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Occupational Tuberculosis

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Tuberculosis (TB), the "White Plague" of the nineteenth and early twentieth centuries, progressively declined with the introduction of public health measures at the turn of the century and then with the widespread use of antituberculous therapy in the 1940s and 1950s. This decline continued until the 1980s, when an upsurge in the incidence of TB in the United States coincided with the onset of the acquired immune deficiency syndrome (AIDS) epidemic. Relaxation of traditional public health measures aimed at the diagnosis and treatment of tuberculosis and alterations in social demographics—particularly increased immigration from endemic areas and a burgeoning homeless shelter and prison population—also contributed to the reversal of progress in TB control during this period. Coincident with the rise in tuberculosis incidence in the 1980s, the emergence of multidrug-resistant TB increased the risk of serious illness and death in those developing active tuberculosis. The number of new cases of tuberculosis continued to rise until the mid-1990s, when renewed commitment of resources to public health with improvements in recognition and treatment of TB in high-risk individuals combined to decrease the incidence of active and latent tuberculosis.

These trends increased the risk of tuberculosis among segments of the working population, particularly health care workers. The Occupational Safety and Health Administration (OSHA) estimated that over 5 million workers were exposed to TB in the course of their work [1], and while the incidence of tuberculosis continues to decline, health care workers remain at significant risk of exposure and possible infection. Health care has been the second fastest growing sector of the U.S. economy, employing over 12 million workers. The increase in workers with direct contact with infected individuals requires continued efforts to maintain effective measures to prevent tuberculosis, even as its overall incidence again declines in the United States. This chapter reviews the microbiology, pathogenesis, diagnosis, and epidemiology of tuberculosis, focusing on occupational exposure and surveillance measures to prevent tuberculosis infection among workers employed in health care and other high-risk jobs.

Pathogenesis and Transmission

Tuberculosis is caused by *Mycobacterium tuberculosis,* a member of a large and diverse genus of aerobic and nonmotile bacilli that differ in microbiology, biochemistry, and virulence. *M. tuberculosis* has a length of 1–4 µm and a thickness of 0.3–0.6 µm. Several characteristic biologic properties are clinically important. It is an obligate aerobe and grows best under conditions of high oxygen tension; as a result, infection typically involves the lungs in both animals and humans. Its cell wall has a high lipid content that resists both usual microbiologic stains and decolorization with alcohol. It also has a slow growth rate, with generation times between 12 and 18 hours, so laboratory isolation by culture typically may take weeks.

Almost all cases of tuberculosis are spread by person-to-person transmission through the respiratory route. Patients with active pulmonary or laryngeal tuberculosis shed infectious organisms into the ambient air through coughing, sneezing, or speaking. Larger droplets settle quickly onto nearby surfaces and generally are noninfectious despite containing large numbers of bacilli. In contrast, smaller droplets (1–5 μm in diameter), also called *droplet nuclei,* desiccate and remain suspended in the air for several hours, traveling substantial distances indoors. These particles, although containing only one to three active TB bacilli, are small enough to bypass upper respiratory defenses and impaction at the level of the bronchioles. They may be inhaled deep into the lungs, and once settling in the alveoli, tubercle bacilli may slowly multiply and initiate infection.

In response to infection, lymphocytes are stimulated and release cytokines that activate macrophages. Most of the bacteria are engulfed and killed, but some may survive and invade lymphatics and the bloodstream, draining to regional lymph nodes, and through hematogenous spread may infect virtually any organ. High blood flow and high local oxygen tension favor the development of infection when disseminated. Predictably, the most frequently infected parts of the body include the apices of the lungs, the renal cortex, the vertebrae, and the metaphyses of long bones. During the first 3 weeks, bacilli can multiply logarithmically; however, by the third week in the previously uninfected host, cell-mediated immune mechanisms have been initiated, and bacterial destruction by activated macrophages is increased. Granulomata form around and isolate foci of infection, encasing initial tuberculous lesions. These granulomatous tubercles characteristically have a necrotic or caseating center, a pathologic hallmark of TB.

M. tuberculosis does not produce enzymes or toxins, and in the immunocompetent host there is little tissue destruction or inflammation initially. Most patients remain asymptomatic after primary infection. In contrast, immunosuppressed individuals are particularly vulnerable to tubercle bacilli and may develop symptomatic primary infection. Primary symptomatic tuberculosis historically was a pediatric disease, but with an increasing number of immunosuppressed adults, this is now observed more commonly among adults. It presents most commonly as an atypical pneumonia, but other common presentations include pleuritis with pleural effusions, pulmonary cavitations, and extrapulmonary tuberculosis. Primary extrapulmonary tuberculosis presented classically in children as cervical adenitis, miliary tuberculosis, or tuberculous meningitis. However, as with primary symptomatic infection, in general, primary extrapulmonary tuberculosis is now seen most commonly among persons infected with human immunodeficiency virus (HIV).

Although granuloma formation will contain the initial TB infection, viable bacteria can persist within granulomata. These can cause reactivation of infection when immunity wanes. Reactivation of latent tuberculous infection (LTBI), although more common soon after primary infection, may occur in an untreated person at any point in time, even decades after primary infection. Postprimary, or reactivation, pulmonary tuberculosis is the most common clinical form of tuberculosis. Reactivation typically occurs in the apical and posterior upper lobes of the lung, a reflection of the organism's affinity for regions of high oxygen tension. Reactivated TB may be manifested by pulmonary infiltrates, cavitations, empyema, fibrosis, and extrapulmonary tuberculosis with spread to other organs.

Although TB reactivation may occur at any time, the risk is greatest in the first years after primary infection. Approximately 5–15% of immunocompetent individuals develop active TB within 2 years of the initial infection. The incidence of reactivation of latent disease then declines to a low level for the remainder of an exposed individual's lifetime unless the immune mechanisms holding the infection in check are disrupted, often a consequence of aging or the development of chronic disease. The cumulative lifetime risk of tuberculosis reactivation has been estimated at 10%. This reflects both the high initial incidence of the infection and ongoing sporadic cases of reactivation among individuals with remotely acquired infection [2].

