countries to the north (306). The disease is considered more severe than louse-borne relapsing fever.

The incubation period is about 1 week (2–10 days). The onset of illness is generally sudden, with:

- fever,
- chills,
- myalgias,
- severe headache,
- nausea,
- vomiting, and
- in a minority of patients, a macular rash.

Other symptoms may include:

- cough (present in approximately 60% and may evolve to frank pneumonia),
- jaundice,
- hepatosplenomegaly, and
- hemorrhage may be present.

Ocular findings are not uncommon, with conjunctival infection most frequent.

The fever may resolve in 3 to 13 days (average, 4–7) by “crisis,” dropping quickly to normal or below. The crisis may be associated with hypotension or shock. There may not be any further fevers, but frequently after an

interval of 5–9 days, the patient will have a relapse. Untreated, relapsing fever may have a case fatality rate up to 40% (306, 307).

Thrombocytopenia and leukocytosis are common. CSF pleocytosis is noted in a minority of tick-borne relapsing fevers. Diagnosis is generally confirmed by the visualization of spirochetes in blood smears of febrile patients. Weil-Felix (OXK agglutinin), syphilis, and Lyme disease serologies may become positive in a minority of patients with relapsing fever (306, 307).

Antibiotic therapy includes:

- tetracycline,
- doxycycline,
- macrolides,
- penicillin, or
- chloramphenicol.

The best means of preventing this infection is avoidance of the rodent-tick cycle, particularly in sleeping areas. It is advisable to separate eating and sleeping locations in areas of endemicity for relapsing fever.

TREATMENT RECOMMENDATION

Tetracycline is the preferred agent, at a dose of 500 mg po q 6 hours for 5 to 10 days. Antibiotics should be given IV to seriously ill patients. The Jarisch-Herxheimer reaction, characterized by fever, chills, and hypotension, often occurs within hours of treatment, but can be ameliorated by meptazinol (308), an opioid agonist-antagonist, and by anti-TNF antibodies (309).



Anthrax

IMPORTANT DIAGNOSIS INFORMATION

Recognition of anthrax requires a high index of suspicion.

Bacillus anthracis (B. anthracis), a gram-positive, non-motile, spore-forming bacillus, is the etiologic agent of anthrax. Anthrax is endemic in Afghanistan and surrounding regions (7). Anthrax infection also is infrequently found in Iraq, where it is related to the presence of infected animals (12 at page 11).

A recent outbreak in neighboring Tajikistan occurred in July 2000. Year-to-year incidence of anthrax is not published, but 90 cases of anthrax were reported in Afghanistan in 1981 (310). There have been several other reports of anthrax in Afghanistan (311, 312). Most recently, multiple outbreaks have been reported by the media and cited on-line (313). Hides and soil contaminated by anthrax spores can remain infectious for decades.

Biological Warfare

In addition to naturally occurring outbreaks, there is special concern about use of anthrax spores as a bioweapon within Iraq, Afghanistan, and Western countries. Cole (314) reported in 1996 that 17 countries were believed to have offensive biological weapons programs. Some of these countries have weaponized anthrax (315-319). The Germans put anthrax spores into animal feed in World War I (320). In WWII, the Japanese Unit 731 used anthrax, plague, and other agents against prisoners and civilians in China (320).

In recent times, a plume of anthrax spores was accidentally released in 1979 from a Soviet bioweapons factory near the city of Sverdlovsk, killing 68 people, and many more livestock (318-321). The Japanese cult, Aum Shinrikyo, tried unsuccessfully to disperse aerosols of anthrax and botulinum in Tokyo on eight separate occasions (315). Importantly, Iraq admitted in 1995 to having weaponized anthrax during the Gulf War (316-318, 320, 322). Weaponized anthrax spores were intentionally spread in the U.S. in the fall of 2001 via the U.S. mail. Although postal deployment of infectious spores is highly inefficient, the damage from primary aerosolization and secondary contamination has caused government paralysis, economic disaster, and five deaths (323-333).

Weaponized, dispersible anthrax spores are well suited as weapons of mass destruction. The U.S. Congressional Office of Technology in 1993 estimated that 100 kg released upwind of Washington, D.C., would kill 130,000 people and possibly as many as 3 million depending on the aerosol and

environmental conditions (315, 322, 334). The highly concentrated anthrax in the letters mailed to the U.S. Congress in 2001 was estimated to have up to 1 trillion spores per gram of powder (335).

Natural History

Whether spread in nature or by terrorists, there are 3 major forms of clinical anthrax that depend on route of entry of the infective spores.

1. Cutaneous anthrax - About 95% of natural anthrax is cutaneous and caused by contamination of abrasions or other skin lesions. The areas of skin that are uncovered and exposed to infected animals and their products, contaminated mail, or other fomites are most likely to be affected:
 - a. face,
 - b. neck,
 - c. feet,
 - d. legs,
 - e. hands, and
 - f. upper extremities.
2. Gastrointestinal anthrax is rare and usually reported in Africa or Asia from ingestion of infected animals.
3. Inhalational anthrax is also rare but occurred sporadically in wool mills before institution of modern protective practices (336-338). The inhalational form of the disease spread by aerosolized spores has the greatest potential for biological terrorism.

B. anthracis grows well on blood agar at 37° centigrade, producing flat, irregular colonies that may be evident within 18–24 h under aerobic conditions. Growth on media reveals end-to-end chains of bacilli likened to boxcars or jointed bamboo under the microscope (318, 319, 334-337). Anthrax spores are the infective form and measure about 1 µm in diameter. They may survive harsh environmental conditions for decades in the soil or on animal hides, wool, or other fomites. Within an animal host, the spore is transformed into its vegetative form.

Pathogenicity depends on production of an antiphagocytic capsule and two binary toxins formed from three factors: the protective antigen (primary component of the FDA approved vaccine), lethal factor, and the edema factor (315, 319, 334-337). After spores gain entry into an animal host through the skin, by inhalation, or after ingestion, the bacteria are taken up by macrophages and transported to regional lymph nodes. The spore is transformed into its vegetative, toxin-producing form and exponentially reproduces, and disseminates, causing death from toxemia (319, 334, 336).

Mortality Rates

Cutaneous anthrax

- 10%–20%, but is reduced to < 1% with appropriate and timely antibiotic therapy.

Gastrointestinal anthrax

- exceeds 50% despite therapy.

Inhalational anthrax - difficult to assess (315, 319, 334, 336-338).

- In the U.S., 18 cases reported in the 20th century.
 - 16 deaths, a mortality rate of 89% (315).

The 1979 Sverdlovsk accident caused 79 cases of inhalational anthrax, with 68 deaths, (86% mortality) (315, 334, 336, 338).

More exact mortality statistics exist from the recent terrorist attack in the U.S.

