

A Brief Review on Extra-Pulmonary Tuberculosis

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Abstract

Review Article

Tuberculosis is an omnipresent, highly contagious chronic granulomatous communicable bacterial infectious disease caused by *Mycobacterium tuberculosis* and other species of same genera. Tuberculosis usually affects the lungs, but can also affect other parts of the body. The aim of the present review to illustrate the various sites and co-morbidities associated with extra-pulmonary tuberculosis along with their diagnosis and treatment approaches.

Keywords: *M. tuberculosis*, Extra-pulmonary Tuberculosis (EP), sites and co-morbidities & treatment approaches.

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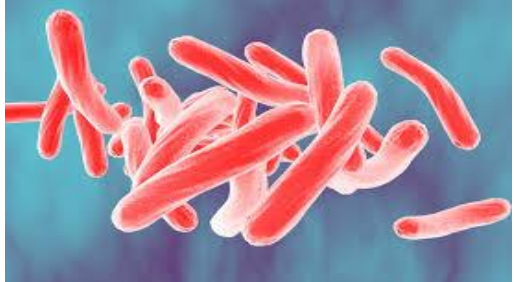
INTRODUCTION

Tuberculosis is a omnipresent, highly contagious chronic granulomatous communicable bacterial infectious disease caused by *Mycobacterium tuberculosis* and other species of same genera. In 1993, the World Health Association confirmed TB a “Global emergency”, as approximately one-third of the world population is infected with *M. tuberculosis*. Tuberculosis, which is easily transmitted through the air, already infects 1.9 billion people, and takes the lives of about two million people each year in which up to 25% of tuberculosis cases present extra-pulmonary association. The situation has been exacerbated because of the presence of several other complicating factors like multi drug resistant tuberculosis and HIV-coinfection. Tuberculosis is a chief cause of death amongst infectious diseases. Furthermore, this re-emerging disease has become one of the most important infections affecting human immunodeficiency virus

(HIV)-positive patients worldwide. TB also is becoming increasingly resistant to existing drugs. It is predictable by the World Health Organization (WHO) that more than 2 billion people in the world are infected with *Mycobacterium tuberculosis* [1]. *Mycobacterial* infection is a demanding health problem that requires particular attention worldwide. According to WHO classification criteria EP is defined as an infection by *M.tuberculosis* which affects outside the pulmonary parenchyma including tissues and organ outside. Approximately 20 and 25% of all TB cases represented EP [2]. The spread of *M.tuberculosis* bacilli at hematogenous and lymphatic resulted to Extrapulmonary TB [3, 4].

CAUSES AND SYMPTOMS

Two type of tuberculosis bacilli that affect the human [5, 6]



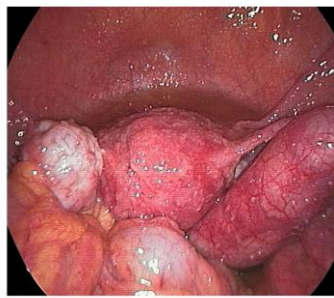

Causes	Symptoms
<p><i>Mycobacterium tuberculosis</i> (endemic in man) is transmitted by inhalation of the organism in droplets</p> 	<p>Tuberculosis pleuritis May occur in 10 % of people who have the lungs disease from tuberculosis. These people have a non-productive cough, chest pain and fever.</p> <p>Miliary tuberculosis In a minority of people with weekend immune system, tuberculosis bacteria may spread through their blood to various parts of their body. The symptom produces fever, weakness, and loss of appetite.</p>



Mycobacterium bovis (endemic in cattle) is transmitted by ingestion of infected milk.