Reactivation of TB depends on many factors related to an individual's immune response to infection, which determines whether the infecting bacilli will be contained or will multiply and disseminate. Patient factors that appear to impair immunity and increase the risk of reactivation include older age, poor nutritional status, and concomitant illnesses such as HIV infection, AIDS, diabetes mellitus, renal insufficiency, hematologic malignancies, and silicosis. Chemotherapeutic agents and corticosteroids also impair the immune system and also may lead to reactivation of TB. The greatest incidence of reactivation occurs in individuals with HIV infection, up to 10% per year. Although overall prevalence of infection with *M. tuberculosis* is not increased in people with HIV infection, they do develop primary active TB at a higher rate and in a shorter period of time (as soon as 1 month after exposure) than do persons without HIV infection. Additionally, the clinical presentation of active tuberculosis in persons with HIV infection may differ, particularly once severe immunosuppression occurs, producing infections that are more widespread and severe.

Epidemiology of Occupational Tuberculosis

Since the 1950s, extraordinary progress has been made in the control and eradication of tuberculosis in the United States. Prior to the twentieth century, tuberculosis was the leading cause of death. With the advent of screening and public health programs beginning in the 1930s, followed by effective TB therapy in the 1940s and 1950s, the incidence of tuberculosis continued to decline every year from 1953 through 1985. The annual number of TB cases decreased by 74%, from 84,304 to 22,201 cases, and the case rate decreased by 82% from 53 to 9.3 cases per 100,000 population. In the early 1970s, many considered it no longer a public health problem, federal funding began to decrease, and TB public health services began to close. By the late 1980s, TB began to emerge again, and in 1986, a 2.6% increase in the number of TB cases marked the beginning of a resurgence of TB.

Several factors contributed to the resurgence: inadequate funding and dismantling of public health services providing screening and treatment of TB, the HIV and AIDS epidemic, the emergence of multidrug-resistant TB (MDRTB), and an increase in TB among the homeless, prison inmates, and other institutionalized persons. HIV infection is one of the greatest risk factors for active TB infection, and significant numbers of HIV-related TB outbreaks were reported among patients and health care workers and in correctional facilities and homeless shelters. There also was a proportionate increase among foreign-born persons. Excess cases of active TB infection (those that would not have been seen if previous trends had continued) in the period 1985–1992 were estimated at 52,100 [3].

The resurgence peaked in 1992 at 26,673 cases, or 10.5 cases per 100,000 persons. In response, renewed public health efforts, particularly targeted to well-defined risk groups and geographic locations, marked the beginning of a decrease in TB rates. Since 1993, rates of TB have once again declined, reaching an all-time low in 2004, with 2.6 cases per 100,000 persons. This represents a 61.9% decline in the incidence of tuberculosis since 1992 [4]. This trend has been attributed to the introduction of effective antiviral therapy for HIV infection, which has reduced the number of AIDS patients and their complications, including tuberculosis, combined with renewed public health efforts to identify and treat persons with both active and latent tuberculosis. During the same period, the incidence of MDRTB has declined by 76.5%. In 2003, about 1% of the 11,040 cases of TB were caused by MDRTB strains, a reduction owing primarily to public health efforts to ensure patients complete treatment for active or latent tuberculosis [4].

Despite the overall downward trend in rates of TB, not all groups have been affected equally. Rates among foreign-born residents of the United States, African-Americans, and Hispanics, although decreased, remain elevated in comparison with U.S.-born and white residents. Rates among foreign-born residents, although declining about 33% from the levels of the early 1990s, remain nearly 10 times higher than those of U.S.-born whites, at 22.5 cases per 100,000 persons. Worldwide, tuberculosis remains the second leading cause of infectious death after malaria, and it is estimated that 2 billion people, or one-third of the world's population, are infected. There are nearly 8 million new cases a year, with 3 million deaths, a figure that may be expected to increase because of the ongoing HIV epidemic in developing countries.

The recognition of TB as an occupational hazard, particularly among health care workers, lagged behind improvements in general public health measures aimed at its control. Standard texts from the 1920s and 1930s maintained that there was no danger from workers' breathing the expired air of consumptive patients or being coughed on by TB patients [5]. Pioneering studies by Heimbeck in Oslo in the 1920s demonstrated 95% tuberculin test conversion in nursing students by the time of graduation; furthermore, 22% of these initially negative nurses developed clinical tuberculosis compared with 1.5% of 200 initially tuberculin-positive nurses [5]. Despite similar compelling data from other studies, the recognition and control of TB as an occupational hazard were delayed decades after effective methods of diagnosis and therapy were available. With the advent of antituberculous therapy in the 1940s and 1950s, occupationally acquired TB became less frequent but, paradoxically, more conspicuous in light of the general trend toward reduced incidence of the disease.

One of the first comprehensive epidemiologic studies of the risk of tuberculosis among workers was a 1973–1974 survey of employees of the New York City Board of Education. This study found an overall 12% tuberculin reactivity in 61,000 employees; differences in prevalence within this cohort were related to ethnic group, socioeconomic status, age, and gender [6]. A second study by Berman and colleagues analyzed results of a 5-year (1971–1976) tuberculin-screening program in a Baltimore hospital [7]. The authors calculated an annual risk for TB infection of 1.4% among employees of the hospital, although the authors attributed the higher-than-expected conversion rate to a booster effect and to exposure in the community. Other studies among health care workers during this period found conversion rates of 0.11–4.5% depending on such factors as location and patient population. Despite evidence that tuberculin reactivity was prevalent in as much as one-fourth of some segments of the population, screening and treatment programs during the 1970s became underfunded, and previously successful public health measures atrophied, allowing for a substantial increase in incidence and prevalence of tuberculosis in the next decade.

An increase in TB, as a concomitant opportunistic infection in patients with HIV infection, paralleled the worldwide AIDS epidemic in the 1980s. Except for the period from 1979–1981, when an influx of refugees had slightly increased the incidence of tuberculosis, rates of tuberculosis in the United States had declined by about 6% a year since 1953. As noted earlier, between 1985 and 1992, the combination of the HIV and AIDS epidemic, homelessness, and an underfunded public health system led to an almost 20% increase in the rates of tuberculosis. As expected, risks to health care workers of TB infection became disproportionately skewed toward institutions that provided care to the homeless, indigent, and inner-city populations. Additionally, with the rise in cases of MDRTB, the perception of increased risk of severe illness and even death from TB became more widespread. Evidence for the increased risk to health care workers was drawn both from prevalence data on skin test conversions and from incidence data on new skin test conversions in outbreaks of TB in facilities. Postexposure rates of employee purified protein derivative (PPD) conversions have been noted to range from 4–77%, with most reported incidence rates from 15–30% [8]. Eight cases of active MDRTB developed in health care workers in New York and Miami hospitals in the period 1990–1991. Epidemiologic evidence linked these cases to nosocomial transmission from infected patients [9].