As of 30 December 2001:

- 11 confirmed cases of inhalational anthrax
 - 5 deaths, for a mortality of 43% (327, 333).
- 8 patients presented in the initial phase of illness
- 6 were given expeditious and appropriate multiple antimicrobial therapy and all survived.

The high mortality rate reported can be reduced with early recognition and modern intensive care and appropriate treatment (327).

IMPORTANT DIAGNOSIS INFORMATION

Recognition of anthrax requires a high index of suspicion.

Diagnosis

For inhaled anthrax, radiographs may allow early evidence of infection. Among the first 10 cases of inhalational anthrax that occurred in the United States in 2001, all 10 patients had abnormal chest radiographs, with:

- 70% showing mediastinal widening,
- 70% infiltrates or consolidation, and
- 80% pleural effusions (327).

CT was done for 8 patients and yielded abnormal results for all, with:

- 100% showing pleural effusions,
- 88% mediastinal lymphadenopathy or widening, and
- 75% infiltrates or consolidation.

For inhaled anthrax, culture of blood is highly sensitive and generally yields positive results within 24 hours, even if previous antibiotics have been given (324-327). Results of culture of CSF, pleural fluid, vesicular fluid, or swabs of skin ulcers are frequently positive (315, 318, 319, 327, 336, 337).

Examination of the buffy coat of spun blood may yield a rapid presumptive diagnosis for a suspected patient with bacteremia (325, 327).

The CDC recommends that clinical anthrax specimens be handled only in biological safety level II or III facilities and that all specimens be handled under a biological safety level II laminar flow hood (315, 330).

Confirmation of *B. anthracis* requires

- PCR,

- direct fluorescent antibody assay,
- immunochemistry,
- phage lysis,
- gas-liquid chromatography,
- virulence testing in rodents, or
- other confirmation that may be available only at level B reference laboratories (315, 318, 319, 334, 336).

Serological tests are available, but are generally not useful clinically.

Treatment

In nature, *B. anthracis* is almost always susceptible to penicillin, which has been the standard of therapy (315, 318, 336, 337). However, penicillin should probably be used as a single agent only when treating uncomplicated naturally occurring cutaneous anthrax. Naturally occurring complicated cutaneous, inhalational, or gastrointestinal anthrax may be best treated with combination therapy (which could include penicillin), on the basis of limited data of lower mortality rates compared with historical cases (315, 326, 327).

In the event of a known or suspected bioweapon-related illness, penicillin is not recommended, given the possibility of penicillin resistance. For uncomplicated cutaneous disease, the CDC recommends:

- ciprofloxacin (500 mg orally b.i.d.) or
- doxycycline (100 mg orally b.i.d.) for adults (328).

If tests reveal penicillin susceptibility and no penicillinase:

- Amoxicillin may be substituted: 500 mg orally t.i.d. for adults.
- Therapy for at least 60 days is advocated for illness related to bioterrorism or in other events in which aerosolization may have occurred.

For inhalational, gastrointestinal, or complicated cutaneous anthrax, combination empirical antimicrobial therapy is recommended on the basis of data collected about victims of the terrorism-related anthrax attack in the U.S. (324-327, 335, 339). Intravenous ciprofloxacin or doxycycline, plus 1 or 2 other antibiotics, is advocated. Antibiotics that may be useful in combination include:

- ampicillin,
- penicillin,
- clindamycin,
- clarithromycin,
- imipenem,
- vancomycin,
- rifampin, and
- chloramphenicol.

Other fluoroquinolones are likely to be as effective as ciprofloxacin. Steroids have been recommended by some experts for severe edema or meningitis,

but proof of benefit is not available. Clindamycin has been advocated as an adjunctive antibiotic because of potential decrease in toxin production. After stabilization, therapy can be changed from IV to oral to complete at least 60 days of treatment (335).

Guidelines have been recently published for post-exposure prophylaxis for prevention of inhalational anthrax after exposure to *B. anthracis* (315, 318, 323, 339-341).

- The CDC is currently advocating ciprofloxacin or doxycycline for at least 60 days.
- Adult dosing is ciprofloxacin at 500 mg po b.i.d. or doxycycline at 100 mg po b.i.d.

An anthrax vaccine was FDA-approved in 1970 for pre-exposure prophylaxis. The vaccine is manufactured by Bioport (previously by Michigan Biologics) from a killed and disrupted attenuated, strain of *Bacillus anthracis* that primarily contains protective antigen. Anthrax vaccine was offered under protocol for post-exposure prophylaxis to victims of the mail-borne anthrax attack in the U.S. (342, 343). Britain, Russia, and South Africa also have produced anthrax vaccines (334, 337, 344).



12

Leptospirosis

Leptospirosis is a potential problem for both displaced persons and relief workers in Southwest Asia because of the close association of tribal people with their infected domestic animals and limited water resources. A common route of infection is contact with water contaminated with animal urine because leptospire can survive in water for many months.

Leptospirosis is a group of zoonotic diseases usually spread by contact with contaminated animal urine. The disease is caused by spirochetes of the genus *Leptospira*. On the basis of serological evidence, the risk is year-round and includes urban areas. Two basic types of foci likely occur:

1. peridomestic or agriculturally associated foci, with rats as the primary reservoir host, and
2. sylvatic foci, with small rodents serving as the reservoir.

Animal serological studies in Afghanistan detected antibody titers $> 1:800$ in 15% of domestic animals tested (345). Antibodies to some serogroups were found in:

- 50% of buffalo and camel,
- 25% of cattle, and about
- 2% of sheep, goats, and zebus examined.

Leptospirosis is thought to be present in Iraq as well, although there are no data on the incidence of disease.

Clinical Findings

Clinical manifestations are protean, commonly including sudden-onset of:

- fever,
- headache,
- chills,
- myalgias, and
- conjunctival suffusion.

In South-Central Asia, the majority of infections are probably inapparent or misdiagnosed as:

- meningitis,
- encephalitis,
- viral hepatitis, or
- influenza.

Recognized outbreaks of leptospirosis have been described in Kazakhstan (346). Up to 6% of febrile military patients in Pakistan were found to have leptospirosis in 1989 (347).

Diagnosis

Diagnosis is by serological test with a panel of locally occurring leptospire. Confirmation relies on rising titers or isolation of the organism from blood (within the first 7 days of acute illness), CSF (days 4–10), or urine (after day 10). Rapid diagnostic tests are available (348). Effective chemoprophylaxis may be achieved by oral doxycycline, 200 mg administered once weekly (349). Prevention of leptospirosis and scrub typhus may be an added benefit of using doxycycline for chemoprophylaxis against malaria. A 7-day course of IV penicillin or doxycycline constitutes effective treatment for clinical leptospirosis (350, 351).



13 Sexually Transmitted Diseases

Sexually transmitted diseases (STD's) historically are a problem for deployed military forces. STD's typically are highly endemic in lesser-developed countries with limited resources for treatment, prevention, and education.

