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Chapter 8

ENT Manifestations in Tuberculosis

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Additional information is available at the end of the chapter

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1. Introduction

Tuberculosis (TB) is one of the oldest diseases that afflicts mankind, and has re-emerged as a significant cause of morbidity and mortality in several countries [1]. It is an infectious and contagious disease caused by a bacterium, *Mycobacterium tuberculosis*, also called Koch´s Bacillus (KB) [2]. According to the location of the outbreak, it can be classified as pulmonary TB, primary TB, TB reactivation and extrapulmonary TB [3].

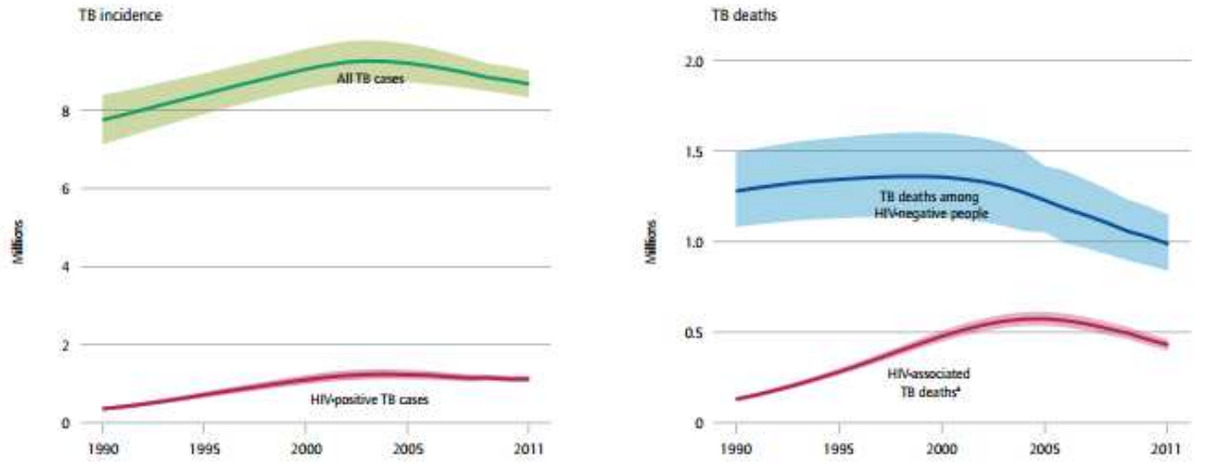
2. Epidemiology

According to the World Health Organization (WHO), there were nearly nine million new cases in 2011, and about 1.4 million TB deaths (990,000 among Human Immunodeficiency Virus (HIV) negative people and 430,000 TB deaths associated with HIV). TB is also more common in men than in women, affecting in particular adults in economically productive age groups [4].

Figure 1 shows the estimated number of TB cases and deaths [4].