Routine exposure to patients in some hospitals has resulted in conversion rates of 5–10% per year [10]. In an attempt to quantify risk for a proposed standard, OSHA had calculated estimates of relative risk for TB skin test conversion ranging from 1.47–9.0, based on results from a 1994 Washington State hospital survey, a statewide survey in North Carolina, and data from 1989–1991 at Jackson Memorial Hospital in Miami [1]. Higher risks of PPD conversion (14.5% over 4 years) were found in employees who worked on wards where patients with culture-confirmed TB were cared for compared with 1.4% in those who did not work around these patients [11]. Furthermore, risk was not limited to those with direct patient contact; it also was increased in other workers, such as clerks, on the same wards. Health care tasks that increase the likelihood of contact with airborne bacilli also carry a particularly high risk. Pulmonary fellows converted at an 11% rate during their 2-year training period; this incidence compares with a 2.4% conversion rate in infectious disease fellows who would have cared for a similar patient population, indicating that respiratory aerosol generation by patients, particularly during instrumentation or procedures such as bronchoscopy, was an important determinant of infectivity [12].

Data on occupational risk outside hospital-based health care are sparse. Increased numbers of individuals with TB are isolated or cared for in settings such as prisons, homeless shelters, medical laboratories, hospices, and home health care services. Populations in correctional facilities, where high-risk individuals are overrepresented, have TB case rates that are estimated to be 3–11 times higher than in the general population. A 2-year employee screening program in New York State prisons found a PPD conversion rate of 1.9%. Relative risks for conversion were 1.64 in guards and 2.39 in medical employees in facilities with known TB cases [13]. Occupational exposure was estimated to account for 33% of new tuberculosis infections in this study. A recent multisite study of correctional health care workers found high prevalence rates of TB skin test reactivity (17.7%) and estimated an annual incidence rate of skin test conversion of 1.3%. Risks of a positive test were strongest, however, for those originating from outside the United States and those having a history of bacille Calmette-Guérin (BCG) administration, suggesting that demographic factors for skin test reactivity were more important than occupational risks [14].

Facilities for chronic and long-term care present another setting where workers may be exposed to infection. Facilities for the elderly continue to house a cohort of individuals for whom chemoprophylaxis of tuberculous infection had not yet been instituted and who thus present a risk for reactivation. Positive PPD rates among residents range from 10–40%. In addition, by virtue of age and illness, the uninfected may be particularly susceptible to primary infection from fellow residents. Large-scale screening studies of workers in these facilities do not exist; a smaller study from Canada [15] found a 15.7% rate of positive tuberculin testing in 286 staff members from a hospital and two chronic care facilities, paralleling a 14% rate among residents. A high rate of positive reactions (39.5%) was found among staff in elderly and mental health care services in a New Zealand hospital, implying that exposure may be much higher than had been suspected [16].

A fivefold risk for active TB in laboratory workers was noted in a large 1971 survey study in the United Kingdom [17]. Technicians in "morbid anatomy" departments (those working with tissue) were at the greatest risk for development of disease. Little current data exists on PPD conversion rates or transmission of TB in laboratories. Tuberculosis of the skin from primary inoculation, termed *prosector's wart,* is a well-known phenomenon in pathologists and related technical personnel [18]. Cutaneous inoculation of TB in laboratory personnel as a result of injuries by sharp instruments has been described [19].

The relationship of silicosis to the development of active tuberculosis infection has been well known for the last century and is the subject of an extensive literature. Active tuberculosis has been found to develop in as many as 25% of workers with silicosis; these workers have at least a threefold higher risk of death from TB infection. Work in silica-exposed occupations, such as quarrying, pottery, stone carving, and ship building and repair, is associated with a higher incidence of tuberculosis [20]. Because of the high rate of disease in these individuals, some authorities have suggested prolonged, even lifelong chemoprophylaxis for workers with silicosis who exhibit PPD conversion [21].

Diagnosis of Tuberculosis

Early diagnosis of both active TB and latent TB is key to the effective control and eradication of TB. A high index of suspicion is important to early identification and diagnosis of cases of TB, and no ideal single test is available for the diagnosis of either active or latent TB infection. Instead, diagnosis depends on the combination of clinical symptoms, chest radiography, microscopic examination and staining of appropriate specimens, microbiologic culture, and more recently, nucleic acid amplification assays.

Diagnosis of latent tuberculosis infection (LTBI) is based on the tuberculin PPD skin test, and until recently, the tuberculin skin test (TST) was the only reliable method of diagnosis of LTBI. The delayed-type hypersensitivity (DTH) reaction forms the basis for this common method of diagnosing TB infection. PPD of tuberculin, an extract of the bacterial cell wall prepared from the supernatant of cell cultures, stimulates a cell-mediated immune response when injected intradermally in subjects who have had tuberculous infection. The TST was designed originally for diagnosis of active infection, but its lack of sensitivity and specificity, and particularly its inability to distinguish between latent and active infection, make it unsuitable for the diagnosis of active TB. Both immunocompetent individuals with active TB infection and healthy subjects with LTBI but no evidence of active disease will react to this test. The inflammatory response produces an area of induration, the extent of which is used to assess the likelihood of infection and the need for preventive therapy. In individuals with primary TB infection, the PPD reaction becomes positive 4–12 weeks following exposure and initiation of infection. This time delay should be borne in mind when investigating TB outbreaks or exposure to active cases of TB.

Various TSTs have been available. The Mantoux test, using a single intradermal injection of an intermediate strength of PPD, is the most reliable method and has replaced multipuncture tests, such as the tine test. The preferred method for the test consists of intracutaneous injection of 0.1 mL of 5 tuberculin units (5 TU) of a standardized PPD preparation sufficient to result in a small wheal on the forearm or other injection site. The test is read 48 and 72 hours following injection and should be interpreted by personnel with adequate training and experience. A positive result is based on the extent of induration at the injection site; redness or erythema may be present in many individuals and may extend well beyond the injection site but should not be measured or considered positive.

Both false-negative and false-positive reactions can occur with the TST. Some persons with *M. tuberculosis* infection may not react to the TST. Persons with a weakened immune response from immunosuppressive drug therapy or HIV infection, children younger than 6 months of age, and persons acquiring a TB infection recently may not react to the skin test. The skin test also may be negative in cases of overwhelming infection, and negative skin testing should not be used to rule out active tuberculous infection. Expired PPD or an incorrectly administered skin test also can lead to false-negative results. The PPD must be administered intradermally; deeper subcutaneous injection can lead to a false-negative reaction. If the first test is administered incorrectly, another dose can be given immediately at another site. Table 9-1 summarizes how to administer and read the TST.