Although there are little data on sexually transmitted diseases in Afghanistan and Iraq, some data exist on trends in nearby countries. For example, the prevalence of genital *Chlamydia trachomatis* among Pakistani women was reported to be 15% in an obstetrical study conducted in Karachi (352).

It is important to note that road transport is the main mechanism of transporting raw materials, goods, and food across Pakistan. A survey of Pakistani truck drivers found that most were married, but stayed away from their wives for up to 2 months at a time; a majority were not aware that condoms are an effective way of preventing STD transmission and did not consider themselves at risk of acquiring HIV. It can be surmised that, as in India and Central Africa, truck drivers constitute a highly mobile segment of the work force whose sexual practices place them at high risk of contracting and spreading HIV and other STD's in South-Central Asia (353).

Since the collapse of the Soviet Union, poverty, migration, and unemployment have put large populations at increased risk of STDs in newly independent states (354). Rapid HIV spread has been associated with injecting drug use in Kazakhstan. The sharp increases in the incidence of syphilis emerged in concert with declines in numerous health and welfare indicators in newly independent states (355). In Kazakhstan, a total of 1010 HIV-infected persons were recorded as of January 2000, with:

- 29 reported AIDS diagnoses, and
- Tuberculosis was detected in 13% of HIV-infected examinees and 42% of those with AIDS.

In contrast to states in the former Soviet Union, HIV infection rates in Iraq appear to be low. With extensive testing activities, including HIV screening performed at border checkpoints for both Iraqis and non-Iraqis entering the country, a cumulative 117 AIDS and 150 HIV infections were reported to health authorities by the end of 2000. The majority of HIV infections incurred by young men with hemophilia was through infected blood products (12 at pages 32-38). The World Health Organization estimates that in Iraq the prevalence of co-HIV infection and TB is fewer than 1 per million individuals in 1999. A prospective study of 430 Iraqi TB patients between 1996 and 1998 found none to be positive for HIV (356).



14 Plague

The WHO indicates that no cases of plague from Afghanistan or Pakistan are currently being reported, but natural foci of plague exist in the Central Asian republics of the former Soviet Union (7). There are no recent reports of plague in Iraq.

Plague has previously caused 4 pandemics, killing hundreds of millions of people during the last 2 millennia. The last suspected plague epidemics in Afghanistan were in 1905, extending from Kabul to the Gelmand Valley, and in Kusan and Badghis in 1912 (244). Buck et al., reported on serological investigations in rural areas of Afghanistan in 1972 that failed to show any evidence of plague (357).

Yersinia pestis is a non-motile, gram-negative, bipolar-staining bacillus, which is responsible for bubonic and pneumonic plague. It is aerobic, grows well on blood agar, and is a non-fermenter of lactose on MacConkey agar (358, 359).

This infectious agent has been identified as one of the potential agents for use in bioterrorism, presumably from an aerosolized source. In nature, bubonic and secondary pneumonic plague are the most important forms of disease. Primary pneumonic plague should be expected if plague is used as a biowarfare agent. The incubation period for bubonic plague is 1 to 7 days, with primary pneumonic plague having a shorter range of 1 to 5 days. Disease is spread from the bite of infected fleas, especially *Xenopsylla cheopis*, which are associated with rodents (358-360).

Transmission from person-to-person is rare for bubonic plague, but it can easily be spread via respiratory droplets from those with pneumonic plague (322, 360). Contact isolation is required for bubonic plague. Strict respiratory isolation and treatment of close contacts with chemoprophylaxis is needed for pneumonic plague (360).

Treatment

The preferred treatment for plague is:

- streptomycin, 30 mg/kg/day in divided doses q 12 hours for 10 days, or
- gentamicin, 5 mg/kg/day in divided doses q 8 hours for 10 days.

For plague meningitis:

- chloramphenicol should be administered as a loading dose of 25 mg/kg, followed by
- 60 mg/kg/day in divided doses q 6 hours for 10 days.

Alternative therapy includes:

- doxycycline, 100 mg orally q 12 hours, or
- tetracycline, 2–4 g in divided doses q 6 hours for 10 days (358-360).

Plague pneumonia is virtually always fatal if antimicrobial therapy is delayed for > 24 hours after the onset of illness (359).

Contacts of pneumonic plague or suspected victims of intentional bioterrorism aerosol exposure should be given chemoprophylaxis with:

- doxycycline (100 mg po q 12 hours),
- tetracycline (15–30 mg/kg in divided doses q 6 hours), or
- chloramphenicol (30 mg/kg po in divided doses q 6 hours) for 7 days.

Only an experimental vaccine is currently available. This formalin-killed vaccine is effective in preventing bubonic plague, but was ineffective in preventing infection from aerosol exposures (322, 360).



15

Infectious Diseases of Limited Military Importance

Because the U.S. military routinely vaccinates its recruits against many of these diseases, they are not observed as frequently among military personnel and veterans as other groups. U.S. recruits can receive up to a dozen vaccines, which include: diphtheria, hepatitis A and B, influenza, measles, meningococcal disease, mumps, poliovirus, rubella, tetanus, varicella, and yellow fever (190).

The following infectious diseases are mostly preventable using available vaccines and basic preventive medicine precautions (361).

Polio

Polio virus types 1 and 3 are still endemic in Afghanistan and cause significant morbidity among the local population (362-364). In 1996, polio was the leading cause of disability among those < 15 years of age in the Kandahar Province of Afghanistan (365). Outbreaks of polio also occurred in Iraq during the 1990's (12 at pages 61-63, 366).

Polio is acquired by the ingestion of fecally contaminated water or food. Poliovirus infection has an incubation period of 3 to 35 days (usually 1 to 3 weeks) and generally results in asymptomatic or inapparent infection. In about 5% of cases, an acute febrile syndrome may result. Non-paralytic aseptic meningitis, typical of other enteroviruses, occurs in approximately 2% of cases and paralytic polio in < 2%.

Note: There is no specific treatment for polio.

The preferred method of diagnosis is isolation of virus from stools or a pharyngeal swab. Polio is prevented by vaccination.

International polio immunization programs have eradicated this disease from most of the world. As noted, U.S. military recruits are vaccinated against poliovirus infection.

Measles

Measles transmission has been interrupted in North America, but measles remains one of the most serious disease threats to the local populations of Southwest Asia. This disease has the capacity, in the setting of overcrowding and malnutrition, to cause epidemics resulting in massive morbidity and mortality. A measles epidemic was most recently reported in Afghanistan in April 2000, with at least 1200 fatalities (367). Measles is common in Iraq as

well, and is a major cause of childhood morbidity and mortality (12 at page 6 and pages 50-52). Also, other vaccine-preventable diseases, like pertussis and diphtheria, are common throughout Iraq.

