Chapter 15

TUBERCULOSIS AND MILITARY RECRUITS

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INTRODUCTION

The volume of medical literature about tuberculosis (TB) is immense. Space limitations and the intended focus of this textbook preclude a comprehensive review of all aspects of TB. Instead, the focus of this chapter is on providing the information most useful and pertinent to the diagnosis and management of TB in modern military recruits for both the individual and the total recruit population. Our experience is with US Navy recruits and TB; little to nothing is found in the literature to date (2004) regarding TB and recruits in other services. We presume that all persons who reach the recruit environment are at least superficially healthy and not significantly immunosuppressed.

TB remains one of the world's deadliest diseases. The World Health Organization estimates that, each year, more than 8 million new cases occur and approximately 3 million persons die from the disease.[1] The term "tuberculosis" describes a broad range of clinical and subclinical infections caused by the organism *Mycobacterium tuberculosis*. Although most *M tuberculosis* infections are kept in check by the host's immune defenses and remain latent, some latent infections progress to active and contagious disease. Best estimates of the number of persons with latent TB infection (LTBI) in the United States range from 10 million to 15 million; many cases of active TB arise from this pool of infected persons.[2] Although most commonly found in the lungs, TB may infect almost any organ in the human body.

TB has plagued mankind since antiquity. Mummies and other ancient skeletal remains have shown evidence suggestive of spinal TB.[3] Similar evidence from remains in Peru suggests the presence of TB in pre-Columbian times.[4] TB became a major problem in Europe at the time of the Industrial Revolution as cities grew and populations became denser. TB was the leading cause of death in Western Europe in the 18th and 19th centuries, accounting for nearly one fourth of all adult deaths.[5] In 1882 Robert Koch identified *M tuberculosis* as the cause of TB,[6] thereby providing the scientific foundation for future TB control and prevention programs.

Classification of *M tuberculosis*, still based on Koch's identification is made on the basis of three characteristics[7]:

1. the organism being "acid-fast,"
2. the presence of 60- to 90-carbon mycolic acids that can be cleaved by pyrolysis to 22- to 26-carbon fatty acid methyl esters, and
3. a high guanosine plus cytosine content in the organism's DNA;

Although more than 70 species of the family Mycobacteriae have been identified, most human infections are caused by *M tuberculosis*, *M leprae*, *M avium* complex, *M kansasii*, *M fortuitum*, *M chelonae*, and *M abscessus*. The term "tubercle bacillus" refers to either of two species of mycobacteria: *M tuberculosis* or *M bovis*. Disease as a result of *M bovis* is rare in modern times, however, and now tubercle bacillus usually refers to *M tuberculosis*. The bacteriology of *M tuberculosis* is the subject of Exhibit 15-1.

Despite identification of the etiological organism, no chemotherapy was yet known; fresh air, healthy food, rest, and prolonged stays in TB sanatoria were all that could be offered in the late 19th and early 20th centuries. The modern era of TB management dates from 1946 with the advent of the drug streptomycin, followed in 1952 by isoniazid (INH), and rifampin in 1970.[8] The need for TB sanatoria disappeared with the introduction of effective antitubercular chemotherapy, and many such institutions were closed or converted to other uses.[9]

Organized surveillance of TB mortality began in the latter part of the 19th century. Data that were gathered then, although crude, demonstrated a continuously declining rate in TB mortality, despite the absence of any effective control measures.[5] The rate of decline in TB mortality accelerated with the advent of effective chemotherapy in the mid-20th century, accompanied by a decrease in the incidence of new cases. The declining trend continued until 1985, slowed only by the two world wars and the Korean War.[10]

The continuing decline in TB mortality and incidence of new cases, however, produced complacency and neglect. Funding for TB elimination programs was reduced, and categorical funding for TB was eliminated from the Centers for Disease Control and Prevention (CDC) budget in 1972.[10] The reduction of public health funding for TB resulted in desultory, scaled-down, and ineffective treatment programs. This situation led to a resurgence in the number of cases of TB as well as to the development of multidrug-resistant TB. In 1985, the declining incidence rate leveled off, and the number of new cases began to rise through the late 1980s and into the early 1990s, peaking at 10.5 cases per 100,000 in 1992, a 12.9% increase from the 1985 rate of 9.3 cases per 100,000.[10] Explanations for this increase in TB cases include (*a*) the increasing prevalence of human immunodeficiency virus (HIV) infection; (*b*) increased numbers of homeless, drug abusing, and incarcerated persons; and (*c*) the dissolution of programs that had been designed to treat infected patients until they were cured.

In 1952 Rene and Jean Dubos prophetically ob-

EXHIBIT 15-1

BACTERIOLOGY OF *MYCOBACTERIUM TUBERCULOSIS*

Mycobacterium tuberculosis is an aerobic, non–spore-forming, nonmotile bacillus with a lipid-laden cell wall. It grows slowly, with a generation time of 15 to 20 hours; visible growth on solid media appears in 3 to 6 weeks. Colonies are either nonpigmented or buff-colored on solid media.

Mycobacteria are usually referred to as acid-fast bacilli (AFB), although a few other organisms such as *Nocardia* may also be acid-fast. Acid-fastness refers to the organism's retention of carbol-fuchsin in the face of acid-alcohol decolorization when the Ziehl-Neelsen stain is performed. Most laboratories now use a fluorochrome stain such as auramine or auramine-rhodamine. The fluorescent mycobacteria can then be seen easily under low magnification.

The microscopic detection of AFB in stained smears is often the first evidence for the presence of mycobacteria in clinical specimens. Any biological fluid can be examined directly for mycobacteria. Usually, this is done after digestion and sedimentation by centrifugation. Sputum specimens can be digested and sedimented both for culture and for direct examination of smears for AFB. An estimated 10,000 organisms/mL of sputum are required for a positive smear; a single organism on a slide is a positive finding.[1] A negative smear does not preclude the presence of tuberculosis (TB). Among patients with pulmonary TB, 50% to 80% will have positive sputum smears.[2] AFB seen on sputum smears may represent either *M tuberculosis* or other nontuberculous mycobacteria. However, given the infectious potential of the patient with smear-positive TB, a report of a positive sputum smear should prompt immediate infection control action. Very few specimens are both smear-positive and culture-negative; most such specimens come from patients who are already on anti-TB therapy, or they are the result of errors in the laboratory.[2]

M tuberculosis can be cultured using either solid or liquid medium. As most clinical specimens contain many nonmycobacterial organisms, specimens from tissues or fluids that are not sterile must be liquefied and decontaminated, usually with a substance such as the mucolytic agent *N*-acetyl–L-cysteine in 1% sodium hydroxide. This procedure will kill other organisms without harming the tubercle bacilli. Usually, sterile specimens need not undergo the decontamination step. Specimens for mycobacterial culture are plated on culture media that are either agar-based (eg, Middlebrook 7H11 agar, Acumedia Manufacturers, Inc, Lansing, Mich) or egg-based (eg, Lowenstein-Jensen agar, Remel, Inc, Lenexa, Kan). Most such media contain antibacterial agents that will slightly slow the growth of mycobacteria. Growth will accelerate in the presence of 5% to 10% carbon dioxide.[1] Growth is faster in liquid than on solid media, but liquid media can be used for nonsterile specimens only if antibiotics are added.