Table 9-1
Administering the Intradermal Mantoux Tuberculin Skin Test

1. The tuberculin skin test (TST) is performed by injecting 0.1 mL of tuberculin purified protein derivative (PPD) into the inner surface of the forearm. Select a smooth area on the forearm, and prepare it with alcohol.
2. The injection should be made intradermally with a tuberculin syringe, with the needle bevel facing upward. When placed correctly, the injection should produce a pale elevation of the skin, a wheal, 6–10 mm in diameter. Subcutaneous injection can result in a false-negative test. Another test dose can be given immediately at another site if the first test was administered improperly.
3. The skin test reaction should be read between 48 and 72 hours after administration. A patient who does not return within 72 hours will need to be rescheduled for another skin test.
4. Use a ballpoint pen or finger to measure the area of induration. Using a ballpoint pen, draw a line towards the area of induration. An increase in the resistence to movement of the pen will be noticed when the border of induration is reached. Repeat this step from the other side, and the overall width of the induration then can be measured with a ruler. (The diameter of the indurated area should be measured across the forearm, perpendicular to its long axis). When a pen is not available, the borders of induration can be identified with a finger.
5. The reaction should be measured and recorded in millimeters of induration. Do not measure erythema or redness. *The absence of induration should be recorded as "0 mm" induration and not "negative."*

False-positive results are also possible with the TST. Persons infected with nontuberculosis mycobacteria and those previously vaccinated with BCG can have false-positive reactions. Incorrect interpretation of the test also will lead to false-positive results. Only the area of induration in response to PPD should be measured and recorded. Erythema or redness at the site of injection occurs often but should not be included in the measurement; otherwise, the reaction may be incorrectly interpreted as positive.

The Centers for Disease Control and Prevention (CDC) have established guidelines for the interpretation of the test based on the likelihood of the degree of induration predicting the presence of infection and the risk of developing active TB. Since the predictive value of a positive test depends on the prevalence of a condition in the population, a higher positive threshold is set for use of the test in populations expected to have a low risk of exposure or development of infection and a lower positive threshold for populations at increased risk. For example, 5 mm of induration represents a positive

reaction and is predictive of TB in persons with HIV infection or persons in close contact with patients known to have TB, whereas 15 mm of induration represents a positive reaction in persons with no identifiable risk factors. The CDC classification [22], shown in Table 9-2, outlines the criteria for a positive test in various population groups.

Screening for LTBI previously had been done by widespread tuberculin skin testing with limited consideration of the risk for TB in the population tested. The CDC now recommends TB testing be reserved for persons at high risk, and with the exception of initial testing of persons at low risk whose future work or other activities will place them at increased risk, screening of low-risk persons is no longer recommended. This strategy of targeted tuberculin testing, which should replace less discriminate screening, is a key strategic component of TB control. Targeted tuberculin testing identifies persons at high risk for developing active TB who would benefit from treatment of LTBI. Persons at increased risk include those who have had a recent infection and those with associated conditions that increase the risk of progression of LTBI to active TB. Infected persons at high risk should be offered treatment irrespective of age.

The tuberculin skin test in health care workers should be interpreted according to these same CDC guidelines. Two additional points, however, should be kept in mind in this interpretation. The first is that individual risk factors outside the work environment must be considered in the interpretation. For example, a worker who is receiving therapy that may be severely immunosuppressive or who has HIV infection will be considered to be in a higher-risk group for reactivation, and therefore, a skin test showing 5 mm of induration may represent a positive test. The second point is that in health care settings where TB is treated, close contact with infectious patients places workers at increased risk. In these workers, a skin test showing 10 mm of induration is probably sufficient to indicate a positive result, even in the absence of other risk factors. By contrast, if a facility presents a low or minimal risk for TB exposure, a cutoff point of 15 mm may be used to judge a result positive if the individual has no other risk factors. In general, in facilities that treat TB patients, an increase in skin test induration of 10 mm or more in a 2-year period indicates a skin test conversion; for facilities in which the risk of exposure is minimal, a cutoff point of 15 mm or more may be used. If a known exposure has occurred in a health care setting, an increase of 5 mm or more from a 0-mm baseline in a health care

Table 9-2
Criteria for Positive Tuberculin Reactivity

Size of Induration	Risk Group
Reaction ≥ 5 mm of induration	HIV-positive persons
	Recent contacts of TB case patients
	Fibrotic changes on chest radiograph consistent with prior TB
	Patients with organ transplants and other immunosuppressed patients (receiving the equivalent of ≥15 mg/d of prednisone for 1 month or more)
Reaction ≥10 mm of induration	Recent immigrants (i.e., within the last 5 years) from high-prevalence countries
	Injection drug users
	Residents and employees[a] of the following high-risk congregate settings: prisons and jails, nursing homes and other long-term facilities for the elderly, hospitals and other health care facilities, residential facilities for patients with AIDS, and homeless shelters
	Mycobacteriology laboratory personnel
	Persons with the following clinical conditions that place them at high risk: silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g., leukemias and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck and lung), weight loss of 10% or more of ideal body weight, gastrectomy, and jejunoileal bypass
	Children younger than 4 years of age or infants, children, and adolescents exposed to adults at high-risk
Reaction ≥ 15 mm of induration	Persons with no risk factors for TB

[a]For persons who are otherwise at low risk and are tested at the start of employment, a reaction of 15 mm or more of induration is considered positive.
Source: Adapted from Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49:24.

worker with close contact with the infected patient should be considered a positive result; however, if the employee's original baseline was more than 0 mm, a 10-mm increase remains the recommended cutoff for considering a test conversion [23].