Measles should be easily diagnosed from the constellation of signs.

1. A maculopapular rash, starting on the face and proceeding inferiorly and to the extremities.
2. The rash can become petechial or even purpuric in the compromised host.
3. Coryza and conjunctivitis are prominent, and patients may experience significant diarrhea or respiratory complaints.
4. Pneumonia is the most common severe complication, either primary measles pneumonia or superinfecting bacterial pneumonia.

For diagnosis, the detection of serum IgM antibody by ELISA is the preferred method (368). Koplik's spots should be sought for presumptive diagnosis.

In the refugee setting, it is prudent to give vitamin A to all with measles. The current vaccine for measles-mumps-rubella is safe and effective. If given within 72 hours of exposure, it can also prevent disease.

Immunoglobulin, which is usually given as immune serum globulin, can modify or

prevent disease when administered within 6 days of exposure, at a dose of 0.25 mg/kg (for immunocompromised patients, 0.5 mg/kg) up to a maximum dose of 15 mg (364).

Note: There is no specific treatment of measles, but many complications of measles in the malnourished child can be ameliorated by the administration of vitamin A (364).

Diphtheria

In the 1990's, Russia and all of the former Soviet republics experienced a diphtheria epidemic, largely in the adult population (369–373). Absence of routine adult and pediatric vaccination caused this epidemic, which was eventually controlled by mass

vaccination efforts.

Movement of refugee populations from Afghanistan, and return of Soviet soldiers from Afghanistan, very likely contributed to the massive epidemic. Diphtheria continues to be an ongoing health concern in Afghanistan and Iraq (12, 374). The number of reported cases in Iraq increased during the 1990's (12 at pages 28-31). Diphtheria is traditionally a childhood disease, but occurs among unvaccinated adults.

Note: Vaccination is the most effective form of prevention. Because all U.S. and Canadian military personnel are vaccinated against diphtheria, their risk of disease is low.

Diphtheria is caused by the bacterium, *Corynebacterium diphtheriae*. It can be classified as:

- cutaneous,
- nasal,
- pharyngeal/tonsillar,
- laryngeal,

- combined, or
- severe.

Pharyngeal diphtheria is the most common form, with abrupt or gradual onset. Symptoms may include:

- malaise,
- sore throat, and
- low-grade fever.

Fever, sore throat, weakness, and odynophagia are common complaints.

The disease is characterized by the formation of a white membrane, which may be a localized patch, on the tonsil or extend across most of the soft palate. The color of parts of the membrane may evolve to a green-gray or black. The membrane is adherent to the tissue and bleeds on probing or attempted removal. In more severe cases, significant neck edema or labored respirations may be present.

The diagnosis should be confirmed by culture of the organism from the membrane or the mucosal surface beneath the membrane. Adding cultures from the nose and pharynx increases the rate of isolation (375). Treatment should not be delayed for diagnostic testing (376). Therapy for diphtheria requires both antitoxin and antibiotics. The antitoxin should be given as soon as possible. The patient should be tested for allergy before antitoxin therapy (375). The treatment dose varies depending on the form of disease:

- nasal, 10,000–20,000 U;
- laryngeal, 20,000–40,000 U;
- pharyngeal, 15,000–25,000 U;
- combined-delayed, 40,000–60,000 U; and
- severe, 40,000–100,000 U.

Antibiotic therapy terminates toxin product and clears the organism. Macrolides are the treatment of choice.

1. Traditionally, erythromycin orally or IV (40 mg/kg to 2 g/day in 4 divided doses) has been used.
2. Procaine penicillin in a dose of 300,000 U (for those ≤ 10 kg) or 600,000 U (110 kg) per day for 14 days is also effective.
3. Patients should be placed in respiratory isolation.

All U.S. and Canadian military recruits receive the tetanus vaccine and therefore are at low risk of disease.

Tetanus

Tetanus occurs as a result of toxin production by the bacterium, *Clostridium tetani*. Four types of tetanus occur clinically.

1. Generalized
 - a. Generalized tetanus is the most recognized form, with painful spasms of muscle groups throughout the body. These spasms can result in death from respiratory compromise if the muscles of respiration become involved.

2. Localized
 - a. Localized tetanus involves muscle groups near the site of infection, is caused by the effects of regional toxin production, and tends to resolve spontaneously.
3. Cephalic
 - a. Cephalic tetanus involves the face and may result in cranial nerve palsies.
4. Neonatal

Several hundred cases of tetanus are reported in Afghanistan every year, which presumably reflects a small percentage of the true number of cases (364). Tetanus is also a health threat among indigenous Iraqi populations (11).

Diagnosis-based on clinical findings

There is no definitive laboratory evaluation. Culture of the bacteria from the site does not confirm the diagnosis. Ancillary testing with electromyography may be helpful. The principles of therapy are to:

1. stabilize the airway and respiration,
2. initiate neuromuscular blockade,
3. provide sedation,
4. minimize effects of autonomic instability, and
5. maximize supportive care.

The use of intramuscular human tetanus immunoglobulin decreases the duration of disease (377).

Adequate vaccination with tetanus toxoid is the best means of prevention. Passive immunization with tetanus immunoglobulin for high-risk wounds in those who are inadequately immunized may prevent disease.

Rabies

Rabies is enzootic in foxes, wolves, and jackals in Southwest Asia, although dogs should be considered the primary source of human exposure.

Packs of wild dogs are common, with essentially no vaccination or public health control. From March to April 2001, 180 people were attacked by rabid dogs in the city of Kabul; WHO estimates four human cases occur daily in the capital city (7). In 1999, a large epizootic cluster occurred in the Afghan provinces of Kabul and Ghazni. Post-exposure human rabies vaccine has typically been unavailable in recent times in Afghanistan.

Urgent post-exposure treatment, particularly

Long-term travelers to Southwest Asia should consider pre-exposure vaccination. Pre-exposure vaccination may provide protection when there is inapparent or unrecognized exposure to rabies and when post-exposure therapy may be delayed.

Note: Rabies causes hundreds of human deaths annually in Afghanistan and therefore poses a potential risk for Western military personnel. Rabies foci also occur in most parts of Iraq (12 at pages 64-66).

after bites of dog, cat, fox, or jackal, for the unvaccinated should include human rabies immune, and initiation of a 5-dose series of human diploid cell strain vaccine. Western military personnel will likely have ready access to vaccine and rabies immunoglobulin. However, humanitarian workers may not have such access, which will delay treatment, and should therefore strongly consider pre-exposure vaccination.

Brucellosis is not usually a military health problem for the U.S. military. However, brucellosis is a major health problem in Afghanistan and Iraq, where it is usually acquired from ingestion of unpasteurized milk and milk products (378-380).

