



Tuberculosis: Pathophysiology, Clinical Features, and Diagnosis

Nancy A. Knechel, RN, MSN, ACNP

PRIME POINTS

- The vulnerability of hospitalized patients to tuberculosis is often underrecognized because the infection is habitually considered a disease of the community.
- Read the article to find out how to obtain a definitive diagnosis of tuberculosis.
- Learn about tuberculosis test like the QuantiFERON-TB Gold test and how it is being used.
- Nurses should advocate for prompt isolation of patients with suspected or confirmed tuberculosis.

Tuberculosis has recently reemerged as a major health concern. Each year, approximately 2 million persons worldwide die of tuberculosis and 9 million become infected.¹ In the United States, approximately 14 000 cases of tuberculosis were reported in 2006, a 3.2% decline from the previous year; however, 20 states and the District of Columbia had higher rates.² The prevalence of tuberculosis is continuing to increase because of the increased number of patients infected with human immunodeficiency virus, bacterial resistance to medications, increased international travel and immigration from coun-

tries with high prevalence, and the growing numbers of the homeless and drug abusers.³ With 2 billion persons, a third of the world population,¹ estimated to be infected with mycobacteria, all nurses, regardless of area of care, need to understand the pathophysiology, clinical features, and procedures for diagnosis of tuberculosis. The vulnerability of hospitalized patients to tuberculosis is often underrecognized because the infection is habitually considered a disease of the community. Most hospitalized patients are in a suboptimal immune state, particularly in intensive care units, making exposure to tuberculosis even more serious than in the community. By understanding the causative organism, pathophysiology, transmission, and diagnostics of tuberculosis and the clinical manifestations in patients, critical care nurses will be better prepared to recognize infection, prevent transmission, and treat this increasingly common disease.

CE Continuing Education

This article has been designated for CE credit. A closed-book, multiple-choice examination follows this article, which tests your knowledge of the following objectives:

1. Identify 3 reasons why the prevalence of tuberculosis is continuing to increase
2. List at least 2 diagnostic tests for tuberculosis
3. Describe 2 medically challenging physiological characteristics of tuberculosis caused by the lipid barrier of mycobacteria.

©2009 American Association of Critical-Care Nurses doi: 10.4037/ccn2009968

Causative Organism

Tuberculosis is an infection caused by the rod-shaped,

non-spore-forming, aerobic bacterium *Mycobacterium tuberculosis*.⁴ Mycobacteria typically measure 0.5 µm by 3 µm, are classified as acid-fast bacilli, and have a unique cell wall structure crucial to their survival. The well-developed cell wall contains a considerable amount of a fatty acid, mycolic acid, covalently attached to the underlying peptidoglycan-bound polysaccharide arabinogalactan, providing an extraordinary lipid barrier. This barrier is responsible for many of the medically challenging physiological characteristics of tuberculosis, including resistance to antibiotics and host defense mechanisms. The composition and quantity of the cell wall components affect the bacteria's virulence and growth rate.⁵ The peptidoglycan polymer confers cell wall rigidity and is just external to the bacterial cell membrane, another contributor to the permeability barrier of mycobacteria. Another important component of the cell wall is lipoarabinomannan, a carbohydrate structural antigen on the outside of the organism that is immunogenic and facilitates the survival of mycobacteria within macrophages.^{5,6} The cell wall is key to the survival of mycobacteria, and a more complete understanding of the biosynthetic pathways and gene functions and the development of antibiotics to prevent formation of the cell wall are areas of great interest.⁶

Author

Nancy Knechel received a BSN from the University of Maryland, Baltimore, in 2003 and then worked in an emergency department in Sacramento, California. She received an MSN from the University of Pennsylvania in the acute care nurse practitioner program and now works at University of California, San Diego Medical Center, in the Division of Trauma.

Corresponding author: Nancy A. Knechel, RN, MSN, ACNP, University of California, San Diego Medical Center, 200 W Arbor Dr, #8896, San Diego, CA 92103-8896 (e-mail: nknechel@ucsd.edu).

To purchase electronic or print reprints, contact The InnoVision Group, 101 Columbia, Aliso Viejo, CA 92656. Phone, (800) 899-1712 or (949) 362-2050 (ext 532); fax, (949) 362-2049; e-mail, reprints@aacn.org.

Transmission

Mycobacterium tuberculosis is spread by small airborne droplets, called droplet nuclei, generated by the coughing, sneezing, talking, or singing of a person with pulmonary or laryngeal tuberculosis. These minuscule droplets can remain airborne for minutes to hours after expectoration.⁵ The number of bacilli in the droplets, the virulence of the bacilli, exposure of the bacilli to UV light, degree of ventilation, and occasions for aerosolization all influence transmission.⁷ Introduction of *M tuberculosis* into the lungs leads to infection of the respiratory system; however, the organisms can spread to other organs, such as the lymphatics, pleura, bones/joints, or meninges, and cause extrapulmonary tuberculosis.