Boosted reactions on TST can occur among hospital workers and other groups and may be mistaken for conversion. Reaction to tuberculin skin testing may wane gradually, and if many years have passed since initial TB infection or repeated antigenic challenge by skin testing, an individual beginning a screening program may have an initially negative skin test. However, after repeated testing, the reduction in cell-mediated hypersensitivity may be reversed, and the TST may become positive again, a phenomenon termed *boosting*. If not recognized in testing an individual, boosting can be misinterpreted as new PPD conversion, and the individual may be mistakenly diagnosed as a new case of TB. A two-step testing protocol has been recommended to avoid misinterpretation of the boosting phenomenon in subjects, including health care workers, who may need repeated testing [22]. An initially negative PPD test is followed by placement of a second 5-TU skin test 1–3 weeks later. If this second test is judged to be positive, any induration can be attributed to the booster phenomenon and considered to represent previous primary TB infection rather than a new conversion. If the second test remains negative, a subsequent test with a positive result indicates a newly converted case. In elderly populations, the booster phenomenon may not be present until three or more tests have been performed. All patients with positive TSTs, if not treated previously, should receive preventive therapy once active TB is excluded.

BCG vaccination also may complicate the diagnosis of TB infection because the PPD reaction that results cannot be distinguished from that produced by mycobacterial infection. BCG is used in many parts of the world to immunize individuals, primarily as a control measure in regions where TB incidence is high. The protection afforded by BCG vaccination is variable and may depend on host, environmental, and bacterial virulence factors. Reactivity to a TST develops soon after vaccination. Postvaccination skin test results may range from 3–19 mm of induration. The size of skin test reaction does not correlate with the degree of protection against TB that may be afforded by BCG [24]. Tuberculin reactivity owing to BCG vaccine wanes over time, however, and after 10 years may be minimal or absent. Previously, TSTs were interpreted differently in persons vaccinated with BCG. However, the CDC now recommends persons at high risk be tested irrespective of prior BCG administration and the results interpreted as if BCG vaccination had not occurred. For example, an adult health care worker who was immunized with BCG as a child in a country with a high TB prevalence would be considered to have a positive tuberculin skin test with a PPD reaction of 10 mm or greater. BCG vaccination should neither preclude participation in PPD screening nor lead the interpreter to conclude reflexively that BCG administration is the sole cause of an indurated skin test.

Subjects who, because of immunosuppressive illness, may be anergic previously were tested with other companion antigens at the time of PPD testing. Mumps, *Candida*, and tetanus toxoid antigens were administered in addition to PPD as an anergy panel; the absence of a response to these common antigens indicated a state of anergy, or inability to mount a delayed-type hypersensitivity reaction. The results of anergy panels were used to help interpret the results of PPD testing in individuals with impaired cell-mediated immunity, most notably HIV infection. A negative PPD test in the setting of a positive response to an anergy panel was considered a true negative and evidence of no infection. However, a negative PPD test in the setting of a negative response to an anergy panel was considered a false-negative result and did not exclude the possibility of TBI infection. However, because of such factors as selective loss of PPD reactivity and the booster phenomenon, anergy testing is unreliable and no longer routinely recommended in evaluating for tuberculous infection among patients with impaired cell-mediated immunity. Individuals with HIV infection should be assessed according to CDC guidelines, which describe reactions of 5 mm or greater as a positive result. Evaluation for preventive therapy in those who exhibit no response to skin testing should be made on the basis of additional clinical and epidemiologic information, such as evidence of exposure to another individual with active TB, and not the results of anergy testing.

Until 2001, the TST was the only test used to diagnose latent TB infection. Newer in vitro enzyme-linked immunosorbent assays (ELISAs) now have been approved for use in detection of LTBI by the U.S. Food and Drug Administration (FDA). This testing has been available since 2004 under the brand name QuantiFERON-TB Gold (QFT-G). The assay tests for interferon-gamma released from sensitized lymphocytes in whole blood incubated overnight with synthetic peptides simulating two proteins present in *M. tuberculosis:* early secretory antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10). Compared with TST, QFT-G offers several advantages: It can be interpreted after a single patient visit, results are less subject to reader error, and the testing does not require that anamnestic immune responses be boosted for accurate interpretation. PPD contains hundreds of antigens, many shared by other mycobacteria common in the environment. The antigens used in QFT-G are more specific to *M. tuberculosis* and are absent from all BCG vaccine strains and many common nontuberculous mycobacteria, except *M. kansasii, M. szulgai,* and *M. marinum.* The CDC recommends use of QFT-G in all circumstances in which the TST is currently used, including contact investigations, evaluation of recent immigrants, and surveillance programs for infection control [25]. As with the tuberculin skin test, QFT-G testing should be targeted at diagnosing infected patients who will benefit from treatment. Before using QFT-G routinely, arrangements need to be made with a qualified laboratory to guarantee quality assurance and collection and transport of blood within 12 hours. Also QFT-G, like the TST, cannot differentiate between latent and active infection, a decision that must be made on other clinical grounds following a positive test.

For all individuals who exhibit a positive TST or QFT-G test, radiography is used to determine whether evidence of active or prior pulmonary tuberculosis infection is present. Additionally, any patient with symptoms suggestive of pulmonary TB infection should have radiography performed regardless of test results. A posteroanterior (PA) view is the standard radiographic procedure; additional views, such as apical lordotic views, may be needed. The classic, though infrequent, finding of healed initial TB infection is the *Ghon complex,* calcification of both a granuloma and its draining lymph node. Other diagnostic findings include multiple fibrotic or calcified pulmonary nodules; in many, if not most, subjects with LTBI, the chest radiograph is normal. A normal chest radiograph in an asymptomatic, healthy-appearing individual with a positive PPD test excludes the possibility of active pulmonary TB. Active pulmonary TB is characterized by patchy or nodular infiltrates in the apical or subapical upper lobes or the superior segments of the lower lobes, although radiographic abnormalities may occur throughout the lungs. In HIV-infected persons, particularly those with AIDS, pulmonary TB may present atypically, and infiltrates may be seen in any zone of the lungs, usually in conjunction with prominent hilar and mediastinal adenopathy. Cavitation, adenopathy, empyema, and pleural effusions also occur in active TB. Miliary spread of the disease appears as multiple nodular densities throughout the lung fields.

Microscopic examination and cultures of appropriate sputum specimens are still the cornerstones of diagnosis of active TB. To avoid mistakenly culturing saliva and nasal mucus, sputum specimens preferably should be obtained by individuals skilled in the appropriate techniques. Up to 30% of patients are unable to provide an expectorated sputum sample, but sputum production may be induced with saline aerosols. Failure to demonstrate acid-fast bacilli (AFB) on a smear does not exclude the diagnosis of TB; only 60% of patients with a positive culture have a positive AFB smear. Culture for mycobacteria is the diagnostic standard, with up to 93% sensitivity and 98% specificity. Culture with liquid media can provide results in as few as 2 weeks, in comparison with the 6–8 weeks required with solid media. A positive culture for *M. tuberculosis* makes the definitive diagnosis of TB. Since cultures may take up to 8 weeks to yield a positive identification, therapy may be instituted for a provisional diagnosis of active TB on the basis of clinical signs, symptoms, radiographic findings, and AFB smear results. Drug susceptibility testing is essential for all positive initial cultures, and the results should be used to guide modifications of antibacterial therapy. To assess effectiveness of, and response to, therapy, as well as to ascertain potential infectiousness of the patient, follow-up sputum examination and culture should be obtained at least monthly until cultures become negative.