Brucellosis

Brucellosis is a zoonotic bacterial disease caused by *Brucella sp.* The disease is found nearly worldwide and is acquired primarily from goats, sheep, camels, cattle, hogs, and dogs. Infection usually results from ingestion of untreated milk products, including cheese. Brucellosis most often presents as an acute febrile illness with:

- chills,
- sweating,
- headaches,
- myalgias, and
- fatigue.

However, this infectious disease can have a wide range of presentations.

Brucellosis can resemble malaria and typhoid. Diagnosis is usually made by serology (antibody titer) and blood culture. Up to three months of combination antibiotic therapy is needed with:

- doxycycline,
- aminoglycosides, and
- rifampin.

The risk of infection among U.S. military personnel should be low unless there is sustained, personal contact with an infectious case.

Leprosy

Leprosy remains a serious health problem in many undeveloped countries. The disease is endemic in Afghanistan, but is not a major health threat, with a reported prevalence of one case per 100,000 population (381). The

prevalence of leprosy in Iraq is unreported, but is likely to be low.

Leprosy is caused by *Mycobacterium leprae*, a slow-growing bacterium preferring cooler parts of the body, including:

- skin,
- peripheral nerves,
- eyes,
- respiratory tract, and
- male genitalia.

Clinically, leprosy is a complex disease with variable presentation that depends on the host response, and many cases have a mixed presentation (382). Treatment of leprosy depends on the burden of infection and relies primarily on:

- rifampin,
- dapsone, and
- clofazimine (382).

Echinococcosis

Echinococcal infections in humans are caused by the larval stages of the parasitic helminths (tapeworms) of the genus *Echinococcus*. The two species endemic to Central Asia are:

1. *Echinococcus granulosus* (*E. granulosus*) - the cause of cystic hydatid disease of the liver, lung, bone, or brain, and
2. *Echinococcus multilocularis* (*E. multilocularis*) - the cause of alveolar hydatid disease that manifest as a solid tumor-like masses, which begin in the liver and expands in a highly invasive manner (383).

Echinococcosis has a worldwide distribution (384). The definitive hosts of *Echinococcus* sp. are carnivores, mostly dogs, which shed the embryonated eggs. The eggs are scattered in the pasture and ingested by intermediate hosts, usually sheep (385). Once hatched, the larvae migrate through the intestinal wall and penetrate the animal's organs, especially the liver and lungs. The life cycle is completed when the carnivore ingests the viscera of the intermediate host. Humans become accidental hosts when they ingest food contaminated with dog feces that contains echinococcal eggs, which can survive several days in the environment. In rural areas, the custom of slaughtering sheep at home, among dogs, is an important dissemination factor (386).

For reasons that are unclear, echinococcal disease has recently increased dramatically in Kazakhstan and Uzbekistan (387-389). In Central Asia, both forms of echinococcal disease can be considered re-emerging diseases (390).

Clinical findings

The initial growth period of primary hydatidosis is frequently asymptomatic, and symptoms may first occur months to years after exposure. In cystic hydatid disease, cysts enlarge slowly over years until they are one to > 10 cm.

- cysts are round and unilocular,

Deployed Western troops should limit contact with dogs and domestic animals, take care in the handling of infected animals, and ensure that food and water are clean.

Note: No information is available on the incidence of echinococcal disease in Afghanistan; however, the presence of intermediate and definitive hosts and a high prevalence in surrounding countries make it highly likely that it occurs in Afghanistan. Echinococcosis is known to be a common infection in Iraq (391-395).

- have a thick wall,
- may calcify with time,
- most frequently found in the liver and lungs, but
- also found in bone, brain, and other organs.

When signs and symptoms do develop, they are related to cyst size and location. Rupture of cysts can result in anaphylaxis or widespread secondary echinococcosis. Complications include:

- bronchial fistulization,
- intrapleural rupture (rare, but severe), and
- metastatic hydatidosis resulting from the breaking of a primary cyst into a blood vessel (396).

Diagnosis

This disease is suspected when clinical symptoms occur after possible exposure in a region of endemicity. Ultrasonography, CT, and MRI can identify lesions and reveal others not readily apparent by conventional radiography (396). Indirect hemagglutination and EIA are the most effective immunologic methods for screening for hydatid disease. These, combined with immunoelectrophoresis, confirm the diagnosis in 80%–94% of hepatic disease and 65% of pulmonary disease. Western blot and PCR may be used for further identification, especially when cysts are calcified (397, 398). All seropositive patients should undergo further clinical examination and continued follow-up (399).

Treatment

Echinococcosis can be treated by medical, surgical, and percutaneous methods. The prognosis has improved recently, but complications occur and operative mortality is still 1%–2% (396). Most patients require surgery or guided percutaneous drainage, but about 30% will respond to medical therapy alone.

- Albendazole has largely supplanted mebendazole because of its better absorption.
- Praziquantel can be used in combination with albendazole and is recommended to reduce the likelihood of secondary cysts if rupture of a primary cyst occurs or is likely to occur (400).

Ultrasound-guided cyst puncture has been used successfully in selected patients, although, the risk of anaphylaxis from spillage of cyst contents exists.

Surgery is usually indicated for large cysts with:

- multiple daughter cysts,
- superficially located single liver cysts,
- complicated cysts,
- compression or obstruction, and
- cysts located in vital organs.

However, surgical therapy has significant risks, and medical therapy with or without a guided aspiration procedure may be a more reasonable alternative for uncomplicated cysts, and for those at high surgical risk (400).

Prevention

Control measures include:

- avoiding contact with dog feces,
- hand washing,
- reducing the dog population,
- treating high-risk dogs with praziquantel, and
- incinerating infected organs.

Vaccines are currently being tested successfully in animals and have potential for use in humans (401).

Schistosomiasis

Schistosomiasis is found in Iraq, but infection is thought to be infrequent (402, 403).

Schistosoma haematobium, which causes urinary schistosomiasis, is the only species of *Schistosoma* reported in Iraq (12 at page 67). *Western military personnel would not be at risk of schistosomiasis unless they waded or swam in infested water* (404). Schistosomiasis is not reported in Afghanistan.



16

Recent Outbreaks: Norovirus (Norwalk Like Virus) Infections

Norovirus infection has been reported in Afghanistan but not Iraq, even though it almost certainly occurs in Iraq because infection is widespread in Kuwait (413).

Treatment of acute Norovirus infection is supportive. There is no specific therapy. Most individuals do not have serious illness, but a small percentage may require intravenous fluid dehydration.

Noroviruses, which were formally called Norwalk-like viruses, are responsible for possibly two thirds of all food-borne gastroenteritis in the U.S., with 23 million cases per year (405). During the Gulf War deployment in 1990 and 1991, U.S. military personnel in Saudi Arabia suffered from large outbreaks of Norovirus, particularly during the cooler winter months (114, 406). The magnitude of outbreaks in crowded military populations can be staggering, with over 700 cases occurring on large U.S. Navy ships (407-412). Many outbreaks of Norovirus aboard commercial cruise ships also have been reported.