Automated, commercial broth systems have been a major improvement in culturing these organisms. For example, the BACTEC MGIT 960 System (Becton, Dickinson and Co, Franklin Lakes, NJ) advanced fluorometric method for culturing mycobacteria is used in many laboratories as a rapid and sensitive method for the recovery of *M tuberculosis* organisms from clinical specimens.[3] Some laboratories may use the older radiometric BACTEC method. Growth is usually detected in these liquid culture methods within 9 to 16 days. Cultures are generally held for 6 weeks before being signed out as negative.

Mycobacteria can be definitively identified using standard biochemical tests,[4] high-performance liquid chromatography,[1] or genetic probes (such as the AccuProbe [Gen-Probe, San Diego, Calif]).[5] AccuProbe is a nucleic acid hybridization test that uses a single-stranded DNA probe. Thus, results with probes can be obtained within 21 days after the specimen is processed.

Nucleic acid amplification methods have been used for the direct detection of mycobacterial DNA or RNA from clinical specimens. Because the number of organisms present in a clinical specimen may be quite small, amplification methods such as polymerase chain reaction, ligase chain reaction, or transcriptase-mediated amplification are used. These methods are specific for M tuberculosis but are relatively insensitive. The US Food and Drug Administration–approved commercial examples of such methods include the AMPLICOR MTB Test (Roche Molecular Diagnostics, Branchburg, NJ) and the Amplified MTD Test (Gen-Probe, San Diego, Calif).[6] Such tests can enhance diagnostic certainty but are not a substitute for AFB smears, mycobacterial culture, or the exercise of clinical judgment.

Drug susceptibility testing is necessary to guide therapy. Drug susceptibility tests should be performed on all initial isolates from all patients to facilitate choice of the most appropriate drug regimen. There are several methods for carrying out drug susceptibilities; one of the most rapid uses the BACTEC MGIT 960 System.[7]

Data sources: (1) Centers for Disease Control and Prevention. Screening for tuberculosis and tuberculosis infection in high-risk populations: Recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR.* 1995;44(RR-11):19–34. (2) Morse D, Brothwell DR, Ucko PJ. Tuberculosis in ancient Egypt. *Am Rev Resp Dis*. 1964;90:524–541. (3) Becton, Dickinson and Co. Available at http://www.bd.com/Clinical/products/mycob/mgit960.asp. Accessed November 5, 2003. (4) Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA, eds. *Medical Microbiology.* St Louis, Mo: Mosby; 2002: Chap 40. (5) Labombardi VJ, Carter L, Massarella S. Use of nucleic acid probes to identify mycobacteria directly from Difco ESP-Myco bottles. *J Clin Microbiol.* 1997;35:1002–1004. (6) Labombardi VJ, Carter L, Massarella S. Use of nucleic acid probes to identify mycobacteria directly from Difco ESP-Myco bottles. *J Clin Microbiol.* 1997;35:1002–1004. (7) Becton, Dickinson and Co. Available at http://www.bd.com/Clinical/products/mycob/pza.asp. Accessed January 29, 2004.

served, "Obviously the equilibrium between man and the tubercle bacillus is very precarious. If war can so rapidly upset it, other unforeseen events might also cause recurrences of the tuberculosis epidemic in the Western world."[5(p196)] Diminished immunity (caused, for example, by HIV infection or illicit drug use); crowding (eg, in prisons, onboard ship, in recruit barracks, in refugee camps); wars; and failure to adequately treat the disease all constitute "unforeseen events" that upset this delicate balance. The failure to assure appropriate and complete treatment regimens among infected populations also resulted in a concomitant epidemic of TB that was resistant to both INH and rifampin. This multidrug-resistant form of the disease spread from HIV-positive to HIV-negative populations, including healthcare workers.[10]

The decline in TB case rates resumed in 1997 and in 2002 reached an all-time low of 5.2 cases per 100,000 (vs 53 cases per 100,000 in 1953).[11] The major reasons for this decrease were (*a*) a substantial strengthening of TB-control resources and programs with intensified screening, diagnosis, treatment, and prevention; and (*b*) the advent of greatly improved antiretroviral therapy for HIV-infected patients.

EPIDEMIOLOGY

TB remains the leading cause of adult death worldwide due to any single infectious agent. The global incidence of this disease is increasing at approximately 0.4% per year, albeit much faster in sub-Saharan Africa and the countries of the former Soviet Union.[12] In the United States, the criteria for diagnosis of TB are profoundly influenced by the epidemiology of the disease, including social and medical risk factors and the varying prevalence of disease among different populations.

Incidence and Prevalence

TB is a disease heavily influenced by social circumstance. It occurs disproportionately among populations that are disadvantaged, malnourished, and overcrowded. Additional factors profoundly influencing the epidemiology of TB include the explosion of HIV infection and accelerated immigration of persons from areas of high incidence.

In the United States, the number of reported TB cases decreased from 84,304 in 1953 to 22,201 in 1985, an average annual decline of 5.8%. However, between 1985 and 1992, the number of cases increased 20% to 26,673. These increases were concentrated among racial and ethnic minorities, persons 25 to 44 years of age, males, and foreign-born individuals. Excess (more than would have been expected based on prospective calculations) cases occurred in both sexes, all racial and ethnic groups, and all age groups. Foreign-born cases accounted for 60% of the total increase, particularly among Asians, Hispanics, females, and persons other than those 25 to 44 years of age. HIV infection had the greatest impact on TB morbidity among whites, blacks, males, and persons between 25 and 44 years of age.[13] In the 10 years since 1992, the number of cases has declined 43.5% to 5.2 cases per 100,000 population. In 2002, for the first time since birth country was added to case report forms in 1986, the proportion of total cases occurring in foreign-born persons exceeded 50%.[11]

US subpopulations who are considered high-prevalence groups include

- persons born in countries with a high prevalence of TB;
- groups with poor access to health care;
- persons who live or spend time in congregate facilities such as nursing homes, correctional institutions, homeless shelters, and drug treatment centers; and
- individuals who inject drugs.

In the federal prison system, foreign-born inmates were 5.9-fold more likely than US-born inmates to have a positive tuberculin skin test (TST), and foreign-born inmates accounted for 60% of recently diagnosed cases of TB.[14] Other high-risk groups include[1]

- children younger than 4 years of age;
- persons with HIV coinfection;
- persons who are close contacts of persons with infectious TB;
- persons with a positive TST conversion within the past 1 to 2 years;
- persons whose chest radiographs suggest old TB; and
- persons with other immunosuppressive medical conditions, including diabetes, silicosis, prolonged therapy with corticosteroids, other immunosuppressive therapy, Hodgkin's disease, head and neck cancers, severe kidney disease, some gastrointestinal diseases, and malnutrition.