Pathophysiology

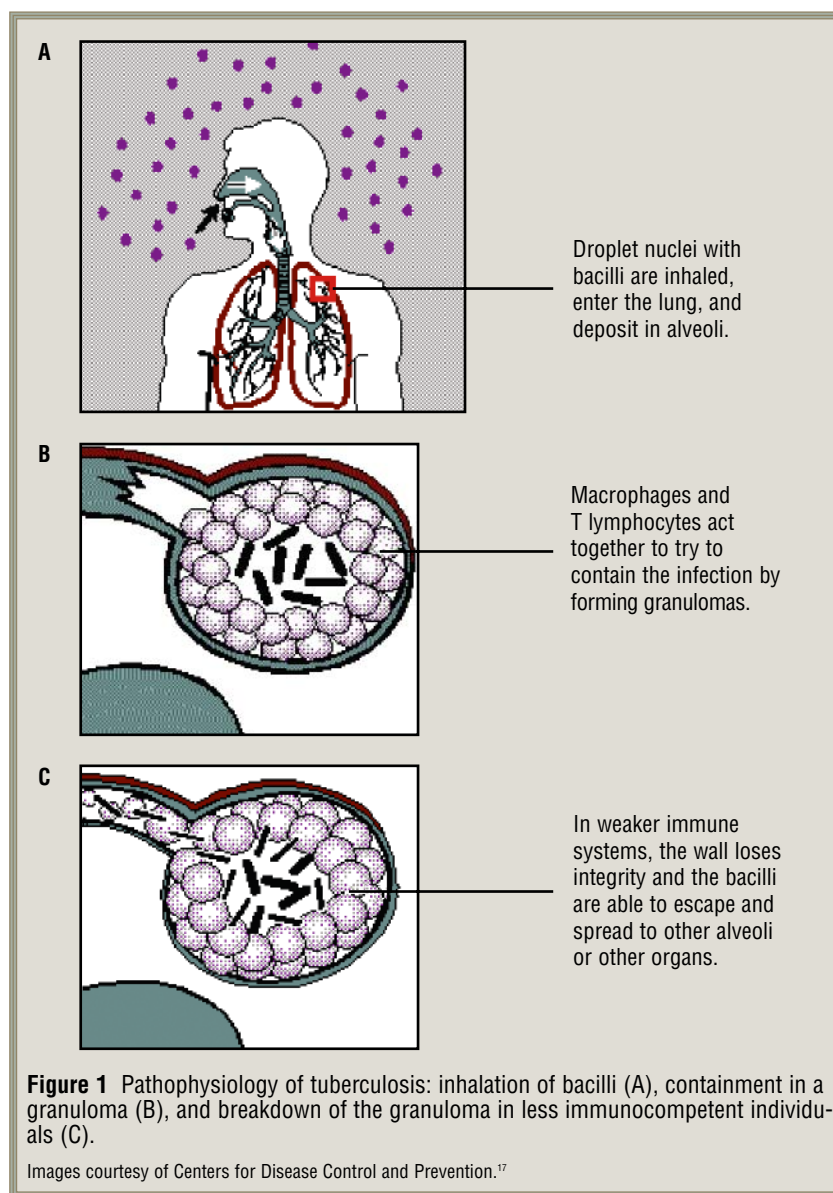
Once inhaled, the infectious droplets settle throughout the airways. The majority of the bacilli are trapped in the upper parts of the airways where the mucus-secreting goblet cells exist. The mucus produced catches foreign substances, and the cilia on the surface of the cells constantly beat the mucus and its entrapped particles upward for removal.⁸ This system provides the body with an initial physical defense that prevents infection in most persons exposed to tuberculosis.⁹

Bacteria in droplets that bypass the mucociliary system and reach the alveoli are quickly surrounded and engulfed by alveolar macrophages,^{7,8} the most abundant immune effector cells present in alveolar spaces.¹⁰ These macrophages, the next line of host defense, are part of the innate immune system and provide an opportunity for the body to destroy the invading mycobacteria and prevent infection.¹¹ Macrophages are readily available phagocytic cells that combat many pathogens without requiring previous exposure to the pathogens. Several mechanisms and macrophage receptors are involved in uptake of the mycobacteria.¹¹ The mycobacterial lipoarabinomannan is a key ligand for a macrophage receptor.¹² The complement system also plays a role in the phagocytosis of the bacteria.¹³ The complement protein C3 binds to the cell wall and enhances recognition of the mycobacteria by macrophages. Opsonization by C3 is rapid, even in the air spaces of a host with no previous exposure to *M tuberculosis*.¹⁴ The subsequent phagocytosis by macrophages initiates a cascade of events that results in either successful control of the infection, followed by latent tuberculosis, or progression to active disease, called primary progressive tuberculosis.⁸ The outcome is essentially determined by the quality of the host defenses and the balance that occurs between host defenses and the invading mycobacteria.^{11,15}

After being ingested by macrophages, the mycobacteria continue to multiply slowly,⁸ with bacterial cell division occurring every 25 to 32 hours.^{4,7} Regardless of whether the infection becomes controlled or progresses, initial development involves

production of proteolytic enzymes and cytokines by macrophages in an attempt to degrade the bacteria.^{11,12} Released cytokines attract T lymphocytes to the site, the cells that constitute cell-mediated immunity. Macrophages then present mycobacterial antigens on their surface to the T cells.¹¹ This initial immune process continues for 2 to 12 weeks; the microorganisms continue to grow until they reach sufficient numbers to fully elicit the cell-mediated immune response, which can be detected by a skin test.^{4,8,11}

For persons with intact cell-mediated immunity, the next defensive step is formation of granulomas around the *M tuberculosis* organisms¹⁶ (Figure 1). These nodular-type lesions form from an accumulation of activated T lymphocytes and macrophages, which creates a microenvironment that limits replication and the spread of the mycobacteria.^{8,12} This environment destroys macrophages and produces early solid necrosis at the center of the lesion; however, the bacilli are able to adapt to survive.¹⁸ In fact, *M tuberculosis* organisms can change their phenotypic expression, such as protein regulation, to enhance survival.¹³ By 2 or 3 weeks, the necrotic environment resembles soft cheese, often referred to as caseous necrosis, and is characterized by low oxygen levels, low pH, and limited nutrients. This condition restricts further growth and establishes latency. Lesions in persons with an adequate immune system generally undergo fibrosis and calcification, successfully controlling the infection so that the bacilli are contained in the dormant, healed lesions.¹⁸ Lesions in persons with less effective immune



systems progress to primary progressive tuberculosis.^{4,8,13,18}

For less immunocompetent persons, granuloma formation is initiated yet ultimately is unsuccessful in containing the bacilli. The necrotic tissue undergoes liquefaction, and the fibrous wall loses structural integrity. The semiliquid necrotic material can then drain into a bronchus or nearby blood vessel, leaving an air-filled cavity at the original site. In patients infected with *M tuberculosis*, droplets can be

coughed up from the bronchus and infect other persons. If discharge into a vessel occurs, occurrence of extrapulmonary tuberculosis is likely. Bacilli can also drain into the lymphatic system and collect in the tracheobronchial lymph nodes of the affected lung, where the organisms can form new caseous granulomas.¹⁸

Clinical Manifestations

As the cellular processes occur, tuberculosis may develop differently in each patient, according to the

Table 1 Differences in the stages of tuberculosis

Early infection	Early primary progressive (active)	Late primary progressive (active)	Latent
Immune system fights infection	Immune system does not control initial infection	Cough becomes productive	Mycobacteria persist in the body
Infection generally proceeds without signs or symptoms	Inflammation of tissues ensues	More signs and symptoms as disease progresses	No signs or symptoms occur
Patients may have fever, paratracheal lymphadenopathy, or dyspnea	Patients often have nonspecific signs or symptoms (eg, fatigue, weight loss, fever)	Patients experience progressive weight loss, rales, anemia	Patients do not feel sick
Infection may be only subclinical and may not advance to active disease	Nonproductive cough develops	Findings on chest radiograph are normal	Patients are susceptible to reactivation of disease
	Diagnosis can be difficult: findings on chest radiographs may be normal and sputum smears may be negative for mycobacteria	Diagnosis is via cultures of sputum	Granulomatous lesions calcify and become fibrotic, become apparent on chest radiographs
			Infection can reappear when immunosuppression occurs

status of the patient's immune system. Stages include latency, primary disease, primary progressive disease, and extrapulmonary disease. Each stage has different clinical manifestations (Table 1).