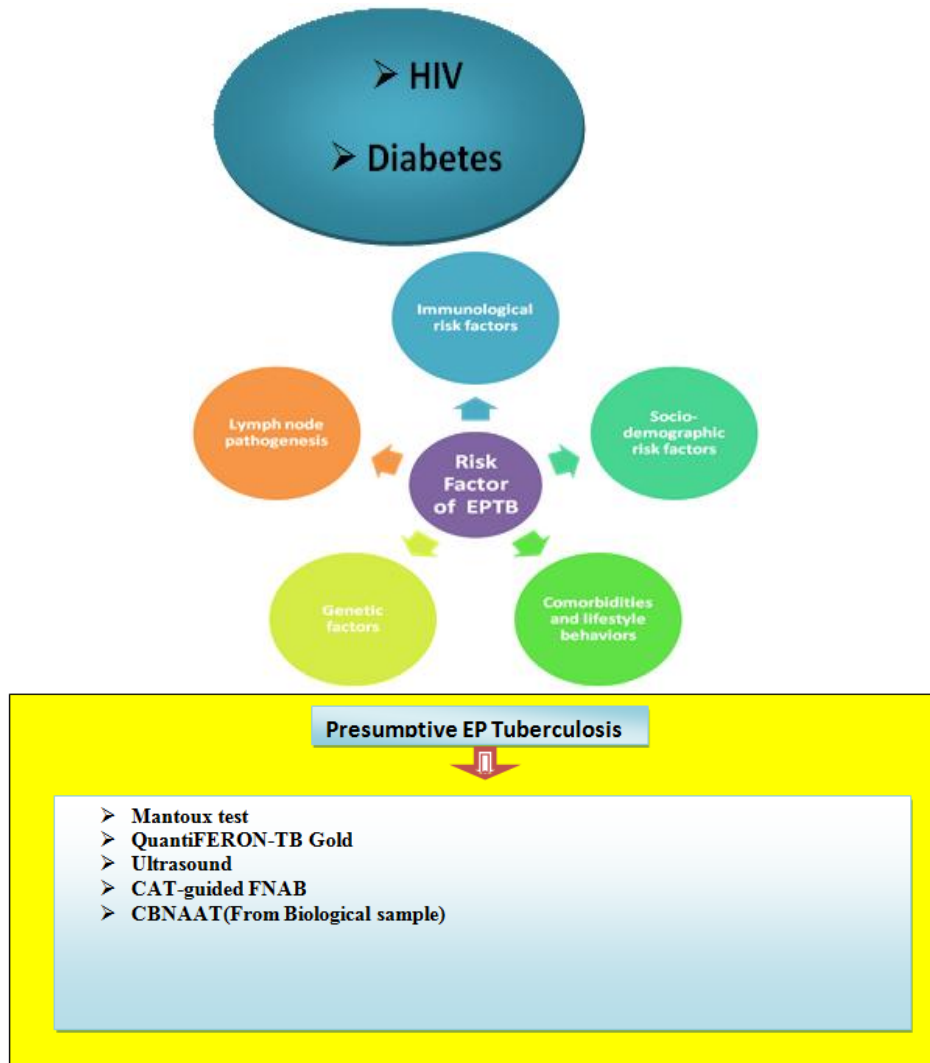
Symptoms of active tuberculosis include Ongoing cough, that brings up thick cloudy and sometimes bloody mucus (sputum) from the lungs. Fatigue, weight loss, night sweats and fever, rapid heartbeat, swelling in the neck, shortness of breath and chest pain (in rare cases)

Various type of extra pulmonary Tuberculosis

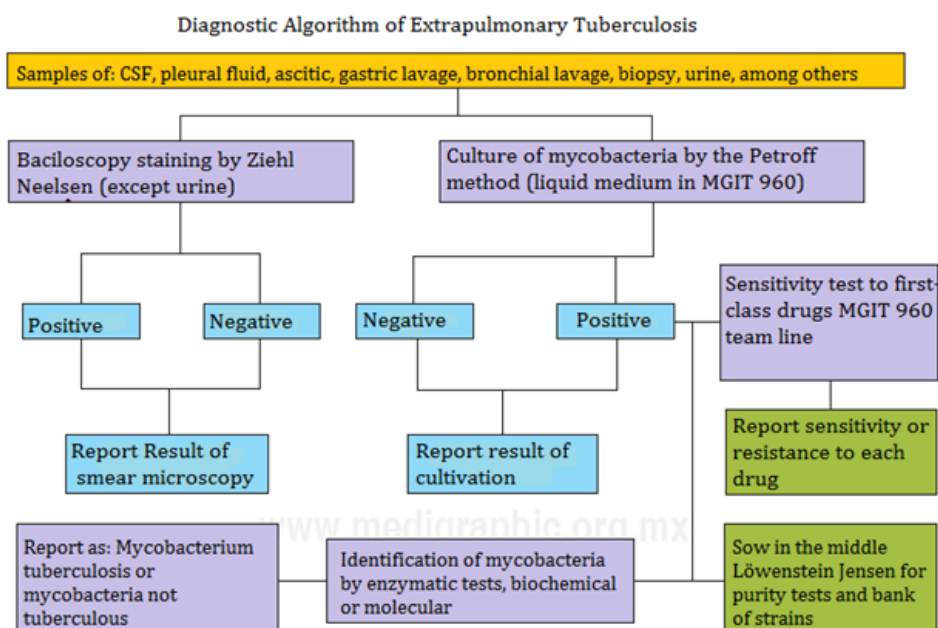
Extra-pulmonary Tuberculosis	Description	
LYMPH NODE TUBERCULOSIS	Occur due to reactivation of healed focus involved during primary infection and progressive primary tuberculosis. Some of the clinical manifestation includes enlarged, firm, mobile, discrete nodes, large rubbery nodes fixed to surrounding tissue & central softening abscess [7].	
OSTEOARTICULAR TUBERCULOSIS	Predominantly affects large joints (hip and knee). Tuberculous spondylitis represents about 50% of musculoskeletal TB. Generally affects the elderly in developed countries and young adults in the under developed countries. Clinical manifestation includes dominated by joint swelling with mono-arthritis affecting the knee, hip or ankle. Infectious spondylitis should be suspected in inflammatory back pain [8].	
GENITAL TUBERCULOSIS	Genital tuberculosis is characterized by extensive destruction and fibrosis. It occurs from primary reactivation of latent bacilli either in the epididymis or the prostate or by secondary spread from the already infected urinary organs. The epididymis is the commonest involved organs affected primarily by a hematogenous mode of spread [9].	
PLEURAL TUBERCULOSIS	Pleural effusion is a climax of fluid in the space between the lining of the lung and the lung tissue (pleural space) after a severe, usually long-term infection with tuberculosis. Clinical manifestation showed an acute febrile illness characterized by a non-productive cough and pleuritic chest pain, but without an elevation in the peripheral white blood cell count. Night sweats, chills, weakness, dyspnoea, and weight loss are also normally reported [10].	