Sources of US Navy Recruits

Over the past decade, the increased incidence of TB among the foreign-born population is largely attributable to increased immigration. In 2002, an estimated 33.1 million foreign-born persons resided in the United

States, representing 11.8% of the total population.[15] The foreign-born population is concentrated in a few states. More than one half of the foreign born population lives in California, New York, and Texas.[15] New Jersey, Florida, Hawaii, and Nevada also have significant foreign-born populations that surpass the national average of 11.1%. In 2002, 40% of US Navy recruits came from these states.[16]

In 2002, the rate (per 100,000) of TB diagnosis in the United States by race or ethnicity was 1.5 among whites (non-Hispanic), 12.6 among blacks (non-Hispanic), 10.4 among Hispanics, 6.8 among American Indians or Alaskan Natives, and 27.8 among Asians or Pacific Islanders.[11] Among all Navy recruit accessions in 2002, 61.5% were white (non-Hispanic), 17.3% were black (non-Hispanic), 12.8% were Hispanic or Latino, 3.6% were American Indian or Alaskan Native, and 4.8% were Asian or Pacific Islander.[11]

Mexico, the Philippines, Vietnam, India, China, and Haiti are the top countries of origin for immigrants with TB.[11] Mexico is the most common country of origin for foreign-born US Navy recruits.[16] Because the incentive of rapid citizenship is offered to those who serve on active duty, more foreign-born persons are likely to present for recruit training. Additionally, foreign-born recruits are more likely to have been immunized in childhood with the bacille Calmette-Guérin (BCG) vaccine. Receipt of the BCG vaccine may lessen the probability in childhood of disseminated TB and TB meningitis[17] but does not preclude TB infection later in life. However, it makes the interpretation of TST results in such persons more difficult.

Tuberculin Skin Testing and Infectious Disease Control

Tuberculin skin testing is essential to the US Naval Medical Command's infectious disease control effort and is performed routinely for recruits and active duty military members. (The US Army, Air Force, and Marine Corps also conduct skin testing on recruits when they begin basic training.) The prevalence of TST positivity among Navy recruits has varied over time. Between 1958 and 1969, 1.2 million recruits received tuberculin skin testing; 5.2% of the results were positive. This rate showed a downward trend to 1.8% in 1981 and 1.2% in 1986.[18] In 1990, however, 2.5% of recruits were found to be TST-positive. The prevalence varied by race and ethnicity, with the highest prevalence among Asians (26.4%), Hispanics (5.4%), and foreign-born recruits (19.2%); the prevalence among recruits born in the United States was 1.6%. The prevalence among blacks was 5.2% and among whites was 0.8%.[19] The prevalence of TB infection among Navy recruits was studied again in 1998, when the overall prevalence of TST positivity was 3.5%, with higher rates among Asian/Pacific Islanders and foreign-born recruits.[20]

Currently, the mean rate of TST positivity among new Navy recruits arriving weekly for recruit training is 6.4%.[21] This rate excludes recruits with a documented history of TST reactivity, but may include recruits who have previously had a positive skin test but had no record of it. All recruits with a positive test are evaluated further for the presence or absence of active disease. Recruits found to have LTBI (those with TST positivity) are given appropriate chemoprophylaxis. Recruits found to have active TB are begun on appropriate antitubercular treatment and receive an entry-level medical separation.[22]

Molecular Epidemiology

The advent of genotyping has inaugurated the concept of molecular epidemiology and produced multiple challenges to old assumptions about TB. The main methods for determining the genotype of a particular strain of *M tuberculosis* include[23] (*a*) restriction fragment length polymorphism (RLFP)analysis, (*b*) the mycobacterial interspersed repeat units method, and (*c*) spacer oligonucleotide typing, or "spoligotyping."

Genotyping allows the evaluation of isolates with different susceptibility patterns, helps evaluate second episodes of TB, and clarifies outbreaks or clusters of TB. There is broad variability in the genotypes of *M tuberculosis* isolates from patients with epidemiologically unrelated TB, whereas isolates from patients infected by a common source are genotypically identical.[22] Genotyping results have demonstrated that, contrary to previous assumptions, (*a*) the dynamics of TB transmission vary widely by geography and site of transmission,[23–28] and (*b*) recent transmission causes 20% to 50% of cases in urban areas.[25–27,29]

Isolates in the United States may be genotyped at regional laboratories funded by the CDC. Genotyping may take several weeks after recovery of the isolate, limiting its usefulness in immediate clinical management. More rapid genotyping methods are being evaluated.

TRANSMISSION AND PATHOPHYSIOLOGY

Almost all transmission of TB takes place through the air. Infectious particles, or droplet nuclei—which are aerosolized by an infectious person coughing, sneezing, talking, or singing—are inhaled. The largest (>5 μm) of these expelled particles settle onto surfaces, whereas smaller (1–5 μm) particles can remain suspended in the air for many hours. Because of the presence of these smaller particles, the air in a room

occupied by a person with infectious pulmonary TB can remain infectious long after that person has left.

Many aspects of military life increase the probability that an individual will encounter the tubercle bacillus. Militarily-specific exposures may occur during deployments for war, peacekeeping, or humanitarian missions to areas of high TB prevalence as well as through exposure to persons (eg, family members, refugees) from such areas.[30–32] Militarily-specific exposures have always heightened the probability of TB acquisition, especially in the US Navy, where an increased probability of TB transmission onboard ship has been recognized for many decades.[33,34] Sailors live aboard ship in close quarters, with controlled ventilation for extended periods of time. Transmission in this environment occurs more easily than in less confined spaces.

A clear example of shipboard transmission occurred in 1966 among the 350 enlisted personnel and officers onboard the USS *Richard E. Byrd*.[35] A seaman aboard this ship acquired TB infection; by the time his condition was recognized, the entire crew had been exposed for at least 6 months to his advanced cavitary disease. Among the 308 enlisted crewmembers, the TSTs of 140 (45.5%) converted; 7 of these individuals were diagnosed with clinically active disease. Among the 42 officers, the TSTs of 9 (21.4%) converted. Meticulous tracking of TB acquisition by berthing compartment and analysis of the ventilation system onboard the USS *Byrd* clearly demonstrated the rapid dispersion of droplet nuclei throughout the closed environment.

In another example, in 1987, a sailor aboard the USS *Saipan* had smear-positive, cavitary pulmonary TB. A contact investigation of the entire ship's crew revealed that 216 of 881 sailors tested (24.5%) had new TST conversions. The risk for new infection was greatest among sailors in the index case's department. The ship's closed ventilation system was found to have contributed to the dissemination of infection.[36]

Even more recently, in 1998, a marine deployed aboard a Navy amphibious ship was found to have smear-positive, cavitary pulmonary TB. A contact investigation showed a new TST conversion rate of 21.3% (721 conversions of 3,338 tested), and there were 21 cases of active TB among the sailors and marines deployed with the index case. Several months later, four persons with LTBI from this investigation developed active TB because of poor compliance with treatment.[37]

When droplet nuclei are inhaled, the larger ones are filtered out in the upper airways or are deposited in large, lower airways where they are removed by mucociliary clearance. But the smaller particles may reach the alveoli and produce infection. Macrophages in the lungs engulf the bacilli, but unless specific cellular immunity is present, most of the bacilli will survive. The surviving bacilli multiply and are transported via the lymphatics to regional lymph nodes. In addition, hematogenic systemic spread occurs, and bacilli may establish sites of infection throughout the body. The most favored site for infection is the apex of the lung, but the lymph nodes, kidneys, brain, and bones may also be infected.

