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Global Burden of Tuberculosis

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Introduction

Tuberculosis (TB) is a major health concern not only in the United States, but in the entire world. TB is an airborne communicable infection which has affected human beings from immemorial times, evidenced by TB being found in the skeletal remains of ancient mummies (Gough & Kaufman, 2011). There are many patho physiological events in TB that concern the entire body, especially the respiratory and immunological systems.

According to Knechel, TB prevalence is rising due to the increased number of patients infected with HIV, bacterial resistance to medications, increased international travel and immigration from countries with high prevalence of TB, and the growing numbers of the homeless and drug abusers. The immune system declines with age. Therefore, the elderly are more susceptible to TB disease, (2009). Latent tuberculosis infection (LTBI) is a type of TB where some producing disease bacilli evade the immune system response, which causes their survival and persistence in a non-replicating state in the host.

The importance of LTBI is that people who have this disease are not contagious, but they are at risk of developing an active infection which is symptomatic and contagious. About 90 % of people who become infected with TB develop a LTBI (Shi, Shi, & Xu, 2011).

Epidemiology

Statistics and Data

- One third of the world is infected with TB. In 2013, there were around 1.5 million TB-related deaths worldwide (Centers for Disease Control and Prevention [CDC], 2014).
- The rate of TB in older adults is increasing. It approached 60,000 cases in 2012 (CDC, 2014).
- TB is the leading killer of people infected with HIV (CDC, 2014).
- In the U.S. TB is primarily a disease of foreign-born people. The TB case rate among Africans in the U.S. is 3 times higher than other foreign-born people and 27 times higher than U.S. born people (Bennett, Brodine, Waalen, Moser, & Rodwell, 2014).
- Latently infected individuals produce most cases of active disease in low TB incidence countries, as opposed to high TB burden countries, where most cases of active disease come from active transmission (Ahmad, 2011).

Epidemiology Continued

Epidemiological Triad. Tuberculosis is produced by Mycobacterium tuberculosis (M.tb). Mycobacteria are small non-sporing, rod-shaped, acid-fast Gram positive bacilli that are aerophilic, which explains their affinity for the lungs. M.tb enters the host via the respiratory tract. Although M. tb can affect any part of the body, pulmonary TB accounts for almost 60 % of the cases and is the only cause of transmission of infection (Gough & Kaufman, 2011).

The hosts are humans infected with TB. Persons with pulmonary TB are the most important source of infection. Infectiousness of the source case, the closeness of contact, bacillary load inhaled, and immune status of the potential host are factors that determine the risk of infection. (Gough & Kaufman, 2011; Ahmad, 2011).

Poverty and overcrowding conditions make a favorable environment for TB transmission. Institutionalized and homeless people, and illicit drug and alcohol abusers are at risk for latent to active disease progression. Likewise, persons with weakened immune systems such as the elderly and diabetics, as well as untreated or inadequately treated active TB infected patients have increased risk of disease progression (Hartman-Adams, Clark, & Juckett, 2014; CDC, 2012).

Pathogenesis and Immune Response

Infection is initiated by inhalation of particles of 1-5 micrometers in diameter that contain M. tuberculosis. These particles are called droplet nuclei and are expectorated by patients who have active TB, especially when they cough. Inhaled droplet nuclei penetrate into the terminal alveoli where they are engulfed by macrophages and dendritic cells (Gough & Kaufman, 2011; Ahmad, 2011).

Once the M. tb is internalized, intra cellular replication occurs. According to Russell and Ramakrishnan (as cited in Guirado & Schlesinger, 2013), granulomas are well organized lesions that contain blood-derived infected and uninfected macrophages, foamy macrophages, epithelioid cells, Langerhans cells, B and T lymphocytes, and fibroblasts around the

Pathogenesis and Immune Response Continued

foci of infected cells (p. 1). Granuloma formation starts shortly after infection, when inhaled M. tb is ingested and transported across the alveolar epithelium into the lungs and adjacent lymph nodes. Then, dissemination occurs through lymphatics and blood stream. As dissemination takes place, there is production of pro and anti-inflammatory cytokines and chemokines. The immune response generated stimulates the phagocyte antimicrobial activities which lead to the recruitment of additional mononuclear leucocytes into the site of infection. Granulomas contain the growing necrotic tissue and limit replication and spread of the bacteria (Guirado & Schlesinger, 2013).

M. tb can persist for decades within the granuloma in a non-replicating state. This is known as LTBI. As a result of a subsequent defect in cell-mediated immunity, 5 % to 10 % of these individuals will develop reactivation of TB many years after the infection and will have active tuberculosis. A balance of pro and anti-inflammatory immune responses is essential for controlling proliferation of bacteria within granulomas and the resolution of these granulomas over time. Dysregulation in the immune response leads to granuloma progression and disease (Guirado & Schlesinger, 2013).