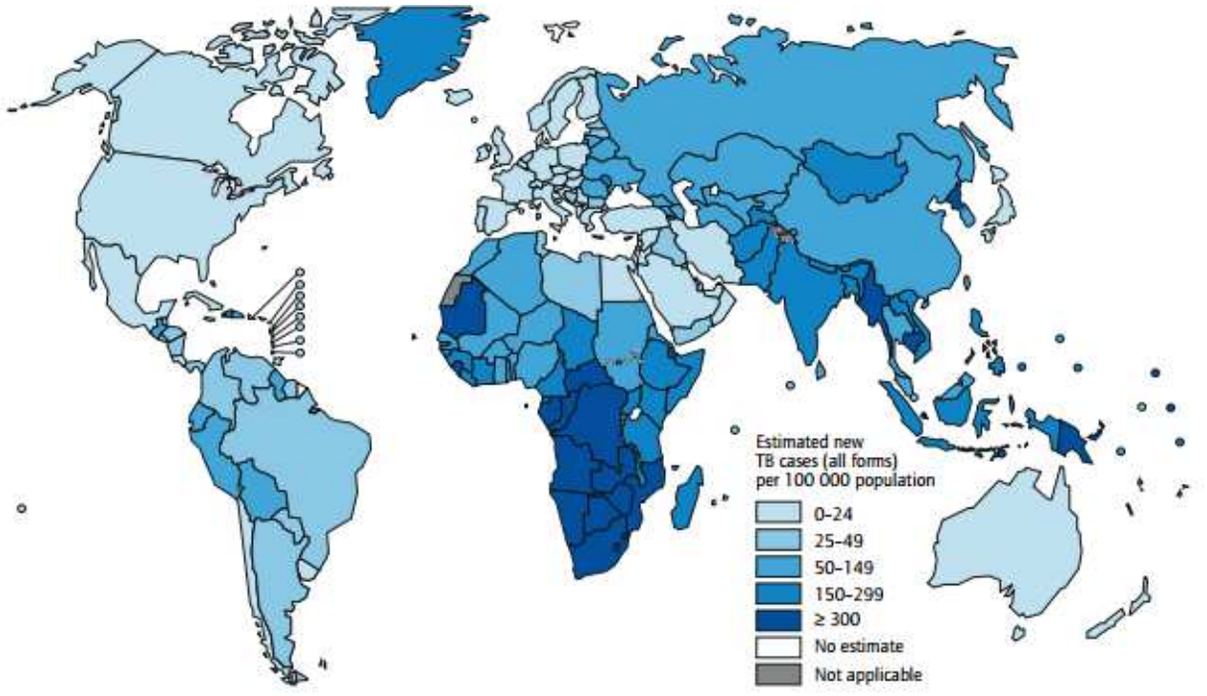
The estimates show that most cases have occurred in Asia (59%) and Africa (26%). Smaller proportions of the global total have occurred in the Eastern Mediterranean Region (7.7%), Europe (4.3%) and the Americas (3%) [4].

Figure 2 shows the estimated incidence rates of TB in each country [4].



Source: World Health Organization. Global Tuberculosis Control Report 2012. Available at: http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf (accessed on 18 June 2014).

Figure 1. Estimated absolute numbers of TB cases and deaths (in millions), 1990–2011.



Source: World Health Organization. Global Tuberculosis Control Report 2012. Available at: http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf (accessed on 18 June 2014).

Figure 2. Estimated TB incidence rates, 2011.

In Brazil, TB is still a serious health problem. Each year, approximately 70,000 new cases are reported and 4,600 deaths occur due to the disease [5]. In Pernambuco in 2012, the incidence rate of TB was 52.21 per 100 thousand inhabitants with 3,879 new cases of pulmonary TB reported, of which 2,657 were in the metropolitan region of Recife [6].

3. Transmission

Transmission usually occurs through direct contact of the patient with a healthy person. Indirect contagion by handling contaminated material and animals can take place, but this is exceptional. When one coughs, sneezes or talks, Flügge droplets are exhaled, which can lead to contagion in a healthy individual. The gateway in about 90% of cases is the airway. Therefore, pulmonary TB is the dominant form. Other pathways, may, however, be conduits, such as the digestive system, skin, tonsils, eye and others that might have direct contact with the aggressor agent [7].

4. Clinical manifestations

Manifestations of TB in cervico-cephalic regions are among the most frequent, and have attracted interest mainly because of the changes in the pattern of attack of the disease. This is because it is currently uncommon to find acute or rapidly progressive forms, it being more frequent to find forms that evolve with a subclinical pattern [8].

In the region of the head and neck, TB manifests itself predominantly in the larynx; less frequently, it is found in the middle and external ear, tonsils, cervical lymph nodes, pharynx, oral cavity, and salivary glands [9].

4.1. Laryngeal TB

One of the organs that can be secondarily affected by TB is the larynx, even although in some cases, laryngeal TB may have a primary involvement [7].