Preventive Therapy

Isoniazid (INH) is the most widely used treatment for LTBI. It is bactericidal, relatively nontoxic, easily administered, and inexpensive. Treatment with INH has been demonstrated to reduce the risk of progression to active TB by as much as 90% in adults if a full course is completed. The recommended dose of INH for adults is 300 mg once daily. A minimum of 6 months of treatment with INH is essential. Nine months is often recommended, and there is a small but definite benefit to 12 months of therapy. The 2003 American Thoracic Society (ATS)/CDC/Infectious Diseases Society of America (IDSA) guidelines recommend a 9-month regimen of INH as the optimal regimen for almost all patients irrespective of HIV status or age [22,26]. Individuals with silicosis should receive a full 12-month course; more prolonged, even lifelong therapy in silicosis has been recommended by some [27].

INH should be dispensed only in monthly allotments to allow screening for symptoms of hepatotoxicity. From 10–20% of individuals taking INH develop asymptomatic transaminase elevations; many of these elevations resolve even if the drug is continued. Baseline laboratory is not routinely recommended at the start of treatment but is recommended in patients with a history of HIV infection or liver disease, in women who are pregnant or in the first 3 months of the postpartum period, and in patients whose history or physical examination suggests undiagnosed liver disease. Elevations of three to five times the upper limits of normal or symptomatic adverse reactions should lead the clinician to strongly consider halting therapy. Peripheral neuropathy also may develop as a side effect of INH therapy and generally can be prevented or ameliorated by concomitant pyridoxine (50 mg once daily) administration. Individuals with existing peripheral neuropathy or conditions such as diabetes that may predispose to its development should be evaluated and monitored carefully while undergoing prophylactic therapy.

Rifampin, once a day for 4 months, may be prescribed as an alternative to INH but should be reserved for individuals exposed to a patient with INH resistant but rifampin-sensitive *M. tuberculosis.* The CDC previously also had recommended a 2-month regimen of daily rifampin and pyrazinamide; data indicating high rates of hospitalization and death from liver injury associated with the use of rifampin and pyrazinamide prompted the CDC to issue a report recommending that this regimen generally should not be offered to persons with LTBI [28]. Rifampin and pyrazinamide should continue to be used as part of multidrug regimens to treat active TB.

Prevention and Control Strategies

ENGINEERING AND PROTECTIVE EQUIPMENT

Primary prevention strategies include rapid identification of patients with active TB and prompt isolation until they are determined to be noninfectious. The CDC recommends airborne infection isolation for all patients with pulmonary TB. Engineering controls, including negative-pressure isolation rooms, increased room ventilation, local exhaust ventilation, high-efficiency particulate air (HEPA) filtration, and ultraviolet (UV) radiation, are appropriate mechanisms for reducing the concentration of airborne droplet nuclei, limiting their dispersion throughout an institution and thus decreasing the potential for inhalation of pathogenic bacilli. The isolation area should receive at least 12 air changes per hour (ACH) for new construction as of 2001 and at least 6 ACH for construction before 2001 [29]. Increased ventilation to a patient or isolation room significantly reduces airborne particle concentration through dilution and will reduce the concentration of droplet nuclei by 99.75% under ideal conditions.

The room should be under negative pressure so that the direction of airflow is from the outside adjacent space into the room. Negative-pressure airflow, which results from maintenance of a pressure gradient between the interior of a hospital room and the surrounding work area, is an effective strategy for limiting the spread of airborne pathogens in hospitals and related facilities. Combined with appropriate ventilation controls, these systems reduce the risk of transmission to workers in adjacent areas. Negative-pressure mechanisms, however, are delicate and susceptible to a variety of disturbances, particularly in large facilities, where a number of influences can disrupt them. Reversal of normal pressure patterns can result from simply opening the door to the room, thus obviating the protective effect of airflow into the room. Maintenance and inspection of pressure systems must be frequent and systematic.

The air in the isolation room preferably is exhausted to the outside but may be recirculated, provided that the return air is filtered through a HEPA filter. HEPA filters designed to capture particles 0.3 μm in diameter with an efficiency of 99.97% will be effective in removing the 1- to 5-μm droplet nuclei that are infectious. HEPA filtration of a room or confined area generally is considered an adjunct to other ventilatory controls, particularly in situations in which ventilation is substandard or circulated air must, for engineering reasons, be reentrained back into the building. Disadvantages of HEPA filtration include the filters' resistance to entrainment of air through them, with consequent costs in energy and potential for leakage around the filter; the need for periodic maintenance and replacement, without which effectiveness is considerably reduced; and the failure of local or free-standing units to capture particulates in the vicinity. OSHA has recommended the use of HEPA filtration in cases in which air from isolation rooms cannot be exhausted away from employees, intake vents, and the public or must be recirculated within the building [1].

Ultraviolet germicidal irradiation (UVGI) has been suggested for use as a bactericide in several settings within hospitals, including isolation rooms, air-system ductwork, and recirculating room air cleaners. There remain differences of opinion regarding the efficacy of UVGI in reducing the airborne burden of *M. tuberculosis.* Claims have been made that irradiation results in reduction of viable organisms equivalent to over 20 ACH [30]. By contrast, other investigators have estimated the result of bacterial inactivation by UVGI at only 1.6 ACH and thus have not considered it an appropriate method of reducing bacterial aerosols in areas where they may be constantly generated [31]. The CDC recommends the use of UVGI as a supplemental air-cleaning mechanism in isolation, treatment, and waiting rooms; emergency facilities; and other areas where undiagnosed patients with active TB may be found [21]. It is not recommended as a stand-alone substitute for negative pressure in isolation rooms or for HEPA filtration of air that must be recirculated.