Before the development of hypersensitivity, microbial growth—both at the initial and metastatic sites—is uninhibited. Tuberculin hypersensitivity develops within 3 to 8 weeks, marking the onset of cellular immunity. In most people the infection is controlled, the only marker being the development of a positive TST. The presence of latent infection carries the risk of disease activation at any time, because persons with a positive TST who have received no chemotherapy continue to harbor live tubercle bacilli in those parts of the body seeded by the early hematogenic dissemination of the organism. The risk of latent infection becoming active is greatest in the first 2 years after infection,[1] during which 5% of infected persons progress to active disease. Another 5% of infected persons progress to active disease sometime later during their lifetimes. Ninety percent of infected individuals never develop TB.[38]

HIV infection promotes the progression of TB infection to active disease, and TB accelerates the course of HIV disease, leading to more opportunistic infections and earlier death.[10] Up to 50% of HIV-infected persons who become infected with TB develop active TB within 2 years; individuals with untreated LTBI who acquire HIV infection develop active TB at a rate of 5% to 10% per year.[1]

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Early pulmonary TB is usually asymptomatic. As the number of tubercle bacilli increases, nonspecific but suggestive symptoms appear (eg, productive cough, anorexia, fatigue, fever, weight loss, chills, and night sweats). Mucopurulent sputum production is nonspecific and may be ignored if the cough is attributed to chronic bronchitis. Hemoptysis resulting from caseous sloughing or endobronchial erosion is usually mild but connotes advanced disease. Life-threatening hemoptysis is rare. There may be chest pain when pleural involvement is present. Abnormal physical findings are few or absent, likely limited to dullness on percussion and posttussive rales.

Diagnosis of TB depends on the use of a TST and

chest radiograph. Currently, tuberculin skin testing is the most widely available method for detecting infection with *M tuberculosis* among persons without overt TB disease. TST methodology is possible because infection with *M tuberculosis* produces a delayed-type hypersensitivity reaction to antigens derived from culture filtrates of tubercle bacilli. In the United States, these antigens are referred to as purified protein derivative. This test is usually applied intradermally to the volar surface of the forearm using a 5-tuberculin unit dose; the hypersensitivity reaction is measured (ie, it is read) within 48 to 72 hours, when hypersensitivity is maximal. This is known as the Mantoux method. The hypersensitivity reaction is manifested as induration, which occurs when previously sensitized T cells secrete lymphokines that produce local vasodilation, edema, fibrin deposition, and recruitment of other inflammatory cells. The diameter of the induration on the forearm is measured transversely to the long axis of the arm and is recorded in millimeters of induration.[1] Absence of induration should be recorded as "0 mm," not as "negative," because the criteria for "negative" are variable and are based on the population being tested.

The interpretation of a TST is based on the prevalence of tuberculous infection in the population being tested as well as the millimeters of induration recorded at 48 to 72 hours. Bayes theorem tells us that the positive predictive value of any test is dependent on the prevalence of the disease in the population being tested,[39] which introduces the concept of targeted tuberculin testing. Targeted testing means that testing is initiated for specific populations based on the projected prevalence of TB in those populations. Targeted tuberculin testing should be conducted among people who are at high risk for TB and is generally discouraged among low-risk populations.

Among US Navy personnel, annual screening is usually required for all members of deployable units, all shipboard personnel, all healthcare workers, and others as specifically recommended by military authority.[40] All new US Navy personnel, including enlisted recruits and officer accessions, are screened as they enter the military at their first training command. Other low-risk military personnel are screened triennially. Based on the sensitivity and specificity of the TST and the prevalence of disease among different populations, three cutoff points for defining a positive test have been recommended: ≥5 mm, ≥10 mm, and ≥15 mm of induration. The criteria for TST positivity by various populations at risk are shown in Table 15-1.

For recruits in the US Army, "[i]ndividuals with a tuberculin reaction 10 mm or greater and without evidence of residual disease are qualified once they have been treated with chemoprophylaxis."[41] The Air Force follows CDC guidelines "…for persons with no health risk."[42,43] New guidance advises against testing (except on accession or for occupational reasons) for those with no risk; however, if testing is done, >15 mm of induration is the cutoff point for a positive reading.[44]

The US Navy criteria differ from CDC guidelines. Although most Navy recruits are members of a low-risk population with regard to TB infection, the cutoff threshold for a positive TST for recruits with no risk factors is 10 mm of induration.[40] This threshold for a positive TST increases the likelihood of a false positive, particularly in someone infected with nontuberculous mycobacteria or someone who was immunized with BCG in childhood. This risk was acknowledged when the threshold was chosen, and it is balanced by the concern that a person infected with TB might not be treated with chemoprophylaxis and go on to develop active disease aboard ship or in a deployed setting.

Classification of Persons Exposed to or Infected With *Mycobacterium tuberculosis*

The American Thoracic Society, in concert with the CDC, has adopted diagnostic standards for classification of TB.[1] This classification system parallels the pathophysiological progression of infection.

Class 0 represents "no tuberculosis exposure, no infection." Individuals in class 0 have no history of exposure and have a negative TST.

Class 1 represents "tuberculosis exposure, no evidence of infection." Individuals in class 1 have a history of exposure but have a negative TST. Appropriate management of persons in class 1 depends on how recently they have been exposed and on their immune status. Individuals who have been exposed within 3 months should have a repeat TST 10 weeks after the last exposure. In the interim, treatment for LTBI may be considered, especially in children and those infected with HIV.

Class 2 represents "latent tuberculosis infection, no disease." Individuals in class 2 have a positive reaction to a TST but have no clinical, bacteriological, or radiographical evidence of active TB. A bacteriological investigation of persons in class 2 may not be required if the chest radiographs are negative. Class 2 individuals have LTBI and are candidates for chemoprophylaxis if they have not already received it.