Caseum accumulation in the core of the granuloma promotes necrotic tissue formation and the breakdown of the granuloma center. When the granuloma center collapses, there is release of infectious bacilli to other tissue parts, where more lesions will be formed. Collapse of granulomas within the airways can lead to the transmission of bacteria to other individuals (Guirado & Schlesinger, 2013). Tumoral Necrosis factor (TNF) produced by infected macrophages and T cells maintains sustained levels of chemokines and cellular recruitment and retention. This role is crucial in maintaining the granuloma structure during the early stages of granuloma formation. In the regional lymph nodes, the accumulation of antigen presenting cells leads to the development of the adaptive immune response against M. tb. CD4, CD8 T cells, and the natural killer cells produce interferon gamma which works in collaboration with TNF-alfa to recognize

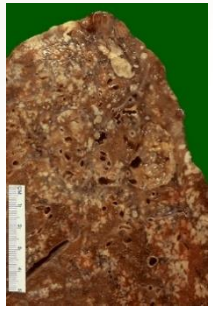
Pathogenesis and Immune Response Continued

and activate macrophages to kill intracellular bacilli. Interleukin-17 is associated with a pro-inflammatory response. It has been suggested that this interleukin promotes polymorphonuclear leukocytes recruitment and organization around the foci of infection during early stages of granuloma formation (Guirado & Schlesinger, 2013).

The most important single factor for progression to active disease in adults is HIV infection. HIV causes depletion of CD4 T cells and functional abnormalities of CD4 and CD8 T cells which play a key role in providing protection against active TB (Ahmad, 2011). Likewise, alterations in the immune system that affect T cells function such as decreased cytokine production, cytotoxic activity, and T cell proliferation, occur during the aging process. Other diseases (e.g., diabetes mellitus), poor nutrition, and immune suppression are other factors that also impact the protective granulomatous response against M. tb during aging.

On one hand, the role of the granulomas is to localize and contain the bacilli while concentrating the immune response to a limited area. On the other hand, since M. tb has its own strategies to persist within the granuloma and to reactivate and scape during certain conditions, complete eradication does not occur. 80 % of the time reactivation occurs in the lungs, whereas in 20% of the cases TB reactivates at other tissues such as pleural space, lymph nodes, bone, and kidneys, due to the early dissemination process that occurs during primary infection (Guirado & Schlesinger, 2013). Some classic symptoms of active TB are cough of at least three weeks of duration, hemoptysis, weight loss, fever, and nocturnal diaphoresis (Hartman-Adams al., 2014).

Above: Representation of an adult sick with TB. http://tb.med.cam.ac.uk/tuberculosis/



Above: Pattern of multiple caseating granulomas in reactivation TB. http://library.med.Utah.edu

Screening

Tuberculin skin test (TST) and interferon gamma release essay (IGRA) are the tests available to diagnose TB. The two step TST is internationally recognized and is an accurate assessment of LTBI status in immuno-competent adults even if they have received the Bacillus Calmette-Gerin (BCG) vaccine (Morano, Zelenev, Walton, Bruce, & Altice, 2014). One major problem of TST is that it is not possible to make a reliable distinction of individuals infected with M. tb from individuals sensitized to other mycobacteria, including BCG (Dagnew et al., 2012). IGRA results can be obtained after a single visit. Therefore, IGRA has processing requirements and higher cost.

According to Hartman-Adams et al. (2014) "neither the TST nor the IGRA can distinguish between latent and active disease" (p. 893). In a person without overt signs of the disease a LTBI is indicated by the delayed-type hyper sensitivity response to the TST (Ahmad, 2011).

Implications for Nursing

As family nurse practitioners, we emphasize in health promotion and disease prevention in our daily practice. We can impact the clinical faith of persons with LTBI. By identifying persons at high risk and educating them in the importance of screening and appropriate preventive treatment, their infection may never progress to active TB. Educating the community and individuals on the signs and symptoms of the disease is important, so that they can seek medical attention and initiate measures to control the spread of the disease. As we educate patients, the possibility of their decision to be screened and adhere to treatment is higher.

Knowing the community where we work is important. We can perform assessments that identify persons more vulnerable to be sick, screen for the disease, and monitor treatment. According to Shimamura et al, patients that believe the nurse had a positive and genuine regard for him or her as an individual, was a key factor for successful treatment completion. The involvement of patient's family members to assist in treatment adherence offered positive outcomes. In addition, emphasizing the importance of treatment compliance to patients, so their family members and other citizens would be protected from contracting the disease, was a great encouragement for patients to complete the treatment (2013).

Conclusion

The presence of an M. tb immune response in the absence of active TB is defined as LTBI (Chee, Sester, Zhang, & Lange, 2013). The inability of otherwise an effective immune response to completely eliminate the pathogen is the hallmark of M. tb (Ahmad, 2011). Although the mycobacterial granuloma is a host defense mechanism for walling off M. tuberculosis, the bacilli can also survive, protected from killing by immune cells, and persists in a latent form until a circumstance arises for reactivation and dissemination.

In the U.S. and other high income countries with a low incidence of TB, most new cases of TB arise from reactivation of LTBI. Therefore, screening and treatment especially for groups at high risk for reactivation, such as contacts of patients with pulmonary TB, immunocompromised persons, and migrants from high-incidence

Conclusion Continued

areas, are key to prevent active disease and control TB (Stagg et al, 2014). The screening for LTBI should be widely practiced in persons at high risk followed by treatment as a preventive measure against active TB (Lee, Meintjes, Kamarulzaman, & Leung, 2013). In general, testing should only be offered when preventive treatment will be accepted, in the case of a positive result (Chee et al., 2013). In the U.S. the greatest incidence and prevalence of LTBI is among foreign-born populations (Morano et al, 2014). It can be concluded that TB is a preventable and curable disease.

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