Latent Tuberculosis

Mycobacterium tuberculosis organisms can be enclosed, as previously described, but are difficult to completely eliminate.¹⁵ Persons with latent tuberculosis have no signs or symptoms of the disease, do not feel sick, and are not infectious.¹⁹ However, viable bacilli can persist in the necrotic material for years or even a lifetime,⁹ and if the immune system later becomes compromised, as it does in many critically ill patients, the disease can be reactivated.

Although coinfection with human immunodeficiency virus is the most notable cause for progression to active disease, other factors, such as uncontrolled diabetes mellitus, sepsis, renal failure, malnutrition, smoking, chemotherapy, organ transplantation, and long-term corticosteroid usage, that can trigger reactivation of a remote infection are more common in the critical care setting.^{8,19} Additionally, persons 65 years or older have a disproportionately higher rate of disease than any does other age group,²⁰ often because of diminishing immunity and reactivation of disease.²¹

Primary Disease

Primary pulmonary tuberculosis is often asymptomatic, so that the

results of diagnostic tests (Table 2) are the only evidence of the disease. Although primary disease essentially exists subclinically, some self-limiting findings might be noticed in an assessment. Associated paratracheal lymphadenopathy may occur because the bacilli spread from the lungs through the lymphatic system. If the primary lesion enlarges, pleural effusion is a distinguishing finding. This effusion develops because the bacilli infiltrate the pleural space from an adjacent area. The effusion may remain small and resolve spontaneously, or it may become large enough to induce symptoms such as fever, pleuritic chest pain, and dyspnea. Dyspnea is due to poor gas exchange in the areas of affected lung tissue. Dullness to percussion

Table 2 Diagnostic tests for identifying tuberculosis

Variable	Sputum smear	Sputum culture	Polymerase chain reaction	Tuberculin skin test	QuantiFERON-TB test	Chest radiography
Purpose of test or study	Detect acid-fast bacilli	Identify <i>Mycobacterium tuberculosis</i>	Identify <i>M tuberculosis</i>	Detect exposure to mycobacteria	Measure immune reactivity to <i>M tuberculosis</i>	Visualize lobar infiltrates with cavitation
Time required for results	<24 hours	3-6 weeks with solid media, 4-14 days with high-pressure liquid chromatography	Hours	48-72 hours	12-24 hours	Minutes

and a lack of breath sounds are physical findings indicative of a pleural effusion because excess fluid has entered the pleural space.⁷

Primary Progressive Tuberculosis

Active tuberculosis develops in only 5% to 10% of persons exposed to *M tuberculosis*. When a patient progresses to active tuberculosis, early signs and symptoms are often nonspecific. Manifestations often include progressive fatigue, malaise, weight loss, and a low-grade fever accompanied by chills and night sweats.²² Wasting, a classic feature of tuberculosis, is due to the lack of appetite and the altered metabolism associated with the inflammatory and immune responses. Wasting involves the loss of both fat and lean tissue; the decreased muscle mass contributes to the fatigue.²³ Finger clubbing, a late sign of poor oxygenation, may occur; however, it does not indicate the extent of disease.²⁴ A cough eventually develops in most patients. Although the cough may initially be nonproductive, it advances to a productive cough of purulent sputum. The sputum may also be streaked with blood. Hemoptysis can be due to destruction of a patent vessel located in the wall of the cavity, the rupture of a dilated vessel in a cavity, or the formation of an aspergilloma in an old cavity. The inflamed parenchyma may cause pleuritic chest pain. Extensive disease may lead to dyspnea or orthopnea because the increased interstitial volume leads to a decrease in lung diffusion capacity. Although many patients with active disease have few physical findings, rales may be detected over involved areas during inspiration, particularly after a

cough. Hematologic studies might reveal anemia, which is the cause of the weakness and fatigue. Leukocytosis may also occur because of the large increase in the number of leukocytes, or white blood cells, in response to the infection.⁷

Extrapulmonary Tuberculosis

Although the pulmonary system is the most common location for tuberculosis, extrapulmonary disease occurs in more than 20% of immunocompetent patients, and the risk for extrapulmonary disease increases with immunosuppression.²⁰ The most serious location is the central nervous system, where infection may result in meningitis or space-occupying tuberculomas. If not treated, tubercular meningitis is fatal in most cases, making rapid detection of the mycobacteria essential.⁸ Headaches and change in mental status after possible exposure to tuberculosis or in high risk groups should prompt consideration of this disease as a differential diagnosis. Another fatal form of extrapulmonary tuberculosis is infection of the blood-

stream by mycobacteria; this form of the disease is called disseminated or miliary tuberculosis. The bacilli can then spread throughout the body, leading to multiorgan involvement.²⁵ Miliary tuberculosis progresses rapidly and can be difficult to diagnose because of its systemic and nonspecific signs and symptoms, such as fever, weight loss, and weakness.⁷ Lymphatic tuberculosis is the most common extrapulmonary tuberculosis, and cervical adenopathy occurs most often. Other possible locations include bones, joints, pleura, and genitourinary system.²⁰

Laboratory and Diagnostic Studies

Active tuberculosis may be considered as a possible diagnosis when findings on a chest radiograph of a patient being evaluated for respiratory symptoms are abnormal, as occurs in most patients with pulmonary tuberculosis. The radiographs may show the characteristic findings of infiltrates with cavitation in the upper and middle lobes of the lungs²¹ (Figure 2). However, specific

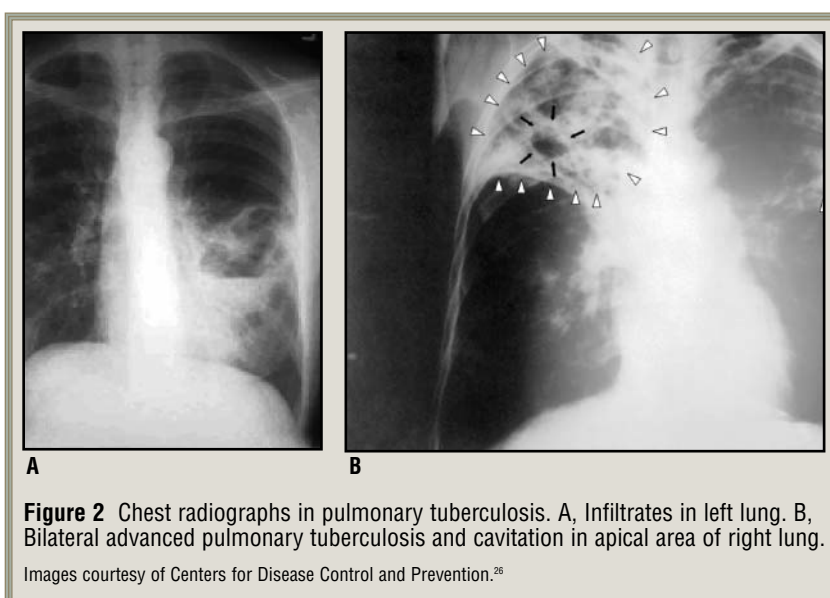


Figure 2 Chest radiographs in pulmonary tuberculosis. A, Infiltrates in left lung. B, Bilateral advanced pulmonary tuberculosis and cavitation in apical area of right lung.