While these methods will reduce the number of infectious particles within an isolation room, the use of personal respiratory protection is also indicated for all persons entering airborne isolation rooms. Respiratory protection is also needed in procedure areas where the generation of aerosols with high infective potential is likely and in enclosed areas where engineering controls are not feasible, such as ambulances and other forms of transport. Respiratory protective devices must meet standards and performance guidelines developed by the National Institute of Occupational Safety and Health (NIOSH):

1. Filtration efficiency of 95% or greater for particles of 1 μm at flow rates of 50 L/min
2. Ability to be reliably quantitatively or qualitatively fitted such that fit testing results in leakage in no more than 10% of cases
3. Ability to fit faces differing in size and other characteristics
4. Ability to check for facepiece fit [32]

HEPA filter negative-pressure respirators, which filter particles of 0.3 μm with 99.97% efficiency, have been considered effective under these guidelines. The use of HEPA filter masks has been problematic because of evidence that particles leak around face seals in 10–20% of subjects, thereby reducing their protective effect. Cost and discomfort of the masks may hinder their widespread acceptance. Under more recent NIOSH criteria, N-95 respirators, which meet particle-removal efficiency standards of 95% for 0.3-μm particles, meet criteria for use in TB prevention guidelines.

Common surgical masks lack effective filtration for small particles and are of little use to the worker exposed to aerosols generated by a patient with TB. However, such a mask can be useful for temporary, short periods in patients who may present a risk within the facility, for example, those being transported for tests or procedures or those who have not yet been admitted to an isolation room. These masks will stop expulsion of most respiratory droplets and reduce the generation of droplet nuclei. Masks should be changed if wet with secretions or sputum because forceful coughing then may expel particles from the mask. Since surgical masks may be uncomfortable and stigmatizing for the patient, they should not be used as a prolonged substitute for effective isolation procedures.

In accordance with the OSHA respirator standard [33], individuals should undergo determination of medical fitness to wear a respiratory protective device. Although infrequent, some medical conditions may result in the inability to wear a respirator mask; individuals with such conditions should be kept from known or direct exposure to patients with active tuberculosis (e.g., direct patient contact or attendance at high-risk procedures). A related issue is the need for greater protection in performing procedures, such as bronchoscopy or chest physiotherapy, that result in the generation of large volumes of potentially infectious droplets. Positive-pressure or powered HEPA filter respirators may be more effective choices for individuals who perform these procedures regularly. Although data regarding the utility and efficacy of respiratory protection in the prevention of TB in institutions are sparse, the CDC recommendations for health care facilities are firm regarding the use of respirators, and individuals responsible for safety and health in these facilities must familiarize themselves with requirements for a respiratory protection program.

While engineering controls and personnel protective equipment are effective in reducing exposure and infection, overemphasis on ventilation and stationary engineering controls does little to reduce nosocomial spread from patients in whom active TB is not suspected [30]. A high index of suspicion, early isolation and institution of protective measures, and rapid diagnosis are essential to preventing the spread of TB throughout a health care facility.

SCREENING AND SURVEILLANCE

Secondary prevention or early diagnosis of LTBI before a person becomes symptomatic, and when treatment is effective, has been accomplished primarily through systematic screening of potentially exposed workers using tuberculin skin testing. The fundamental principles of tuberculin skin testing were outlined earlier; its application to workers exposed to TB is discussed in this section. Previously, tuberculin skin testing was the only test available for the diagnosis of LTBI. QFT-G is now available and may be substituted as an alternative to tuberculin skin testing for surveillance; results are available after a single patient visit, are not subject to reader error, and are not confounded by a waning DTH skin reaction or the booster phenomenon.

Any facility that houses or cares for persons with suspected or confirmed TB, including hospitals, nursing homes, and homeless shelters, should develop an exposure control plan and complete a risk assessment that identifies the job tasks and individuals who potentially will be exposed to *M. tuberculosis.* This exposure assessment determines which workers should be included in a surveillance program and how frequently testing should be done. Every employee who potentially may be exposed to tuberculosis should participate in a medical surveillance program that systematically and periodically tests for LTBI. The exposure control plan also should include provisions for exposure incidents and should include appropriate medical evaluation and follow-up for all employees exposed to tuberculosis regardless of whether the employee had been participating in periodic screening and surveillance.

Health care facilities and other worksites should gather complete, reliable information on the baseline PPD skin test status of employees prior to initial assignment to jobs with occupational exposure to TB. An initial two-step protocol for PPD skin testing should be performed on hire or on initiation of a surveillance program for all employees not known to be previously positive or who cannot document a negative TST in the past 12 months. Individuals who exhibit the booster phenomenon (an initially negative test followed by a second positive PPD test), indicative of past TB infection with subsequent waning of the cell-mediated immune response, can be excluded from subsequent PPD skin testing. All individuals with a boosted reaction should be evaluated by a physician for treatment of LTBI. BCG vaccination should not be considered a contraindication to PPD testing; it is important to remember that these individuals also may exhibit a boosted reaction on two-step testing. The application and reading of skin tests (see Table 9-1) and interpretation of positive tests according to the CDC guidelines (see Table 9-2) should be performed by medical professionals trained in their interpretation. The employee should not, and should not be expected to, read and interpret his or her own test results.

Following the baseline PPD test, periodic retesting should be performed at least annually for employees at risk of exposure to TB. The CDC recommends that the frequency of PPD testing be based on a risk assessment of the health care facility, including the number of cases of infectious TB present and the potential for transmission to workers. The frequency of retesting will vary for different facilities; testing as frequently as every 3 months is suggested for workers in facilities with the highest risk, defined as areas with an elevated rate of skin test conversions, evidence of a cluster of conversions, or evidence of transmission between patients or from patients to workers [23, 25]. At the very least, employers should provide TB skin testing every 6 months for employees who routinely enter AFB isolation rooms, perform or are present during high-hazard procedures, transport suspected or confirmed infectious patients in enclosed vehicles, or work in intake areas of facilities where six or more confirmed cases of infectious TB have been encountered per year. These workers are considered to be exposed more intensely and frequently. In contrast, other workers with lower risks of exposure should be retested yearly.

Individuals in health care and other exposed work settings who have a positive PPD should have chest radiography performed to exclude the possibility of active tuberculosis. In the absence of radiographic evidence and clinical signs and symptoms of tuberculosis, treatment of latent tuberculosis with INH is indicated. When the source patient is known or strongly suspected to have MDRTB, a careful assessment of the exposed worker's health and immunologic status is mandated. Individuals at greater risk of developing active TB, particularly persons with HIV infection, immunosuppressed persons because of other medical conditions or therapies, the very young, and the elderly, should be considered for multiple-drug prophylactic therapy. This usually consists of the addition of rifampin to the prophylactic regimen but should be tailored to the known susceptibilities of the isolate or to the pattern of drug resistance in the facility. An infectious disease specialist with expertise in the treatment of MDRTB should be consulted.