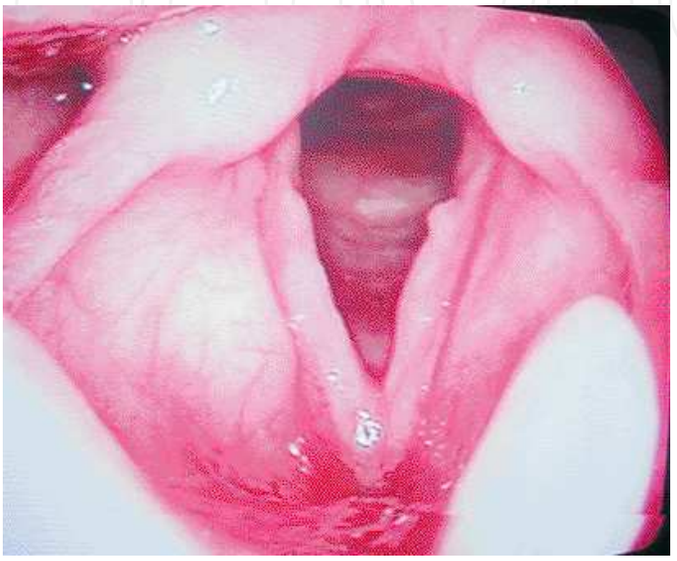
There are two theories that attempt to explain its pathogenesis: bronchogenic theory, which is the most accepted, says bronchogenic secretions are responsible for contaminating the larynx through the direct contact of the secretions with the laryngeal mucosa; and hematogenous theory, which says that *Mycobacterium tuberculosis* reaches the blood and lymph vessels and thus affects the larynx, it being possible for there not to be any pulmonary damage [10].

Before the use of antibiotic therapy, laryngeal TB was considered one of the most serious complications of pulmonary TB and was often fatal. In the 1940s, after the development of various treatment regimens, the incidence of pulmonary TB decreased and pharyngolaryngeal involvement became less frequent. However, in the last two decades due to the decline in the quality of treatment and supervision worldwide, and as a consequence of the emergence of AIDS as a global epidemic and the development of multidrug-resistant strains of TB, the number of cases of the disease has been increasing progressively [11].

In the clinical framework of laryngeal TB, the most common symptom is dysphonia, which is present in 100% of patients in many studies, and this can progress to aphonia. In addition, other important manifestations include dysphagia due to ulceration of the laryngeal vestibule or perichondritis of the cricoid cartilage; cough and hemoptysis because of the

affect on the lungs; dyspnea due to edema or laryngeal granulomas that may obstruct light from the larynx [12].

In laryngeal TB, the most commonly affected site is the region of the vocal folds, followed by the vestibular folds and may involve the epiglottis, the aryepiglottic fold, the arytenoids, the posterior commissure and the subglottis [10]. Figure 3 shows a lesion in the posterior third of the left vocal fold [7].



Source: Garcia, 2004, p.257.

Figure 3. A lesion in the posterior third of the left vocal fold.

4.2. TB of cervical lymph nodes

Lymph node TB may result from dissemination via the blood stream, of bacillary pulmonary foci [13], as well as from the bacilli gaining entrance via the tonsils, dental or pharyngeal foci [14]. It is located most frequently in the cervical, supraclavicular and hilar and mediastinal regions. However, any lymph node may be affected [13].

It is one of the most prevalent forms of TB in the head and neck. In general, it presents itself insidiously with a gradual increase in the lymph node and evolution to caseification [14].

No gender difference was found among those suffering from TB in cervical lymph nodes. However, what was verified is that there was greater prevalence in the 35-44 year-old age group [15].

4.3. TB of the ear

TB located in the middle ear as the primary focus is uncommon. Classically it affects children more than adults [9].

Several theories attempt to explain the infection of the middle ear by TB, but its pathogenesis is still controversial. It is suggested that routes may be through the bloodstream by direct extension from the nasopharynx through the Eustachian tube via the lymphatic system; externally, by perforation of the tympanic membrane; by direct extension from adjacent structures, the central nervous system, congenital infection (via the placenta) or during passage through the birth canal [9].