Images courtesy of Centers for Disease Control and Prevention.²⁶

groups of patients, such as the elderly and patients with advanced infection by human immunodeficiency virus, may not have these typical findings. Compared with other patients, both groups have the classic cavitation less often and may have lower-lobe infiltrates as a prominent finding.^{7,21} Although abnormal findings on a chest radiograph may suggest tuberculosis, they are not diagnostic for the disease.¹⁹

Traditionally, the first laboratory test used to detect active tuberculosis in a patient with abnormal findings on chest radiographs is examination of a sputum smear for the presence of acid-fast bacilli (Table 2). Also, because the bacilli have entered the sputum, the patient is infectious to others. According to the Centers for Disease Control and Prevention,¹⁹ 3 sputum specimens should be used for detection of pulmonary tuberculosis, with specimens collected in the morning on consecutive days. However, recently, investigators have questioned the need for 3 specimens. Leonard et al²⁷ concluded that examination of 2 specimens is just as sensitive.

For the test, sputum is smeared on a slide, stained, dried, and then treated with alcohol. Any bacilli that are present will remain red because they will not destain. The test is not specific for tuberculosis, because other mycobacteria give the same results, but it does provide a quick method to determine if respiratory precautions should be maintained while more definitive testing is performed. Results of sputum smears should be available within 24 hours of the specimen collection.¹⁹

Diagnosis

The Standard

Definitive diagnosis of tuberculosis requires the identification of *M tuberculosis* in a culture of a diagnostic specimen. The most frequent sample used from a patient with a persistent and productive cough is sputum. Because most mycobacteria grow slowly, 3 to 6 weeks may be required for detectable growth on solid media. However, a newer, alternative method in which high-performance liquid chromatography is used to isolate and differentiate cell wall mycolic acids provides confirmation of the disease in 4 to 14 days.¹⁹ Conventionally, 3 sputum samples were also used for culture diagnosis, but the use of 2 specimens, as mentioned earlier for smears, also applies for cultures.²⁷

After medications are started, the effectiveness of the therapy is assessed by obtaining sputum samples for smears. Once again, the traditional requirement of 3 sputum smears negative for *M tuberculosis* may be unnecessary when determining if respiratory isolation can be discontinued.²⁸ A patient is considered to have achieved culture conversion when a culture is negative for the mycobacteria after a succession of cultures have been positive; culture conversion is the most important objective evaluation of response to treatment.¹⁹

Alternatives

Unfortunately, not all patients with tuberculosis can be detected by culture of sputum specimens, a situation that can lead to delayed or missed diagnosis.^{20,29} Additionally, many critically ill patients have trouble producing the necessary

material from the lungs and instead produce saliva or nasopharyngeal discharge. For patients who have difficulty generating sputum, inhalation of an aerosol of normal saline can be used to induce sputum for collection.^{4,7,19} However, if sputum specimens are still inadequate, or the index of suspicion for tuberculosis is still high despite cultures negative for *M tuberculosis*, alternative approaches are available.

Bronchoscopy with bronchial washings or bronchoalveolar lavage can provide sputum for diagnosis.¹⁹ In bronchial washing, a fiberoptic bronchoscope is inserted into the lungs, and fluid is squirted in and then collected, essentially washing out a sample of cells and secretions from the alveolar and bronchial airspaces. Aliquots obtained from subsequent lavages constitute bronchoalveolar lavage specimens.³⁰

In patients with involvement of intrathoracic lymph nodes, as indicated by adenopathy suggestive of tuberculosis, who have sputum smears negative for *M tuberculosis*, culture of specimens collected by transbronchial needle aspiration can be used to accurately and immediately diagnose the disease. With this technique, specimens are collected by inserting a 19-gauge flexible histology needle through a bronchoscopy tube; patients are sedated but conscious, and computed tomography scans are used for guidance.³¹

Technological Advancements

Newer diagnostic techniques for faster detection of *M tuberculosis* include nucleic acid amplification tests. In these tests, molecular biology methods are used to amplify



Figure 3 Measuring induration, not erythema, in a tuberculin skin test.

Image courtesy of Centers for Disease Control and Prevention.³⁴

Table 3 Positive tuberculin skin tests

Diameter of induration	Considered positive for
≥5	Persons at high risk for tuberculosis: Patients with chronic diseases (eg, infection with human immunodeficiency virus) Persons with recent exposure to tuberculosis Patients with findings on radiographs suggestive of tuberculosis Employees of hospitals and long-term care facilities
≥10	Persons at risk for tuberculosis: Injectable drug users Persons in close living conditions Persons born in countries with high prevalence of tuberculosis
≥15	Persons who do not belong to either of the other groups

DNA and RNA, facilitating rapid detection of microorganisms; the tests have been approved by the Food and Drug Administration.³² One method is the polymerase chain reaction assay, which can be used to differentiate *M tuberculosis* from other mycobacteria on the basis of genetic information and provides results within hours. Although the test can provide rapid confirmation of *M tuberculosis* in sputum specimens positive for acid-fast bacilli, it has limitations, including high cost, low sensitivity, and low availability. A polymerase chain reaction assay positive for *M tuberculosis* in conjunction with a sputum smear positive for the organism indicates true tuberculosis, but in a patient with a sputum smear negative for the organism, the positive polymerase chain reaction assay should be considered carefully along with clinical indicators. The results of these assays can not be relied on as the sole guide for isolation or therapy.³³

Diagnosing Latency

Once patients recover from a primary *M tuberculosis* infection and

the infection becomes latent, sputum specimens are negative for the organisms, and findings on chest radiographs are typically normal. These patients also do not have signs or symptoms of infection, and they are not infectious to others. Tuberculin skin testing is the most common method used to screen for latent *M tuberculosis*.³