Class 3 represents "tuberculosis, clinically active." Individuals in class 3 have undergone a complete diagnostic evaluation and have been found to have clinically active TB. If the diagnostic evaluation is incomplete, the person should be classified as a TB suspect (class 5). Criteria for class 3 include clinical,

TABLE 15-1

CRITERIA FOR TUBERCULIN SKIN TEST POSITIVITY FOR POPULATIONS AT RISK

Reaction (mm of Induration)*	Population at Risk
≥ 5	HIV-positive persons
	Recent contacts of patients diagnosed with TB
	Persons whose chest radiographs are consistent with prior TB
	Persons with organ transplant and other forms of significant immunosuppression
≥ 10	Recent immigrants from high-prevalence countries
	Injection drug users
	Residents and employees of high-risk congregate facilities (eg, prisons, jails, nursing homes and other long-term care facilities for the elderly, healthcare facilities, residential homes for patients with AIDS, homeless shelters)
	Healthcare workers
	Mycobacteriology laboratory workers
	Persons with clinical conditions that place them at high risk: diabetes; chronic renal failure; leukemias, lymphomas, and other malignancies; gastrectomy; jejunoileal bypass
	Children younger than 4 years of age
	Infants, children, and adults exposed to adults at high risk
	Shipboard personnel
	Members of deployable units
	Military recruits
≥ 15	Persons with no known risk factors for TB

*lower limit
AIDS: acquired immunodeficiency syndrome
HIV: human immunodeficiency virus
TB: tuberculosis
Data sources: (1) Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR*. 2000;49(RR-6):24. (2) US Department of the Navy. *Tuberculosis Control Program*. Washington: DC: Headquarters, USN; 8 Feb 93. BUMED INSTRUCTION 6224.8. (3) US Department of the Navy. *Tuberculosis Control Program—Clarification*. Washington, DC: Headquarters, USN; Apr 2001. BUMED Message 241350Z APR 01.

bacteriological, or radiographical evidence of current TB. The best demonstration of current active disease is isolation of the *M tuberculosis* organism. A person who had TB in the past and has current TB remains in class 3 until the course of treatment is complete.

Class 4 represents "tuberculosis, not clinically active." Individuals in this class have had at least one previous episode of TB, or they have abnormal but stable findings on the chest radiograph, a positive TST, and no bacteriological evidence of current disease (if bacteriological evaluation is done). This class presupposes that no clinical or radiographic findings suggest current disease and is not changed by whether or not the person has received or is receiving chemotherapy.

Class 5 represents "tuberculosis suspect." Individuals in this category are undergoing a diagnostic evaluation that is not yet complete. This classification applies regardless of whether or not treatment has begun, but no one should remain in this classification longer than 3 months.

Evaluation and Treatment of Patients With Tuberculosis

Treatment regimens for all forms and classifications of TB infection are complicated and beyond the scope of this chapter. The American Thoracic Society, the Infectious Diseases Society of America, and the CDC have formulated comprehensive treatment guidelines for TB,[45] which can be accessed online.[46] However, treatment issues that are most pertinent to recruits are

addressed below.

The goals of TB treatment are to cure the infected individual and to minimize transmission of *M tuberculosis* to others. All treatment regimens must address host factors (presence or absence of immunosuppression), stage or classification of TB, and social factors that influence the infected individual. The recruit training environment is artificial and unique. Recruits from all 50 states and many foreign countries are crowded together for 9 weeks and placed under various types of physical and psychological stress. They have no individual home to go to, and, unless they receive an entry-level medical separation, must remain in the recruit environment. These circumstances influence both the diagnostic evaluation performed and the treatment given to recruits.

Most recruits who receive antitubercular treatment are treated for LTBI. A chest radiograph to rule out active TB is indicated for everyone being considered for treatment of LTBI. In patients with LTBI, the chest radiograph is usually normal, although changes suggestive of old, healed disease may be present. Changes that suggest old TB include dense, possibly calcified, pulmonary nodules found in the hila or the upper lobes. Smaller nodules may also be seen, sometimes accompanied by fibrotic scars and loss of volume in the upper lobes. Nodules and fibrotic scars indicating healed disease are well demarcated in appearance and have sharp edges. The presence of calcification in such lesions lessens the probability of recrudescence and is further evidence of old, healed disease.[47]

Sputum examination is not usually indicated for persons being evaluated for treatment for LTBI, unless the chest radiograph reveals changes that suggest either active disease or old, healed TB. When the chest radiograph is abnormal, three consecutive sputum samples should be obtained for acid-fast bacillus (AFB) smears and culture.[47] If the only lesions on the chest radiograph are calcified pulmonary nodules, then bacteriological sputum evaluation may not be necessary. Single-drug therapy for LTBI should *not* be instituted until the medical officer is reasonably sure that active TB is not present. If uncertainty persists, a multidrug regimen should be started pending culture results.

The three regimens recommended for the treatment of adults with LTBI are shown in Table 15-2. The 9-month regimen of INH is preferred to the 6-month regimen. If twice-weekly dosing is used, directly observed therapy must be used. This intervention, the most likely to improve adherence to treatment of LTBI, requires that the patient be observed while ingesting each dose of medication. In the recruit setting, this observation may be accomplished either in the clinic or in the recruit compartments. Previous recommendations for the treatment of LTBI in adults included a 2-month regimen of either daily or twice-weekly rifampin and pyrazinamide. This regimen is no longer recommended because of reports of severe and fatal

TABLE 15-2

RECOMMENDED TREATMENT REGIMENS FOR LATENT TUBERCULOSIS INFECTION IN ADULTS

Drug	Dose	Duration (in Months)	Comments
Isoniazid	300 mg daily or 900 mg twice weekly (DOT)	9	Preferred regimen, mandated by instruction for recruits Twice-weekly dose *must* be with DOT
Isoniazid	300 mg daily or 900 mg twice weekly (DOT)	6	Not indicated in HIV-positive persons or in persons with fibrotic lesions on chest radiograph Twice-weekly dose *must* be with DOT
Rifampin	600 mg daily	4	For persons who are contacts of patients with isoniazid-resistant, rifampin-susceptible TB

DOT: directly observed therapy
HIV: human immunodeficiency virus
TB: tuberculosis
Data sources: (1) Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR*. 2000;49(RR-6):24. (2) US Department of the Navy. *Tuberculosis Control Program.* Washington: DC: Headquarters, USN; 8 Feb 93. BUMED INSTRUCTION 6224.8. (3) US Department of the Navy. *Tuberculosis Control Program—Clarification.* Washington, DC: Headquarters, USN; 2001. BUMED Message 241350Z APR 01. (4) Centers for Disease Control and Prevention. Update: Adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection—United States, 2003. *MMWR*. 2003;52(31):735–739.

liver injury associated with it.[48–50]

Completion of therapy is based on the total number of doses taken, not on the duration of therapy. The 9-month regimen of INH should consist of 270 doses taken within a period of no more than a 12 months. The 6-month regimen should include 180 doses taken within a 9-month period. Adverse reactions to INH include

- rash,
- nausea,
- vomiting and epigastric distress,
- hepatic enzyme elevation,
- hepatitis,
- peripheral neuropathy,
- agranulocytosis, and
- rare central nervous system effects (eg, convulsions, toxic psychosis, optic neuritis and atrophy, toxic encephalopathy, and memory impairment).