<p>ABDOMINAL TUBERCULOSIS</p>	<p>Mostly affected gut, the peritoneum (the lining of the abdominal cavity) and abdominal lymph nodes. The bacilli can be affected the mucosal layer which lead formation of epithelioid tubercles in the lymphoid tissue of the submucosa. Furthur necrosis of tubercles leads to ulceration [11]. Clinical manifestation showed abdominal pain, weight loss, anemia, and fever with night sweats.</p>	
<p>CENTRAL NERVOUS SYSTEM TUBERCULOSIS</p>	<p>CNS tuberculosis leads development of small tuberculous foci (Rich foci) in the brain, spinal cord, or meninges [12]. Fever, stiff neck and seizures are some of the common symptom.</p>	

Major Co-morbidities associated with Tuberculosis



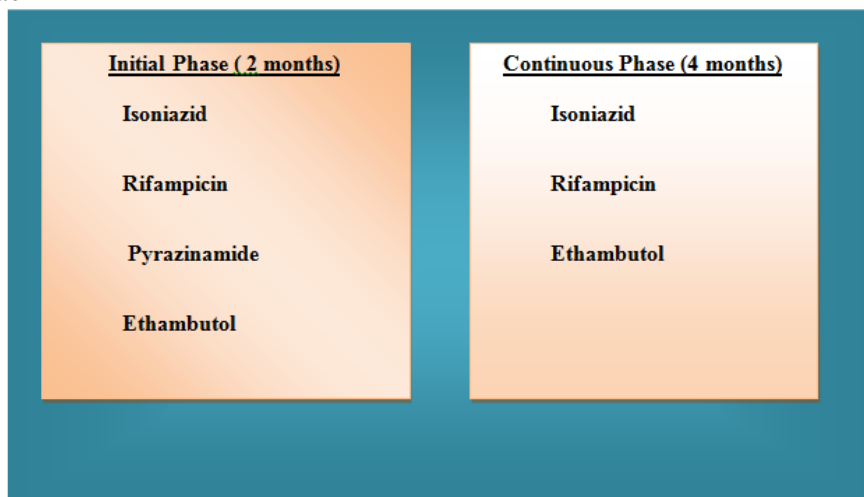
Diagnostic Approaches Extra-pulmonary tuberculosis