The tuberculin skin test is performed by intradermally injecting 0.1 mL of intermediate-strength purified protein derivative (PPD) that contains 5 tuberculin units. After 48 to 72 hours, the injection site is examined for induration but not redness (Figure 3, Table 3). Although the test is useful because the PPD elicits a skin reaction via cell-mediated immunity when injected in patients previously infected with mycobacteria, it is limited because it is not specific for the species of mycobacteria. Many proteins in the PPD product are highly conserved in various species of mycobacteria. Also, the test is of limited value in patients with active tuberculosis because of its low sensitivity and specificity. False-negatives can occur in patients who are immunocompromised or

malnourished, because these patients cannot mount an immune response to the injection, and in 20% to 25% of patients who have active tuberculosis, because there is a time lag of 2 to 10 weeks between infection and the T-lymphocyte response required for a positive skin reaction. False-positives can occur in patients who have infections caused by mycobacteria other than *M tuberculosis* or who have been given BCG vaccine.³⁵

The tuberculin skin test was the only test available to detect latent tuberculosis until an interferon-release assay, called QuantiFERON-TB test, was approved by the Food and Drug Administration in 2001. Then, in 2005, a new interferon-assay, called QuantiFERON-TB Gold was approved and is intended to replace the QuantiFERON-TB test, which is no longer commercially available. In both tests, the cell-mediated reactivity to *M tuberculosis* is determined by incubating whole blood with an antigen and then using an enzyme-linked immunosorbent assay to measure the amount of interferon- γ released from white blood cells. In the QuantiFERON-TB Gold test, 2 synthetic antigenic proteins specific

in PPD are used rather than a PPD admixture, making this test more sensitive than its predecessor. QuantiFERON-TB Gold provides results in less than 24 hours and can be used to detect both active and latent tuberculosis. The results of the QuantiFERON-TB Gold test are similar to those of the tuberculin skin test, and the Centers for Disease Control and Prevention now recommend that the QuantiFERON-TB Gold test be used in all instances in which the tuberculin skin test formerly would have been used.³²

Implications for Critical Care Nurses

With the reemergence of tuberculosis, being well informed about this disease is more important than before. Tuberculosis can be difficult to diagnose promptly, resulting in delayed isolation of patients and potential spread of the disease. Detection of extrapulmonary tuberculosis is generally even more difficult because this type is often less familiar to clinicians.⁷ Nurses play an important role in recognizing the clinical signs and symptoms of tuberculosis, a situation that places them in a position for early recognition of the disease, leading to diagnosis and early isolation to prevent transmission. Importantly, diagnosis may be based on clinical manifestations even without a culture positive for *M tuberculosis*.¹⁹ Nurses are also in a position to optimize nutrition, educate, provide emotional support, and prepare patients and patients' families for discharge from the hospital.

Nearly every type of health care setting has been implicated in the transmission of *M tuberculosis*.⁹ The

emergency department can play a vital role in control because it is a point of entry into the hospital. However, because of the nonspecific signs and symptoms and dated screening protocols, initial detection of tuberculosis is still missed in emergency department triage.³⁶ Consequently, a patient with tuberculosis can be discharged into the community or admitted to the hospital without any intervention. Patients admitted because of trauma may also escape screening for tuberculosis, because the focus is almost entirely on injuries. Often trauma patients are admitted to an intensive care unit, where other patients are particularly susceptible to any infection. Intubated patients are compromised directly from the pulmonary standpoint and lack normal upper airway defenses that protect the lungs from bacteria. Many nosocomial tuberculosis outbreaks have been reported,³⁶ emphasizing that nurses and other health care personnel should remember that even hospitalized patients may have tuberculosis.

Isolation

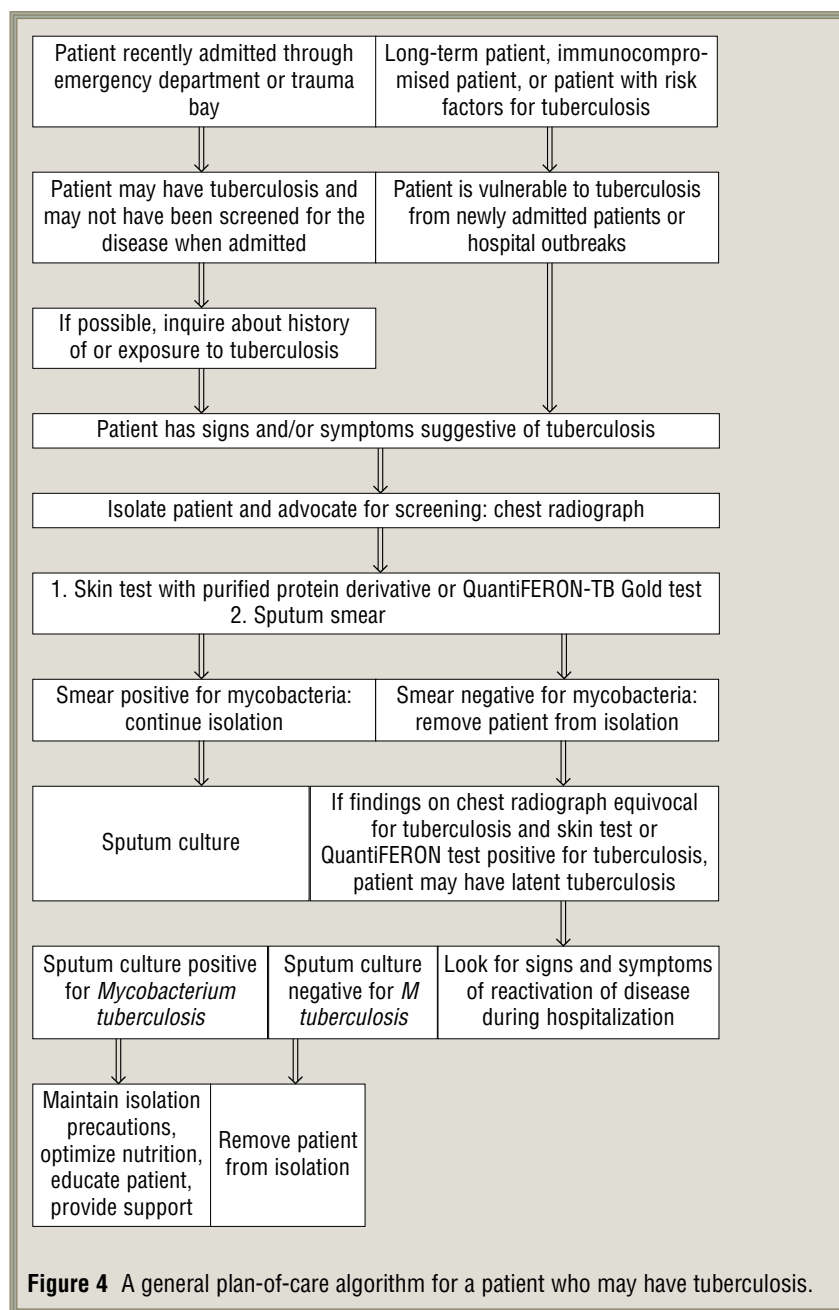
Because nurses play a key role in detecting tuberculosis, they should advocate for prompt isolation of patients with suspected or confirmed *M tuberculosis* infection (Figure 4). Nurses should be familiar with the isolation precautions that must be implemented. Patients with suspected tuberculosis should be placed in a negative-pressure room, and appropriate particulate respiratory masks (N-95/high-efficiency particulate air filters) should be readily available outside the door for anyone entering the room.³⁷ The number of visitors should be minimized, and children