Asymptomatic aminotransferase elevations up to 5-fold higher than the upper limit of normal occur in 10% to 20% of people receiving INH for the treatment of LTBI.[51] These elevations usually return to normal even with continued administration of the drug. About 20% of patients taking INH develop antinuclear antibodies, although fewer than 1% develop symptoms of lupus erythematosus, thus necessitating discontinuation of the drug.[45] Monoamine poisoning, manifested by a flushing reaction, occurs rarely following the ingestion of foods with a high monoamine content; patients should be advised to avoid cheese and wine that are high in monoamines.[45]

Among individuals taking INH, clinical hepatitis occurs less frequently than previously thought. In a study[52] of 11,141 people receiving INH for LTBI, the incidence of clinical hepatitis was 0.1% to 0.15%. The risk of clinical hepatitis increases with advancing age: it is rare in the age range of recruits, but the risk increases to nearly 2% among persons aged 50 to 64 years.[53] The risk is also increased in persons with underlying liver disease; in people with heavy alcohol consumption; and in postpartum women, especially among Hispanic women.[54] Adults should be monitored monthly for symptoms of hepatitis. Anyone who develops signs or symptoms of hepatitis should have liver function studies done. INH should be withheld if[40] (*a*) the symptomatic patient's transaminase levels exceed by 3-fold the upper limit of normal, or *(b)* the asymptomatic patient's levels exceed by 5-fold the upper limit of normal.

Although active TB is rarely found among recruit populations, when AFB cultures are positive for *M tuberculosis,* the recruit has active TB and is processed for entry-level medical separation.[22] The recruit with active TB should be treated according to the comprehensive guidelines established by the American Thoracic Society, the Infectious Diseases Society of America, and the CDC[45] (they are beyond the scope of this chapter but available on the Internet[55]). Susceptibility testing must be performed for all *M tuberculosis* isolates to assure that the isolates are susceptible to the drugs chosen. Additionally, when the recruit with active TB is returned to his or her civilian home, public health authorities in that local area must be contacted and referral of the active TB case made to them (in our experience, public health authorities are grateful for the referral and any information that can be provided). Specific information that should be supplied with the referral includes the name and home address of the recruit, the millimeters of induration of the TST, the chest radiograph findings, the number and dates of positive cultures, and, very importantly, the susceptibilities of the *M tuberculosis* isolate.

RECRUITS AND TUBERCULOSIS

Recruit Environment

The Recruit Training Command (RTC), Great Lakes, Illinois (located 40 miles north of Chicago) is the sole training site for US Navy enlisted recruits. Recruit training is an intensive physical and emotional period of indoctrination into military life, typically lasting 8 to 9 weeks. A distinguishing feature of recruit training is the concentration of a large group of adolescents and young adults of diverse nationalities brought together to live and work in crowded, close quarters. By nature, time at RTC is transitory for recruits; new groups of young people arrive at or depart from RTC daily.

More than 42,000 recruits (83% men, 17% women) began basic Navy training at RTC during 2002. More than half of all recruits enter the military between May and September, a period known as "summer surge." The summer months are a popular time to enter RTC primarily because most US students graduate from high school in May and June, and the harsh climate of the upper Midwest during the winter months deters many prospective recruits.

On arrival at RTC, Navy recruits are separated into divisions of 80 to 90 recruits. The division is the group of people with whom a recruit will spend most of his or her time, eating, sleeping, doing physical training, taking classes, and performing any other scheduled recruit activities. Most divisions are all male, due to

the predominance of male recruits in the Navy. Some divisions have both male and female recruits; however, there are no all female divisions. Direct leadership for the division is provided by recruit division commanders, enlisted Navy personnel who have completed special training. Two or three recruit division commanders guide each division and act as a surrogate parent during the training period, assuming responsibility for the recruits' training and welfare.

Recruits are housed in large buildings, called "ships." Each ship has several large rooms or compartments, where a division sleeps, changes clothes, and attends to personal hygiene. Female recruits, sometimes from more than one division, occupy a separate compartment from male recruits. Compartments are typically large, rectangular rooms lined with 60 to 100 bunk beds arranged in two rows separated by a wide pathway. Bunk beds are approximately 3 feet apart; there are no partitions between beds. Such a setup is referred to as "open bay." At one end of the compartment, there is a bathroom with four or five sinks, toilets and urinals, and showerheads. The recruits in each division are responsible for cleaning the compartment and the bathroom.

Although the compartment is the recruits' living space, recruits spend few of their waking hours there. Most of their time is divided among classrooms, drill halls, and the galley (cafeteria). Divisions of recruits travel from building to building by marching in formation, generally two straight lines in order of height, with the tallest at the back. Recruits maintain a distance of about one arm's length apart. Recruits may stay in these formations for 15 to 20 minutes at a time as they walk from place to place. Sometimes, recruits may need to compress the space between them to fit within a certain area; it is common to see a formation assembled in rows separated by mere inches. This environment likely approximates the close quarters experienced aboard Navy vessels and could facilitate the transmission of TB in a similar manner.

Detection and Management of Tuberculosis Infection in Recruits

In the US Navy, the clinical handling of TB is governed by the Tuberculosis Control Program instruction issued by the Bureau of Medicine and Surgery (BUMED) in February 1993.[40] This instruction requires that all Navy personnel have their TST results documented in their medical treatment record. To comply with this instruction, tuberculin skin testing is conducted on all recruits on arrival at RTC. On the recruit's first day, a TST containing a 5-tuberculin unit is placed using the Mantoux method. TST results are read within 48 to 72 hours in the recruit barracks. All reactions are measured and recorded by enlisted Navy hospital corpsmen. Recruits with reactions measuring 5 mm or larger are considered tuberculin reactors and are taken to the recruit medical clinic for further evaluation, which includes a questionnaire about symptoms of TB, country of birth, and past history of TB infection or disease. The evaluation also includes a chest radiograph, which is reviewed by a radiologist within 72 hours. Both posteroanterior and lateral views are obtained, although only a posteroanterior view of the chest is needed for detection and description of chest abnormalities.

The BUMED instruction also specifies that all new Navy personnel—enlisted recruits and officer accessions—are candidates for treatment of latent TB infection if they have a TST reaction measuring 10 mm or larger, regardless of the presence or absence of risk factors for infection. New personnel are not considered to be at increased risk of active disease; however, they are included to "ensure that persons with pre-existing tuberculosis infection receive preventive therapy before shipboard service or foreign travel."[40] False-positive results may occur among recruits who have infection with nontuberculous mycobacteria or have been vaccinated with BCG. The incidence of these false-positive results is unknown. No reliable method is currently available to distinguish tuberculin reactions caused by BCG from those caused by natural infection, so BCG vaccine status is not considered when evaluating TST results.

Latent Tuberculosis Infection

Recruits with a TST measuring at least 10 mm and a normal chest radiograph are categorized as having LTBI. Some patients with radiographic findings consistent with old TB disease may also be categorized as having LTBI. Radiographic findings consistent with old TB include[1]

- dense pulmonary nodules (with or without calcification) in the hilar area or the upper lobes,
- small nodules sometimes seen with fibrotic scars and volume loss in the upper lobes,
- bronchiectasis of the upper lobes,
- pleural scarring, and
- apical or basal pleural thickening.