After an incubation period of 12-48 hours, the major symptoms include the sudden onset of:

- nausea,
- vomiting, and
- diarrhea, which lasts 24-48 hours (414).

An outbreak can begin from a point-source meal in which most of the cases consume a contaminated food item, but these viruses are usually spread person-to person (415). Noroviruses are exceptionally contagious because they:

1. have a low infectious dose of < 100 viral particles;
2. are shed asymptotically for up to two weeks after clinical recovery;
3. are relatively stable and remain viable in the environment; and
4. resist chlorination (414).

Noroviruses are described as having several immunologically distinct strains that fall into two main genogroups (GI and GII) and two newly described genogroups, GIII and GIV. The unique "Operation Desert Storm" strain identified from one U.S. soldier is a GI, while most cases in the U.S., including the worldwide Farmington Hills strains, are GII (416). In challenge studies, certain individuals do not exhibit symptoms nor develop antibody response when fed stool extracts containing the prototype

Norwalk virus strain. After rechallenge one or two years later, the same response was seen in these individuals:

1. Those who became ill and developed antibodies became ill again.
2. While those with no response remained asymptomatic.

However, few individuals are completely non-susceptible to all Norovirus strains (417-419).

In May 2002, 29 of 350 British military medical personnel staffing a field hospital in Bagram, Afghanistan became ill with an initially unknown disease characterized by:

- nausea,
- vomiting,
- diarrhea,
- fever,
- headache,
- neck stiffness, and
- other symptoms.

The outcomes associated with the illness and hospitalization included:

1. One patient developed disseminated intravascular coagulation (DIC).
2. Two patients were critically ill with circulatory collapse and respiratory failure requiring ventilatory support.
3. Twelve patients were evacuated to hospitals in Europe, where all recovered.
4. Three secondary cases occurred among attending medical personnel, one in England.

After several days of concern over an intentional biological attack, the causative agent was determined to belong to genogroup II of Norovirus (420).

This outbreak of Norovirus among Western troops stationed in Afghanistan demonstrates the confusion that can result during a sudden outbreak of viral gastroenteritis, where symptoms may mimic those of:

- anthrax,
- ricin,
- mycotoxin, and
- other biological warfare agents.

Note: Field detection is usually not possible (410). Diagnosis is difficult because there are no commercial or standardized tests.

Noroviruses can be identified in stool specimens by EM, PCR, or a new antigen-capture ELISA (416). Also, it is possible to measure a specific antibody response in acute and convalescent serum samples using a research assay.

Interdiction of the person-to-person spread is difficult, especially in the close quarters of a naval or pleasure cruise ship, or military barracks (421). Removal of personnel for several days, combined with extensive cleaning with chlorine disinfectants appears to work on cruise ships, but is not usually an option in military or refugee situations.



17 Long-Term Health Concerns

Veterans, their families, and health care providers must anticipate these deployment-related health problems following current deployments to Iraq and Afghanistan. In response, VA in the U.S. has developed new programs for providing treatment and assistance-based on experience with veterans returning from recent conflicts abroad (422).

Most military veterans seeking health care present with well-known diagnoses and receive effective treatments. However, a small percentage of veterans will return from overseas deployments with unusual illnesses, like the infectious diseases described in this VHI. In addition, it is now understood that some veterans will return from hazardous military deployments with difficult-to-diagnose, but nevertheless serious symptoms. In fact, concerns about chronic symptoms have arisen after every major military conflict (20). The same types

of health problems also are frequently seen among civilians, particularly after life-threatening disasters.

Health Care Resources for Returning Veterans

Note: This law means that combat veterans will have access to high-quality health care at VA medical facilities for 2 years.

The VA has expanded health care benefits for veterans who have served in a war zone. In 1998, VA was authorized to provide a broad range of health care services to U.S. veterans who served on active duty in a designated theater of combat operations.

Combat veterans are eligible for 2 years after separating from active duty for free VA hospital care, medical services, and nursing home care for any illness, even if there is insufficient medical evidence to conclude that their illness was a result of their combat service (see Public Law 105-368, Section 102, codified at Title 38 United States Code (U.S.C.) 1710(e)((1)(D).)

The law applies to combat veterans in the Reserves and National Guard. Under this authority, however, health care may not be provided for any disability that is shown to have resulted from a cause other than the service at issue; for example, conditions existing before military service and conditions that began following military combat, like broken bones occurring after separation from active duty.

VA's War-Related Illness and Injury Study Centers (WRIISC)

In the U.S., VA has established two new Centers for the study of war-related

illnesses. These two new centers — begun in 2001 in Washington, DC, and East Orange, NJ — focus on the difficult-to-diagnose illnesses seen in veterans following all wars. VA primary care providers can request an evaluation for appropriate patients at one of these Centers. To request a referral, the VA health care provider must contact VA Central Office at 202-273-8463.

For the Washington Center, the telephone number is 800-722-8340; the Web site is <http://www.va.gov/WRIISC-DC>.

For the East Orange Center, the telephone number is 800-248-8005; the Web site is <http://www.wri.med.va.gov>.

VA/DoD Clinical Practice Guidelines

A clear lesson learned after the Gulf War, is that DoD and VA clinicians need timely education on deployment health risks and on the causes and treatment of chronic symptoms (422). Because knowledgeable health care during the post-deployment period is crucial in preventing long-term health problems, DoD and VA developed a Post-Deployment Evaluation and Management Clinical Practice Guideline (CPG) in 2002. An additional supporting guideline was developed by both agencies to assess veterans for chronic fatigue and pain.

The Post-Deployment Evaluation and Management CPG is designed to assist primary care physicians in the evaluation of patients seeking care following hazardous deployments. This guideline provides a structure, clinical tools, and linked resources, which allow primary care providers to diagnose and treat patients with deployment-associated health concerns. The Post-Deployment Evaluation and Management CPG also applies to family members of deployed troops and is designed to support comprehensive education efforts related to deployment health risks.

The Post-Deployment CPG is patterned on standard outpatient health care practices, but with several critical differences. DoD and VA health care providers are given more thorough education about deployment health risks and have readily available sources of detailed information on these risks. Study guides like the VHI's, including this one on infectious disease risks in Southwest Asia, are linked to the deployment CPGs. As a result, health care providers can more quickly and accurately:

1. identify the causes of veterans' complaints;
2. provide more effective treatment; and
3. more thoroughly inform patients and their families about the nature of the health problem.