A PPD conversion in the workplace may be a sentinel event, indicating that other workers or patients have had similar exposures. A history of contacts and possible exposures should be elicited from the individual with a newly converted skin test. If this history indicates that exposure took place within the facility, contacts of the suspected source should be identified and tested. A similar protocol should be followed in identifying contacts of a suspected or confirmed case of a worker with active TB within a facility; patients and coworkers must be identified and tested for evidence of TB infection [23]. If exposure is recent, sufficient time to convert to a positive skin test may not have elapsed, and any identified contacts that are skin test–negative should have repeat PPD testing in 3 months. If additional positive tests are found on follow-up, they are grounds for assessing current controls and preventive measures against the spread of TB within the facility.

Sometimes the probable source of infection cannot be readily identified within the facility at the time a PPD conversion is noted. The period within which the worker was likely to have become infected can be estimated based on previous negative skin test results and ranges from 10 weeks before the last negative PPD test to 2 weeks before skin test conversion. Hospital records during this time, including those from the laboratory and the infection control service, should be examined to determine possible sources of infection. Additional screening within the new converter's occupational group or among area coworkers may be necessary to determine the likelihood of transmission from a common source. If exposure occurred at work, the effectiveness of procedures and policies for TB control in the facility needs to be reviewed and evaluated. Since contact tracing and investigation require extensive work, it is essential to keep accurate and current records of the PPD status of all workers who may sustain TB exposures.

Workers who exhibit PPD conversion but have no symptoms or signs of active tuberculosis may continue work at their current job without restriction, whether or not they are taking INH. They should be advised to report any signs or symptoms of active TB. Prompt assessment for the possibility of active TB infection is indicated if symptoms develop in any skin test converter. Workers who cannot take INH or must have it discontinued before completing a full course should be made aware of the potential for development of active TB infection.

Workers with active pulmonary or laryngeal TB may transmit the infection to patients and coworkers. These workers should be excluded from the workplace until they have been demonstrated to be noninfectious through appropriate treatment. Adequate and continuing therapy, resolution of cough, and three consecutive negative AFB smears should be documented before an excluded individual is allowed to return to work. Special care must be taken to ensure that an infected individual continues with treatment, that treatment remains adequate (based on laboratory tests of sensitivity), and that sputum and other secretions remain negative for AFB. Patients who discontinue treatment before they are considered cured should be reevaluated immediately, and if evidence indicates that the employee may be infectious, he or she should be excluded from work immediately. Individuals with extrapulmonary TB are generally considered noninfectious with respect to the workplace and need not be excluded from work as long as concurrent pulmonary TB has been ruled out [22]. However, for individuals with cutaneous TB, appropriate precautions should be taken to ensure that exposure to actively infected lesions by direct contact does not occur.

The Future

Over the past decade, renewed public health funding and programs have been effective in reversing the resurgence of TB and renewing its progressive decline. Elimination of TB in the United States requires sustained efforts to identify and target populations at risk and requires adequate resources, a lesson brought home by the events of the 1980s. Major research programs are working to develop a safe and effective vaccine, pharmacologic trials are being conducted to study new drugs for the first-line treatment of TB, and molecular genotyping is becoming available as a tool to investigate outbreaks, to understand patterns of transmission, and to control TB.

Health care facilities and other employers whose workers may come into contact with infectious TB need to continue to define their population at risk, monitor employees' exposure status, institute appropriate and ongoing surveillance measures, and maintain effective controls and measures for the reduction of exposure among their personnel. Although evidence of the efficacy and cost-effectiveness of engineering controls and personal protective equipment may not be complete [7], the failure to rapidly recognize and take adequate control measures for exposure appears to be the single most important factor in nosocomial transmission of TB infection.

Current guidelines provide a framework by which exposure reduction and surveillance can be instituted for the protection of exposed employees. From a public health perspective, reducing exposures also benefits those who may not fall under the immediate protection of health and safety standards but whose work may inadvertently put them at risk. Continued surveillance is needed to reduce the risk a new resurgence of TB may have on workers in health care, human services, and other high-risk jobs.

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Notice: This book describes basic principles of diagnosis and therapy. The information provided in this book is no substitute for individual patient assessment based upon the health care provider's examination of each patient and consideration of laboratory data and other factors unique to the patient. This book should be used as a tool to assist the user in making diagnostic and treatment decisions, bearing in mind that individual and unique circumstances may lead the user to reach decisions not presented in the book. You bear full responsibility to determine the applicability of the information available in this book. The authors and publisher disclaim all responsibility for any liability, loss, injury, or damage incurred as a consequence, directly or indirectly, of the use and application of the contents of this volume.

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This book is dedicated to the memory of

Alain J. Couturier, MD, MS, FACOEM

January 21, 1957–May 25, 2007

Dr. Couturier conceived the textbook, *Occupational and Environmental Infectious Diseases*, and was the editor of the first edition. His work on the second edition was cut short by his unexpected and sudden death. He had a distinguished career that touched many people. Dr. Couturier graduated from the University of Rhode Island with a bachelor of science degree in 1980 and received his doctor of medicine degree from Brown University School of Medicine in 1985. He was awarded a master of science degree in Health Sciences from Purdue University in 1990 and completed a residency in occupational medicine at Boston University Medical Center. His honors included election to Phi Beta Kappa and Phi Kappa Phi. Dr. Couturier was board certified in occupational medicine by the American Board of Preventive Medicine. He became a fellow of the American College of Occupational and Environmental Medicine in 1999 and was active in that organization and in its New England component. During his career he was an assistant professor in the department of family medicine at Wayne State University, served as clinical and executive director in various health networks, published actively in the field of occupational medicine, served as a medical consultant to the U.S. Department of Energy, and was formerly a member of the editorial board of *The Occupational and Environmental Medicine Report* for OEM Press. At the time of his death he was a consultant for the Unum Provident Insurance Company in Portland, Maine. He will be greatly missed by his colleagues and friends. Some will remember him as an avid Boston Red Sox fan. We are proud to carry on his legacy with publication of the second edition. He is survived by his wife, Susan, and two sons, Nicholas and Alexander.