should be discouraged from visiting. Patients should be instructed to cover their nose and mouth with a tissue when sneezing or coughing. Additionally, they should wear a mask when leaving the room, and nonurgent procedures should be postponed until the infectious phase has passed.

Patients receiving mechanical ventilation should also be kept in a negative-pressure room, and respiratory masks should still be used by anyone who enters the room. A closed-system endotracheal suction catheter should be used for suctioning whenever feasible. In order to help reduce the risk of contaminating ventilation equipment or release of *M tuberculosis* organisms into the room air, a bacterial filter should be placed on the endotracheal tube or on the expiratory side of the ventilation circuit. Good oral care and strict adherence to suctioning infection control practices should be a priority, because ventilator-associated pneumonia is already a predominant nosocomial infection and would pose an enhanced threat to a patient with tuberculosis.

Nutrition

Adequate nutrition is an important feature though all stages of infection. Malnutrition appears to increase the risk for tuberculosis; persons with low body mass index are greatly more at risk for tuberculosis than are those with a high index.³⁸ Additionally, among patients underweight at the time of diagnosis, those who increase their weight by 5% during the first 2 months of treatment have significantly less relapse than do patients who gain less than 5%.³⁸ Nurses should take



particular note of underweight tuberculosis patients, recognizing that being underweight is a risk factor for relapse and encouraging aggressive nutritional support.³⁹ Also, because functional recovery often lags behind microbiological cure, the aim of nutritional intervention should be to restore lean tissue.^{23,39} Nurses should also encourage patients to engage in physical

activity to counter the loss of muscle mass and subsequent fatigue. Advocating for a nutritionist and physical therapist to evaluate a patient with tuberculosis to make patient-specific recommendations would be an appropriate action for nurses.

Emotional Support and Education

In addition to the direct responsibilities of nursing, many nurses

are also a key source of emotional support for patients and patients' families during times of illness. Perceived emotional support from nursing staff can improve adherence to therapy. Many patients with tuberculosis experience feelings of guilt and face stigma, and patients' family members often fear associating with the patients.⁴⁰ Nurses can provide education to patients and patients' families about transmission and treatment to help reduce misconceptions and can elicit conversations to communicate concerns. Encouragement combined with education can affect a patient's adherence to therapy, as well as improve the patient's mood and perception of the illness.

Conclusions

Tuberculosis has reemerged as a major public health concern and is the second deadliest infectious disease worldwide. Understanding the pathophysiology of this contagious airborne disease, from the primary infection to primary progressive (active) disease or latency, is important. Understanding the pathophysiology will help critical care nurses be aware of the causes of the classic signs and symptoms for tuberculosis. Many different diagnostic tests can be used to evaluate a patient with suspected tuberculosis, and the stage or progression of the disease markedly affects the results. Even in critical care, each nurse has an



To read more about tuberculosis, read "The Pursuit of Healthcare" by Christopher W. Bryan-Brown and Kathleen Dracup in the *American Journal of Critical Care*, 2004;13: 368-370. Available at www.ajconline.org.

opportunity to contribute to the control of tuberculosis by learning about the signs and symptoms of the disease, risk factors specific to critical care patients, and the appropriate actions to take should such a case occur. The more nurses know about tuberculosis, the more they can contribute to minimizing its transmission, making early diagnoses, and preventing increases in morbidity and mortality due to this disease. **CCN**

eLetters

Now that you've read the article, create or contribute to an online discussion about this topic using eLetters. Just visit www.ccnonline.org and click "Respond to This Article" in either the full-text or PDF view of the article.

Financial Disclosures
None reported.