LTBI is managed according to the recommendations from the CDC[47, 48] and US Navy.[40, 56] Nine months of INH, 300 mg taken once daily, is the preferred treatment for recruits. INH is dispensed as a 30-day supply

to recruits, with return appointments scheduled at 28-day intervals. At return appointments, recruits complete a screening questionnaire for symptoms of active TB and adverse events such as hepatitis and peripheral neuropathy. Typically, by the end of recruit training, a recruit completes 1 month of treatment and receives one refill before leaving RTC.

Suicidal Overdose Involving Isoniazid

Because INH is widely used and generally dispensed in large quantities, suicidal overdose may be expected to occur in many patient populations.[57] Intentional overdose is an uncommon but well-recognized problem.[58] A toxic reaction can occur from ingesting as little as 1.5 g of INH; 6 to 10 g is the usual dose required for more severe toxic reactions, and 15 or more grams is frequently fatal if untreated.[57] The potential of INH to be used in intentional overdose is a significant concern at RTC, because approximately 2,000 recruits per year are prescribed INH. The emotional stress experienced by many recruits may make them more vulnerable to displaying impulsive behavior, particularly during the early acclimation period at RTC. Most of the psychiatric and behavioral issues associated with adjustment to the recruit training environment appear during the first 2 weeks.[59]

Between January 2001 and December 2002, the incidence of suicide attempts using INH among Navy recruits at RTC, Great Lakes, was 1.8 per 1,000 (7 cases/3,778 recruits prescribed INH[60]). There were three cases of status epilepticus, and one patient died. Patients were all men, ranging in age from 18 to 34 years and of multiple ethnicities. All suicide attempts appeared intentional; four patients reported making the attempt impulsively after a specific, inciting event. None of the patients had a history of suicide attempts or ideation before starting INH. Although toxic psychosis is a potential side effect of INH,[61] there was no evidence that psychosis precipitated any of the suicide attempts.

Preventive recommendations advise caution when prescribing INH to those with a history of depression, suicidal ideation, or suicidal gesture,[58] or those deemed at high risk for attempting suicide.[62] Other recommendations include ongoing monitoring of INH chemoprophylaxis by paramedical personnel, inhibiting impulsive ingestion of large amounts by dispensing individually wrapped tablets, or dispensing small amounts of INH at short intervals. Many of these recommendations are followed for recruits; however, some are considered prohibitive in the training environment. Administration of the INH program is managed by hospital corpsmen trained as preventive medicine technicians from Naval Hospital Great Lakes. Recruits who are candidates for INH treatment are screened for a history of suicidal ideation or suicidal gestures during the initial medical screening for active TB disease. INH treatment begins during the third week of training to minimize misuse of INH by recruits who might display psychiatric or behavioral issues early in training. Reducing the quantity of medicine dispensed was considered as an additional safeguard; however, with nearly 2,000 recruits receiving INH therapy annually, the option was not considered as practical. Even dispensing a 14-day supply of INH to recruits would not eliminate the possibility of severe toxicity and would double the time spent in medical and pharmacy visits. The projected loss in training time resulting from implementation of this policy was considered prohibitive.

Active Tuberculosis

Recruits with a positive TST and an abnormal chest radiograph require further evaluation. Recruits with abnormal chest radiographs are recalled for further history, review of prior radiology reports (if available), and scheduling of further radiological studies, if needed. Consultation with the radiologist is helpful in defining the abnormality and determining whether the radiographic findings represent old tuberculous disease or a pulmonary condition other than TB. If the chest radiograph reveals findings suspicious for pulmonary TB (eg, infiltrates, cavitations of the upper lobes), the patient should be admitted to a negative-pressure isolation room to obtain at least three serial sputum samples for AFB staining and culture. Because home isolation is impractical for recruits, hospital admission is required.

Tuberculosis Control

Traditional infection control policies to contain TB within a household are not useful in the training environment, where a "household" consists of up to 80 individuals. The primary method for containing TB in this environment is to employ a low threshold for removing recruits when there is any suspicion of active pulmonary TB. Secondly, a low threshold is also used for initiating four-drug anti-TB therapy under direct observation while awaiting sputum culture results.

The threshold for removal of a recruit from the recruit environment is based on clinical and epidemiological factors that make pulmonary TB a likely diagnosis. Classic symptoms of pulmonary TB (persistent cough, hemoptysis, and fever), in combination

with clinical features of the chest radiograph (upper lobe infiltrates, cavitary lesions, and hilar adenopathy), are seldom seen in this young, otherwise healthy population. Instead, radiographic abnormalities are often seen without *any* clinical symptoms. In addition to the absence of clinical symptoms, the chest radiograph often includes findings such as solitary pulmonary nodules, pleural effusions, and middle- or lower-lobe infiltrates that are not specific to TB. Often, the epidemiological history—including risk factors such as being exposed to someone with TB; being foreign-born or having spent time in a country of high prevalence; or having spent time in a prison, homeless shelter, or nursing home, or among HIV-positive persons—weighs heavily in a decision to hospitalize a recruit for further evaluation. The following case studies illustrate some of the salient issues faced in the evaluation of TB among recruits, especially the need for rapid diagnosis.

Case Study 15-1: Seaman Recruit A, a 24-year-old woman, was born in the Philippines but spent most of her childhood in Japan. She immigrated to San Diego, California, at 19 years of age but traveled frequently to the Philippines until 1 week before to her arrival at RTC, Great Lakes. Her TST on medical inprocessing was 18 mm. The patient's prior TST history was unclear; she denied any history of pulmonary TB. She stated that she had visited a person with known active TB in the Philippines during the 3 months prior to her arrival at RTC. She denied any symptoms of TB, including cough, hemoptysis, fever, weight loss, or malaise. She did report mild sinus congestion and rhinorrhea. The rest of her medical history was unremarkable. A radiograph examination of her chest was performed, but before it was read by the radiologist, she was incorrectly started on INH 300 mg daily for LTBI. Seven days later, the radiograph report noted a left upper lobe infiltrate.

Seaman Recruit A was then hospitalized in negative-pressure isolation and taken off INH therapy. She provided three sputum samples for AFB staining and culture. During her inpatient stay, a pulmonary medicine specialist recommended starting her on four-drug TB therapy while awaiting further evaluation. When three serial sputum smears came back as AFB-negative, the patient was discharged from isolation and placed in temporary quarters within the hospital while awaiting a pulmonary medicine evaluation.

A bronchoscopy was performed 1 week after discharge. Two weeks later AFB were identified from bronchial washings, and DNA probes for *M tuberculosis* were positive. Seaman Recruit A was notified and processed for an entry-level separation from the Navy for pulmonary TB. Before separation, follow-up for continued treatment was arranged with the California Department of Public Health.

A contact investigation was initiated for approximately 160 recruits and staff members with baseline negative TSTs who trained closely with the patient. There were no conversions among her contacts.