Summary of Symptoms and Investigation tools for various types of EP Tuberculosis

S.No.	Type of EP Tuberculosis	Symptom	Investigation Tool
1.	Neuro-tuberculosis (Tuberculous meningitis)	Lethargy Seizures Weight loss Altered sensation Vomiting Diplopia Giddiness	CSF-Lumbar puncture- Cob web formation CBNAAT BACTEC CSF-IGRA test TB-Gold test CT-Scan MRI scan(Hydrocephalus)
2.	Abdominal Tuberculosis	Constipation Abdominal pain Abdominal distension Weight loss Vomiting Ascites	USG(Abdominal) X-Ray(Abdominal) TB-Gold test CT-Scan Adenine deaminase test IFN-T level Laparoscopy Biopsy
3.	Bone Tuberculosis	Chronic back pain(Pott's spot) Difficulty in movement particularly banding forward	X-Ray(Spine) MRI scan(Spine) XPRT CBNAAT CT scan
4.	TB lymphadenitis	Painless Swelling on cocrial vertical & horizontal chain of lymph node Fever weight loss chronic discharging sinus	Biopsy Histopathology of affected Lymph node PCR Aspiration cytology
5.	Renal Tuberculosis	Painless hematuria	PCR U-culture in AFB TB-Gold test
6.	TB Pericaditis/	Chest Fever dysplasia Weight loss	Aspiration fluid ADA>40μ/L Cytology
7.	Pleural effusion	Pain on breathing cough Febrile dysplasia	Fluid Aspiration & Cytology

Treatment Approach



1. Treatment of individuals with active tuberculosis (TB) is the first priority for TB control; but an important second priority is identification and treatment of individuals with latent tuberculosis in order to avoid the disease dissemination.
2. The WHO recommends that chemoprophylaxis of these patients must be included as
3. Part of the TB control program for high income or upper middle-income countries with an estimated TB incidence rate of less than 100 per 100,000 populations per year.
4. For treatment of latent tuberculosis infection in HIV-uninfected adults, the WHO suggested either nine months of self-administered Isoniazid (INH) or three months of weekly INH and Rifampentine (RPT), preferably administered via directly observed therapy. Alternative regimens include daily INH for six months, daily Rifampin (RIF) for four months, or daily INH and RIF for three months. For HIV-infected patients with latent TBC, they are significantly more likely to reactivate with TB disease than HIV-uninfected individuals.
5. Treatment of latent TB is associated with two important benefits:
 - I. Reduction in the likelihood of progression to active TB disease,
 - II. Reduction in TB transmission.

Chemoprophylaxis is warranted for HIV-infected patients in the following circumstances: Individuals with recent contact with a person with active TB disease, individuals with a history of inadequately treated healed TB (fibrotic disease on chest radiograph), regardless of test results for latent TB, individuals with evidence of latent TB by tuberculin skin test or interferon-gamma release assay and individuals living in resource-limited areas of high

TB incidence where testing for latent TB is not available

CONCLUSION

Despite the availability of a restore to health and acquaintance on prevention of transmission, EPTB remains a imperative public health problem for a noteworthy proportion of the world. In developing countries, EPTB is less well addressed by programs than PTB, while its identification is imperative for optimizing care. Therefore, investigate EPTB determinants and identifying patients at higher risk of EPTB involvement is immediately needed in order to improve TB management and to ameliorate the diseases prognosis. TB spreading and acquiring EPTB form depend on a huge number of factors: Co-morbidities, HIV-coinfection, host factors, genetic variance and the site of the infection. Given the current shocking rates of EPTB burden, elimination of the disease at global level is still out of reach. Therefore, prevention of TB spreading must be a public health priority worldwide and immense resource investment is required. Poverty reduction has been emphasized by the United Nations as a tool to reduce TB burden. The key towards achieving the *STOP TB target of global TB eradication by 2050* will be sustained commitment from donors, authorities, effective national TB programs as well as community engagement, which played a fundamental role in identifying the most susceptible groups, assessing their specific needs and promoting good quality of life for TB patients.

Concern of Extra pulmonary can occur in isolation or along with a pulmonary focus as in the case of patients with disseminated tuberculosis (TB). The current human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) pandemic has resulted in changing epidemiology and has once again brought extra pulmonary tuberculosis (EPTB) into focus. EPTB constitute about 15-20% of

all cases of tuberculosis in immunocompetent patients and accounts for more than 50% of the cases in HIV-positive individuals. Lymph nodes are the most common site, followed by pleural effusion and virtually every site of the body can be affected. Since the clinical presentation of EPTB is a typical, tissue samples for the evidence of diagnosis can sometimes be not easy to procure, and the conventional diagnostic methods have a poor yield, the diagnosis is often delayed. Availability of computerised tomographic (CT) scan, magnetic resonance imaging (MRI) laparoscopy, endoscopy has tremendously helped in anatomical localization of EPTB. The disease usually responds to standard anti-tuberculosis drug treatment. Biopsy and/or surgery are required to procure tissue samples for diagnosis and managing the complications. Further research is required for evolving the most suitable treatment for EPTB.

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