References

- Centers for Disease Control and Prevention. World TB day—March 24, 2007. *MMWR Morb Mortal Wkly Rep*. 2007;56(11):245.
- Centers for Disease Control and Prevention. Trends in tuberculosis incidence, United States, 2006. *MMWR Morb Mortal Wkly Rep*. 2007;56(11):245-250.
- Goldrick BA. Once dismissed, still rampant: tuberculosis, the second deadliest infectious disease worldwide. *Am J Nurs*. 2004;104(9):68-70.
- Porth CM. Alterations in respiratory function: respiratory tract infections, neoplasms, and childhood disorders. In: Porth CM, Kunert MP. *Pathophysiology: Concepts of Altered Health States*. Philadelphia, PA: Lippincott Williams & Wilkins; 2002:615-619.
- Lee RB, Li W, Chatterjee D, Lee RE. Rapid structural characterization of the arabinogalactan and lipoarabinomannan in live mycobacterial cells using 2D and 3D HR-MAS NMR: structural changes in the arabinan due to ethambutol treatment and gene mutation are observed. *Glycobiology*. 2005;15(2):139-151.
- Joe M, Bai Y, Nacario RC, Lowary TL. Synthesis of the docosanasaccharide arabinan domain of mycobacterial arabinogalactan and a proposed octadecasaccharide biosynthetic precursor. *J Am Chem Soc*. 2007;129(32):9885-9901.
- American Thoracic Society and Centers for Disease Control and Prevention. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med*. 2000;161(4 pt 1):1376-1395.
- Frieden TR, Sterling TR, Munsiff SS, Watt CJ, Dye C. Tuberculosis. *Lancet*. 2003;362:887-899.
- Jensen PA, Lambert LA, Iademarco MF, Ridzon R; Centers for Disease Control and Prevention. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR Recomm Rep*. 2005;54(RR-17):1-141.
- Korf JE, Pynaert G, Tournoy K, et al. Macrophage reprogramming by mycolic acid promotes a tolerogenic response in experimental asthma. *Am J Respir Crit Care Med*. 2006;174(2):152-160.
- van Crevel R, Ottenhoff THM, van der Meer JWM. Innate immunity to *Mycobacterium tuberculosis*. *Clin Microbiol Rev*. 2002;15:294-309.
- Nicot LP. Immunology of tuberculosis. *Swiss Med Wkly*. 2007;137(25-26):357-362.
- Li Y, Petrofsky M, Bermudez LE. *Mycobacterium tuberculosis* uptake by recipient host macrophages is influenced by environmental conditions in the granuloma of the infectious individual and is associated with impaired production of interleukin-12 and tumor necrosis factor alpha. *Infect Immun*. 2002;70:6223-6230.
- Ferguson JS, Weis JJ, Martin JL, Schlesinger LS. Complement protein C3 binding to *Mycobacterium tuberculosis* is initiated by the classical pathway in human bronchoalveolar lavage fluid. *Infect Immun*. 2004;72:2564-2573.
- Goyot-Revol V, Innes JA, Hackforth S, Hinks T, Lalvani A. Regulatory T cells are expanded in blood and disease sites in patients with tuberculosis. *Am J Respir Crit Care Med*. 2006;173:803-810.
- Rosenkrands I, Slayden RA, Crawford J, et al. Hypoxic response of *Mycobacteria tuberculosis* studied by metabolic labeling and proteome analysis of cellular and extracellular proteins. *J Bacteriol*. 2002;184:3485-3491.
- Transmission and pathogenesis of tuberculosis: TB disease [self-study module]. Centers for Disease Control and Prevention Web site. <http://www2.cdc.gov/phtn/tbmodules/modules1-5/m1/con6a.htm>. Accessed January 29, 2009.
- Dheda K, Booth H, Huggett JF, et al. Lung remodeling in pulmonary tuberculosis. *J Infect Dis*. 2005;192:1201-1210.
- Interactive core curriculum on tuberculosis. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/tb/webcourses/CoreCurr/TB_Course/Menu/frameset_internet.htm. Accessed January 28, 2009.
- Surveillance reports: reported tuberculosis in the United States, 2005. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/tb/surv/surv2005/default.htm>. Published September 2006. Last reviewed May 18, 2008. Accessed January 28, 2009.
- Thrupp L, Bradley S, Smith P, Simor A, Gantz N, et al. Tuberculosis prevention and control in long-term-care facilities for older adults. *Infect Control Hosp Epidemiol*. 2004;129:1097-1108.
- TB elimination: the difference between latent TB infection and active TB disease. Centers for Disease Control and Prevention Web site. <http://cdc.gov/tb/pubs/tbfactsheets/LTBandActiveTB.pdf>. Updated October 7, 2008. Accessed January 28, 2009.
- Paton NI, Chua YK, Earnest A, Chee CB. Randomized controlled trial of nutritional supplementation in patients with newly diagnosed tuberculosis and wasting. *Am J Clin Nutr*. 2004;80:450-465.
- Ddungu H, Johnson JL, Smieja M, Mayanja-Kizza H. Digital clubbing in tuberculosis—relationship to HIV infection, extent of disease and hypoalbuminemia. *BMC Infect Dis*. 2006;6:45.
- Wang JY, Hsueh PR, Wang SK, et al. Disseminated tuberculosis: a 10-year experience in a medical center. *Medicine (Baltimore)*. 2007;86(1):39-46.
- Vaccines and preventable diseases: tuberculosis photos. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/vaccines/vpd-vac/tb/photos.htm>. Last modified September 11, 2007. Accessed January 29, 2009.
- Leonard MK, Osterholt D, Kourbatova EV, et al. How many sputum specimens are necessary to diagnose pulmonary tuberculosis? *Am J Infect Control*. 2005;33(1):58-61.
- Bryan CS, Rapp DJ, Brown CA. Discontinuation of respiratory isolation for possible tuberculosis: do two negative sputum smear results suffice? *Infect Control Hosp Epidemiol*. 2006;27:515-516.
- Jafari C, Ernst M, Kalsdorf B, et al. Rapid diagnosis of smear-negative tuberculosis by bronchoalveolar lavage enzyme-linked immunospot. *Am J Respir Crit Care Med*. 2006;174:1048-1054.
- Rutgers SR, Timens W, Kauffmann HF, et al. Comparison of induced sputum with bronchial wash, bronchoalveolar lavage and bronchial biopsies in COPD. *Eur Respir J*. 2000;15:109-115.
- Bilaceroglu S, Gunel O, Eris N, Cagirci U, Mehta AC. Transbronchial needle aspiration in diagnosing intrathoracic tuberculosis lymphadenitis. *Chest*. 2004;126:259-267.
- Mazurek GH, Jereb J, Lobue P, et al; Division of Tuberculosis Elimination, National Center for HIV, STD, and TB Prevention, Centers for Disease Control and Prevention (CDC). Guidelines for using the QuantiFERON-TB gold test for detecting *Mycobacterium tuberculosis* infection, United States [published correction appears in *MMWR Morb Mortal Wkly Rep*. 2005;54(50):1288]. *MMWR Recomm Rep*. 2005;54(RR-15):49-55.
- Michos AG, Daikos GL, Tzanetou K, et al. Detection of *Mycobacterium tuberculosis* DNA in respiratory and nonrespiratory specimens by the Amplicor MTB PCR. *Diagn Microbiol Infect Dis*. 2006;54:121-126.
- Mantoux tuberculin skin test. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/tb/pubs/Posters/images/Mantoux_wallchart.PDF. Accessed January 29, 2009.
- Anderson ST, Williams AJ, Brown JR, et al. Transmission of *Mycobacterium tuberculosis* undetected by tuberculin skin testing. *Am J Respir Crit Care Med*. 2006;173:1038-1042.
- Sokolove PE, Lee BS, Krawczyk JA, Banos PT, Gregson AL. Implementation of an emergency department triage procedure for the detection and isolation of patients with active pulmonary tuberculosis. *Ann Intern Med*. 2000;35:327-336.
- Toth A, Fackelmann J, Pigott W, Tolomeo O. Tuberculosis prevention and treatment. *Can Nurse*. 2004;100(9):27-30.
- Khan A, Sterling TR, Reeves R, et al. Lack of weight gain and relapse risk in a large tuberculosis treatment trial. *Am J Respir Crit Care Med*. 2006;174:344-348.
- Schwenk A, Hodgson L, Wright A, et al. Nutritional partitioning during treatment of tuberculosis: gain in body fat but not in protein mass. *Am J Clin Nutr*. 2004;79:1006-1012.
- Chalco K, Wu DY, Mestanza L, et al. Nurses as providers of emotional support to patients with MDR-TB. *Int Nurs Rev*. 2006;53(4):253-260.