Case Study 15-2: Seaman Recruit B, a 22-year-old Hispanic man, was born in California. He arrived at RTC, Great Lakes, but did not begin medical in-processing for a week. Before beginning medical in-processing, he sought medical care on three occasions with complaints of cough, low back pain, sore throat, and nasal congestion. His TST at in-processing was measured at 20 mm. The patient could not recall prior tuberculin skin testing and denied any history of pulmonary TB or known contact with an active TB case. A chest radiograph showed interstitial changes in both apices, but the findings were initially overlooked. The patient continued to seek medical attention, with seven additional visits for cough, chills, sore throat, nasal congestion, mouth pain, rash, knee pain, and depression. His physical examinations were notable for tachycardia and a maximum temperature of 100.9°F. At the last visit, the results of his chest radiograph were reviewed, and he was referred for admission to the hospital to rule out active TB.

Seaman Recruit B was hospitalized in negative-pressure isolation. Three serial sputum samples were obtained for AFB staining and culture. When three serial sputum smears were negative for AFB, he was discharged from the hospital and returned to the training environment. No referral to pulmonary medicine was made, and, before the results of sputum AFB cultures were available, the patient was started on single-drug treatment for LTBI with INH. The patient continued to complain of cough and developed coarse breath sounds. Another chest radiograph was obtained, which showed bilateral apical infiltrates, greater on the right side than on the left.

The patient was recalled and hospitalized a second time in negative-pressure isolation. Three additional sputum samples were obtained for AFB staining and culture. *M tuberculosis* grew from the liquid medium of one specimen (first set) at 4 weeks. A contact investigation was subsequently initiated for 144 recruits with baseline negative TSTs who trained closely with the patient. The conversion rate for this group was 4%. Six recruits had TST results of 5 mm or larger (range: 6–15 mm). Chest radiograph examinations of two of the six new reactors showed lower-lobe infiltrates suggestive of primary pulmonary TB.

Future Challenges

Recruits do not all have the same risk of TB: a recruit with no known exposures who has lived all his or her life in the United States has a different risk than a recruit who arrives for recruit training having lived for an extended time in a country with a high prevalence of TB. An epidemiological history provided by the recruit reveals risk factors for TB infection. In the future, TB testing on arrival for recruit training could be reserved for those recruits found to have risk factors for TB infection. Performing TB testing on only those with risk factors and then following both cohorts through their military careers would clarify whether there is any risk in not testing those recruits without risk factors. This effort would be a further refinement of targeted testing. Testing only recruits with risk factors would

not only save money and training time but would also diminish the number of false-positive test findings that result in unnecessary chemoprophylaxis.

This fine-tuning of targeted testing requires further research on the epidemiology of TB infection in recruits. Data are needed about risk factors (past history of a positive skin test; country of birth; exposures to others with TB; prolonged stays in a foreign country; exposure to high-risk populations such as intravenous drug abusers, the homeless, people in nursing homes, prisoners, etc) that recruits bring to recruit training. As described previously in this chapter, methods of molecular fingerprinting of *M tuberculosis* continue to revolutionize concepts of transmission of TB.[23] These methods have not yet been applied to military-specific issues of TB transmission. Using such methods to examine transmission both onboard ship and in the recruit setting would clarify real risks and routes of transmission.

Finding newer and better methods to diagnose TB infection is another provocative area of research. Although it is a time-honored method, TST is flawed in several important ways. Interpretation of the TST is difficult in people with nontuberculous mycobacteria infection or who have received BCG vaccination in childhood. Additionally, the TST requires two visits—one to place the test and another to read it—and compliance with the return visit is not always 100%. A test of TB infection that would produce results with a single visit would be preferable for reasons of cost, logistics, and compliance.

In 2001 the QuantiFERON-TB test (QFT) (Cellestis Limited, Carnegie, Victoria, Australia) was approved by the Food and Drug Administration as a diagnostic aid for the detection of LTBI. The test is based on quantifying the amount of interferon-γ released from sensitized lymphocytes in blood that has been incubated overnight with a purified protein derivative from *M tuberculosis* and control antigens. Release of interferon-γ is a component of cell-mediated immune reactivity to *M tuberculosis*. This test is advantageous because it requires only one visit, effectively differentiates between *M tuberculosis* and nontuberculous mycobacterial infection, and it is not reactive in a person who received BCG in childhood. Currently, the QFT is recommended by the CDC[63] and the Armed Forces Epidemiological Board[64] as a screening test for LTBI in military and other low-risk populations. Current recommendations require that a positive QFT be confirmed with a TST. It is likely that, as the QFT is refined in the future, there will no longer be a requirement for the confirmatory TST. When the requirement for a TST and its subsequent reading is eliminated, adding the QFT to the regular blood examinations performed during recruit medical in-processing will result in saved training time and logistics effort.

SUMMARY

Military life includes living, training, and fighting in close quarters—whether in the field, in garrison, or aboard ship. Although active TB is rare in recruits, failure to detect and properly treat a military member for TB puts other members and the mission at risk. TB control in recruits presents unique challenges. The recruit population often includes persons who are foreign-born or who have resided in geographical areas with a high prevalence of TB. Recruit training is conducted in crowded environments that can facilitate airborne transmission of *M tuberculosis*. Recruits are deliberately stressed, physically and mentally, during recruit training.

Almost all transmission of TB takes place through the air. Persons with active disease aerosolize droplet nuclei by coughing, sneezing, talking, or singing. These infectious particles are then inhaled by others in close proximity. The air in a room occupied by a person with infectious pulmonary TB may remain infectious long after that person has left.

Medical inprocessing of recruits must include assessment for TB, both asymptomatic infection and active disease. Tuberculin skin testing is the current assessment method used. Among civilian populations, criteria for TST positivity vary depending on the characteristics of the population. Because the consequences of missing a recruit with incipient TB are serious, criteria for defining a positive TST are more stringent in the recruit setting. Treatment for LTBI should not be initiated until active disease has been ruled out.

US Navy recruits with a positive TST and a negative chest radiograph are treated for LTBI, usually with INH, 300 mg daily, for 9 months. Because providing recruits with large amounts of INH provides a vehicle for use during a suicidal impulse, however, care should be taken to minimize such opportunities by limiting the amount of drugs dispensed, delaying its provision by a few weeks after the start of training, and carefully monitoring therapy.

Most recruits with active TB are asymptomatic. The diagnosis is suspected on review of the chest radiograph. Radiographic abnormalities compatible with early active disease must be taken seriously. Recruits are hospitalized to collect three sputum specimens, which are examined for AFB and cultured for *M*

tuberculosis. Recovery of *M tuberculosis* confirms the diagnosis of active tuberculosis and mandates four-drug therapy consistent with treatment guidelines.[45] Before treatment, drug susceptibility testing must be performed. Recruits who are found to have active TB are usually returned to their homes. Contact should be made with local public health authorities and pertinent information provided so that appropriate follow-up can take place.

Military medical officers should not hesitate to ask for consultation on specific treatment of individual patients or help with the attendant investigation of contacts and exposed personnel. Control of TB is a complex matter requiring time, effort, personnel, and other resources, as well as steadfast vigilance. The consequences of failure to attend to TB were vividly demonstrated in the rise in TB in the late 1980s and early 1990s and the concomitant development of multidrug-resistant TB. As more foreign-born persons serve in the US military and as the military continues to deploy to the far corners of the world, the threat of TB will not diminish.

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