The CPGs also ensure that there is more complete documentation of health risk, particularly related to a recent deployment. For example, in addition to a routine medical history, the patient is assessed for occupational and deployment history (including possible toxic exposures), traumatic events during deployment, and the use of prophylactic drugs and vaccines. Lastly, the CPGs provide assistance in referring veterans whose health problems remain unexplained to new DoD and VA deployment health clinical centers.

The regular use of CPGs will decrease the need for special clinical evaluation programs. For the first time, troops will be specifically screened in the primary health care setting for illnesses that may be related to a military deployment. The Post-Deployment CPGs will help ensure that the health problems of all U.S. veterans returning from hazardous deployments are addressed whenever they seek care in the DoD or VA health systems.

VA physicians are urged to use the CPG's in the evaluation and care of veterans returning from the recent conflicts in Afghanistan and Iraq. The guideline is available at:

http://www.oqp.med.va.gov/cpg/cpgn/mus/mus_base.htm.

Clinicians can also refer to DoD CPG for Post-Deployment Health Evaluation and Management, found at PDHealth:

<http://www.pdhealth.mil/clinicians/PDHEM/frameset.htm>.

VA's Vet Centers

There are more than 200 community-based Vet Centers located around the United States. This program was originally developed in response to the readjustment needs of returning Vietnam veterans. Based upon their successes, Vet Centers are open today to other veterans who served in combat and who suffer from psychological war trauma. They also offer:

- accessible readjustment counseling,
- extensive case management and referral activities, and
- other supportive social services.

For many veterans who might not otherwise seek VA assistance, the Vet Centers serve as a local resource for VA services.

Phone numbers for local VA Vet Centers can be found in the telephone book, or call 1-877-222-VETS (8387).

Information on the Vet Center's can be found at: <http://www.va.gov/rcs>.

Information on Gulf War Veterans' Health Issues can be found at: <http://www.va.gov/gulfwar>.

Additional Information

Additional health information that may be helpful in caring for veterans returning from recent conflicts in Afghanistan and Iraq can be found at the following Web sites:

U.S. Department of Veterans Affairs, "Iraqi Freedom Veterans: Information for Veterans Who Served in Southwest Asia in 2003," May 2003, at:

<http://www.va.gov/gulfwar/docs/IraqiFreedomMay21.pdf>.

U.S. Department of Veterans Affairs, "Afghanistan Veterans: Information for Veterans Who Served in Afghanistan," March 2002, at: <http://www.va.gov/environagents/docs/afghanVet302.pdf>.

U.S. Army Center for Health Promotion and Preventive Medicine (CHPPM) at: <http://chppm-www.apgea.army.mil>.

U.S. Army Center for Health Promotion and Preventive Medicine, "A Soldier's Guide to Staying Healthy in Southwest Asia" at: <http://chppm-www.apgea.army.mil/deployment/shg/SWA.pdf>.

World Health Organization (WHO) Updates available at: <http://www.who.int/disasters>.

Canada's Experience

Canada has extensive experience in post-deployment health problems as a result of multiple missions over the past few decades, including the 1991 Gulf War and the Afghanistan conflict. Information on the types of medical problems likely to be encountered has been distributed to all Canadian Forces health care workers involved with patient care. In addition, internal medicine specialists with special expertise in deployment health issues are available at major bases across Canada. A Memorandum of Understanding (MOU) was signed between the Department of National Defence and Veterans Affairs Canada in 1998 that provided veterans of any Canadian deployment access to these specialists for diagnosis and treatment strategies. This MOU was necessary because expertise in post-deployment health issues was lacking in the civilian sector, with the result that clinical management was less than optimum, despite being free.

It has been recognized that the stress of deployments has had a significant impact on the health of Canadian Forces members. Operational Trauma and Stress Support Centres were stood up (opened) in 1999, at multiple bases across Canada. Clientele from these Centres frequently present with problems that cross the realms of psychiatry and internal medicine, with the result that joint management is frequently necessary to optimize care.

The Canadian Forces Members Assistance Program (CFMAP) was designed to provide anonymous emergency professional counseling services to service members and their families. Access is through a toll-free number (1-800-268-7708). The intent was to provide a resource for those members and their families with problems they might not otherwise bring to the attention of Canadian Forces Medical Services providers because of concerns about career implications.

The Operational Trauma and Stress Injury Social Support (OSISS) project is a peer support network of former operational stress injury survivors. The OSISS mission is to increase the level of social support available to members, former members, and their families affected by Operational Stress Injury (OSI). The OSISS is a joint Department of National Defence and Veterans Affairs Canada initiative. Education and training to the CF community is provided to create an understanding and acceptance of these injuries.

The Canadian Forces have in place a comprehensive Forces Health Protection strategy designed to provide troops with the resources needed to support overall good health. An enhanced capacity exists to identify, quantify, record, and mitigate potential deployment health hazards through:

1. A significant increase in the number of Preventive Medicine Technicians assigned to headquarters, formations, units, and deploying forces;
2. The establishment and pre-mission deployment of Deployable Health Hazard Assessment Teams (DHHAT) to identify, quantify, conduct risk assessments, and recommend mitigation measures for occupational and environmental hazards on deployed operations; and
3. Updated programs and increased headquarters staff with specialized expertise in toxicology, occupational and environmental health, epidemiology, industrial hygiene, communicable disease control, and entomology.

Canadian Forces medical personnel have used the U.S. VA/DoD CPGs in the management of veterans returning with health complaints. Guidelines specific to Canada are in development. This initiative is being undertaken by the military through a newly created Post-Deployment Health Section in Ottawa, whose mandate includes education of Canadian Forces members and health care workers in post-deployment medical problems. The Post-Deployment Cell is also involved with research in this area, collaborating closely with Veterans Affairs Canada.



18 Conclusion

The current upheavals in Afghanistan and Iraq increase the threat of infectious disease outbreaks among local populations, which can affect Western military personnel and humanitarian aid workers. As recent military experiences in the Persian Gulf, Somalia, and Haiti have shown, Western troops can be effectively protected from infectious diseases through:

1. careful pre-deployment preparation,
2. personal protective measures, and
3. rapid evaluation and treatment of acute illnesses.

Preventing and treating infections among the indigenous population will be a much more difficult task.

In the development of the Veterans Health Initiative (VHI), VA built upon the lessons learned from experiences with previous Gulf War and Vietnam veterans' programs to implement an innovative new approach to health care for veterans. Each VHI is a comprehensive program designed to increase recognition of the connection between military service and certain health effects, to better document veterans' military and exposure histories, and to improve patient care.

As exemplified by this study guide, the education component of VHI prepares health care providers to better serve their patients. This VHI on infectious disease risks in Southwest Asia should be used in conjunction with other VHI's, the Post-Deployment Clinical Practice Guidelines, and with other sources of health information from VA and DoD. Although infectious diseases contracted during deployment usually are a rare problem for returning veterans, it will be important to rapidly recognize these diseases and provide effective treatment.