CE Test Test ID C0923: Tuberculosis: Pathophysiology, Clinical Features, and Diagnosis

Learning objectives: 1. Identify 3 reasons why the prevalence of tuberculosis is continuing to increase 2. List at least 2 diagnostic tests for tuberculosis 3. Describe 2 medically challenging physiological characteristics of tuberculosis caused by the lipid barrier of mycobacteria

1. How many people worldwide become infected with tuberculosis each year?

- a. 2 million c. 14 million
b. 9 million d. 20 million

2. How many people in the world are estimated to be infected with mycobacteria?

- a. 9 billion c. 20 billion
b. 14 billion d. 2 billion

3. What makes an intensive care unit patient's tuberculosis exposure more serious than community exposure?

- a. A suboptimal immune state
b. Mycobacteria infection
c. Resistant bacteria infection
d. Advanced pneumonia

4. Tuberculosis is an infection caused by what rod shaped, non-spore-forming aerobic bacterium?

- a. Aspergillus
b. *Mycobacterium*
c. *Enterococcus*
d. *Streptococcus*

5. Which of the following is a challenge created by the lipid barrier of *Mycobacterium tuberculosis*?

- a. Resistance to antibiotics
b. Immune response
c. Physical defense
d. Misdiagnosis

6. *M. tuberculosis* is spread by which of the following?

- a. Skin contact with bacterium
b. Ingestion of bacteria
c. Airborne droplets
d. Infection by blood stream

7. After being ingested by macrophages, the mycobacteria continue to multiply slowly with bacteria cell division occurring how often?

- a. Every 20 to 32 hours c. Every 25 to 32 hours
b. Every 25 to 30 hours d. Every 20 to 30 hours

8. The initial immune process continues for how long?

- a. 2 to 10 weeks c. 2 to 12 weeks
b. 4 to 12 weeks d. 4 to 10 weeks

9. Which of the following is the necrotic environment that is characterized by low oxygen levels, low pH, and limited nutrients?

- a. Caseous necrosis
b. Frontal necrosis
c. Immune necrosis
d. Fibrotic necrosis

10. What age group has a disproportionately higher rate of disease than any other age group?

- a. 50 years and older
b. 35 years and older
c. 40 years and older
d. 65 year and older

11. Why are the results of primary pulmonary tuberculosis diagnostic test often the only evidence of disease?

- a. Because primary tuberculosis is not diagnosed
b. Because primary tuberculosis is misdiagnosed
c. Because primary tuberculosis exists subclinically
d. Because primary tuberculosis is asymptomatic

12. Upon diagnosing an abnormal chest radiograph, the first laboratory test used to detect tuberculosis will examine which of the following?

- a. Sputum smear for acid-fast bacilli
b. Bronchoscopy findings
c. Purified protein derivative test
d. Sputum culture

Test answers: Mark only one box for your answer to each question. You may photocopy this form.

- | | | | | | | | | | | | |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|--------------------------------|--------------------------------|
| 1. ☐ a | 2. ☐ a | 3. ☐ a | 4. ☐ a | 5. ☐ a | 6. ☐ a | 7. ☐ a | 8. ☐ a | 9. ☐ a | 10. ☐ a | 11. ☐ a | 12. ☐ a |
| ☐ b | ☐ b | ☐ b | ☐ b | ☐ b | ☐ b | ☐ b | ☐ b | ☐ b | ☐ b | ☐ b | ☐ b |
| ☐ c | ☐ c | ☐ c | ☐ c | ☐ c | ☐ c | ☐ c | ☐ c | ☐ c | ☐ c | ☐ c | ☐ c |
| ☐ d | ☐ d | ☐ d | ☐ d | ☐ d | ☐ d | ☐ d | ☐ d | ☐ d | ☐ d | ☐ d | ☐ d |

Test ID: C0923 Form expires: April 1, 2011 Contact hours: 1.0 Fee: AACN members, \$0; nonmembers, \$10 Passing score: 9 correct (75%) Category: A, Synergy CERP A
Test writer: Brenda Hardin-Wike, RN, CNS, MSN, CCNS

AMERICAN
ASSOCIATION
of CRITICAL-CARE
NURSES

**For faster processing, take
this CE test online at
www.ccnonline.org
("CE Articles in this issue")
or mail this entire page to:
AACN, 101 Columbia
Aliso Viejo, CA 92656.**

Program evaluation

	Yes	No
Objective 1 was met	☐	☐
Objective 2 was met	☐	☐
Objective 3 was met	☐	☐
Content was relevant to my nursing practice	☐	☐
My expectations were met	☐	☐
This method of CE is effective for this content	☐	☐
The level of difficulty of this test was:		
☐ easy ☐ medium ☐ difficult		
To complete this program, it took me _____ hours/minutes.		

Name _____ Member # _____
Address _____
City _____ State _____ ZIP _____
Country _____ Phone _____
E-mail _____
RN Lic. 1/St _____ RN Lic. 2/St _____
Payment by: ☐ Visa ☐ M/C ☐ AMEX ☐ Discover ☐ Check
Card # _____ Expiration Date _____
Signature _____

The American Association of Critical-Care Nurses is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. AACN has been approved as a provider of continuing education in nursing by the State Boards of Nursing of Alabama (#ABNP0062), California (#01036), and Louisiana (#ABN12). AACN programming meets the standards for most other states requiring mandatory continuing education credit for relicensure.

CriticalCareNurse

The journal for high acuity, progressive, and critical care nursing

Tuberculosis: Pathophysiology, Clinical Features, and Diagnosis

Nancy A. Knechel

Crit Care Nurse 2009;29 34-43 10.4037/ccn2009968

©2009 American Association of Critical-Care Nurses

Published online <http://ccn.aacnjournals.org/>

Personal use only. For copyright permission information:

http://ccn.aacnjournals.org/cgi/external_ref?link_type=PERMISSIONDIRECT

Subscription Information

<http://ccn.aacnjournals.org/subscriptions/>

Information for authors

<http://ccn.aacnjournals.org/misc/ifora.xhtml>

Submit a manuscript

<http://www.editorialmanager.com/ccn>

Email alerts

<http://ccn.aacnjournals.org/subscriptions/etoc.xhtml>