VA has also completed the following VHI modules.

1. A Guide to Gulf War Veterans' Health
2. American Ex-Prisoners of War
3. Caring for War Wounded
4. Cold Injury *Diagnosis and Management of Long Term Sequelae*
5. Health Effects from Chemical, Biological, and Radiological Weapons
6. Hearing Impairment

7. Military Sexual Trauma
8. Post-Traumatic Stress Disorder: Implications for Primary Care
9. Spinal Cord Injury
10. Traumatic Amputation and Prosthetics
11. Traumatic Brain Injury
12. Veterans and Radiation
13. Vietnam Veterans and Agent Orange Exposure
14. Visual Impairment and Blindness

These important tools are integrated with other VA educational efforts to enable VA practitioners to more quickly and accurately arrive at a diagnosis and to provide more effective treatment.



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NOTE: The Web sites contained in this reference section were current as of the printing of this VHL.

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CME Exam

1. Which of the following diseases is **NOT** identified as an infectious disease causing illness among over 50% of Soviet troops during the occupation of Afghanistan in the 1980's?
 - a. Anthrax
 - b. Dysentery
 - c. Viral Hepatitis
 - d. Typhoid
2. Which of the following is the most numerous Muslim sect in the country of Iraq?
 - a. Hindus
 - b. Shi'a
 - c. Sunni
 - d. Buddhist
3. Which of the following diseases is listed by WHO as the most important infectious cause of death worldwide?
 - a. Viral Hepatitis
 - b. Typhoid
 - c. Malaria
 - d. Dysentery
4. Which of the following diseases is **NOT** identified as an endemic disease of Southwest Asia?
 - a. Anthrax
 - b. Lyme Disease
 - c. Leptospirosis
 - d. Malaria

5. Diseases such as diphtheria, yellow fever, mumps, and tetanus are considered "Of Limited Military Importance" because:
 - a. Every military member had the disease as a child.
 - b. The WHO has publicly stated that the disease has been eradicated.
 - c. The military does not deploy to areas where these diseases are prevalent.
 - d. U.S. military members are vaccinated against these diseases.
6. After an incubation period of about _____ hours, the major symptoms of the Norovirus include nausea, vomiting, and diarrhea.
 - a. 12-24 hours
 - b. 48-72 hours
 - c. 24-48 hours
 - d. 24-72 hours
7. Returning U.S. veterans from war zone deployment in Southwest Asia will have increased access to VA health care for ___ year(s).
 - a. 1 year
 - b. 2 years
 - c. 3 years
 - d. 4 years
8. Which of the following is the main reason for the high prevalence of infectious disease outbreaks in Afghanistan and Iraq?
 - a. Civil unrest and war
 - b. Mismanagement of the public health system
 - c. Religious beliefs associated with vaccination
 - d. Weather patterns causing drought and flooding
9. The typical incubation period of 8-14 days is associated with _____.
 - a. Arboviral Disease
 - b. Shigellosis
 - c. Hepatitis B
 - d. Typhoid

10. Which of the following diseases "Of Limited Military Importance" are U.S. military members **NEVER** vaccinated against?
 - a. Diphtheria
 - b. Rabies
 - c. Schistosomiasis
 - d. Tetanus
11. Which of the following diseases has a prolonged incubation period of 2-8 months, and in rare circumstances may incubate for up to 2 years?
 - a. Cholera
 - b. Leptospirosis
 - c. Leishmaniasis
 - d. Viral Meningitis
12. Giardiasis and amebiasis should be considered when evaluating patients for:
 - a. Encephalitis
 - b. Wound Infections
 - c. Chronic Diarrhea
 - d. Pneumonia
13. Malaria, Leishmaniasis, Crimean-Congo Hemorrhagic Fever, and Sand Fly Fever may be prevented by:
 - a. Inoculation of all deployed personnel
 - b. Spraying Permethrin on clothing.
 - c. Use of a delousing agent such as lindane
 - d. Use of an oral chemoprophylaxis
14. Which of the following diseases often requires fluoroquinolone as treatment because it's resistance to most non-quinolone drugs is high?
 - a. Acute Diarrheal Diseases
 - b. Leishmaniasis
 - c. Rickettsial Type Diseases
 - d. Viral Hemorrhagic Fever

15. Which of the following is **NOT** a prevention measure for Crimean-Congo Hemorrhagic Fever?
- Daily skin inspection for ticks
 - Use of DEET
 - Use of permethrin impregnated clothing
 - Vaccination
16. Which of the following treatments is best used for Spotted Fever Rickettsial Diseases?
- Chloroquine
 - DEET
 - Doxycycline
 - Amphotericin B
17. Which of the following is **NOT** a contraindication for prescribing mefloquine as a chemoprophylaxis for malaria?
- Cardiac Arrhythmias
 - Epilepsy
 - Depression
 - Anemia
18. Sand flies can be the vector for which two diseases?
- Malaria and typhoid
 - Sand fly fever virus and leishmaniasis
 - Viral hepatitis and malaria
 - Sindbis fever and Shigella
19. Which statement is **NOT** true for the West Nile Virus Infection?
- Post-infection confers life-long immunity
 - Infection may be asymptomatic
 - Elderly most likely to suffer from mortality and morbidity
 - Treatment consist of sulfadoxine-pyrimethamine, 10mg/kg single dose
20. Which of the following diseases is **NOT** likely after an individual consumes unpasteurized milk products?
- Dengue Virus
 - Brucellosis
 - M. Bovis
 - Q Fever

21. Iraq and Afghanistan are considered to be located in which geographic location?
- Central Africa
 - Central Asia
 - Southwest Africa
 - Southwest Asia
22. Which of the following diseases is **NOT** caused by the disruption of the public health system in Iraq and Afghanistan?
- Diarrheal Diseases
 - Measles
 - Hepatitis C
 - Respiratory Tract Infections
23. Which disease is currently **NOT** known to be a cause of febrile illness in Iraq?
- Crimean-Congo Hemorrhagic fever
 - P. falciparum* Malaria
 - P. vivax* Malaria
 - Typhoid
24. Use of oral ciprofloxacin for 1-3 days or another fluoroquinolone is the recommended treatment for which disease?
- Anthrax
 - Cholera
 - Bacterial Dysentery
 - Viral Hepatitis
25. Which of the following diseases now uses oral fluoroquinolones and parenteral third-generation cephalosporins as the treatment standard?
- Multidrug-Resistant Viral Hepatitis
 - Multidrug-Resistant Cholera
 - Multidrug-Resistant Tuberculosis
 - Multidrug-Resistant Typhoid

26. Ketoconazole, fluconazole, miltefosine, itraconazole, and dapson are promising oral options for which disease?
- a. Anthrax
 - b. Cutaneous Leishmaniasis
 - c. Smallpox
 - d. Viral Hepatitis