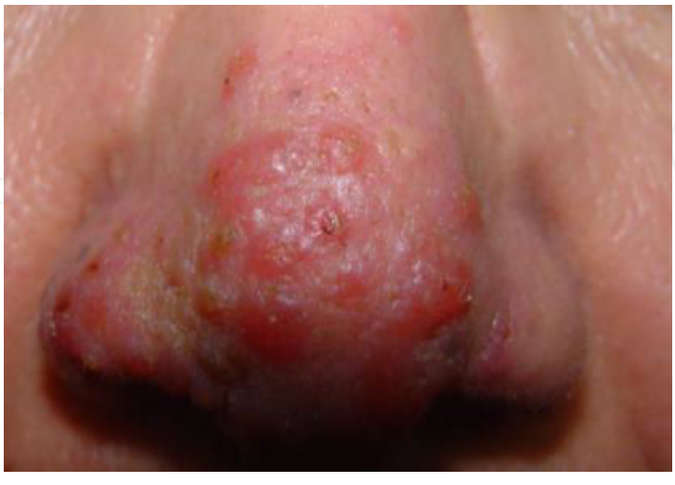
Classically it is presented as the triad: painless otorrhea, multiple perforation of the tympanic membrane, and peripheral facial palsy; but currently its presentation has become polymorphic. Among its complications are the following: peripheral facial paralysis, retro-auricular fistula, labyrinthitis, meningitis, tuberculous osteomyelitis of the petrous pyramid, subperiosteal, cerebral or cerebellar abscess, acute mastoiditis and cellulites [9].

4.4. Nasal TB

Nasal TB is an extremely rare form [16]. Butt in his review of nasal TB in the 20th century identified only 35 reported cases, 12 of which were of the primary form. The most common symptoms were nasal obstruction and aqueous secretions [17].

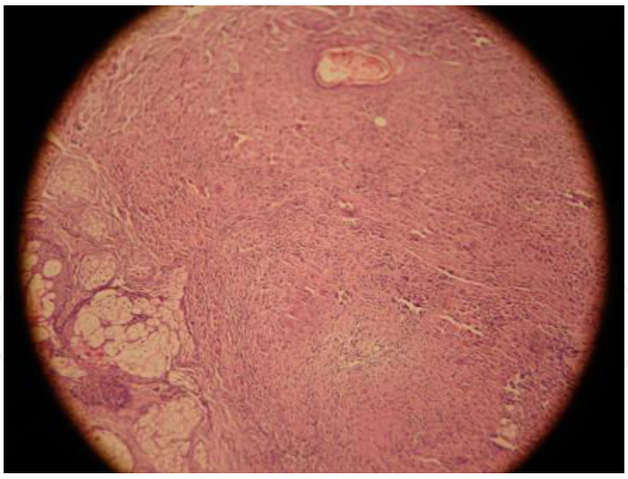
Less common symptoms include nasal discomfort, presence of a mass, epistaxis, crusting, lachrymation, postnasal drip, recurrent polyps, and nasal ulcer [17]. The most common site is the anterior-inferior portion of the nasal septum, in the region of greatest arteriovenous confluence called the Kiesselbach zone. In anterior rhinoscopy, a pale, torpid mucosa is observed and can present with perforation of the nasal septum [14].

Figure 4 shows an image of nasal TB lesions. Figure 5 gives the histopathological assessment which revealed a caseous granulomatous reaction, epithelioid cells lymphatics, and some giant cells [18].



Source: Alavi, 2014, p.50.

Figure 4. Reddish ulcerative lesion on the nose and in the internal mucosal layer.



Source: Alavi, 2014, p.50.

Figure 5. Caseating granulomatous reaction, epithelioid cells, lymphocytes, and a few giant cells.

4.5. TB in the oral cavity

Oral TB is a rare form representing 0.1-5% of the total of TB infections. *Mycobacterium tuberculosis* can infect all parts of the mouth, such as gums, hard and soft palate, lips, maxilla and mandible [19]. It is more frequent in men than in women appearing mainly in the form of ulcerative lesions [20]. The tongue is the most common site of TB oral [19].

The integrity of the oral mucosa, the cleaning action of the saliva, the presence of oral saprophytes and submucosal antibodies represent a natural resistance to the invasion of *Mycobacterium tuberculosis* [19]. Oral trauma, tooth extraction, inflammatory conditions and poor hygiene represent gateways [20].

Its presentation occurred as a secondary infection in 58% of patients and as a primary infection in 42%. Carcinomas have been found coexisting in the same site of the lesion in 3% of patients. In approximately 50%, the oral manifestation of TB led to the diagnosis of systemic infection [20].

4.6. TB in the tonsils

Primary tuberculosis in tonsils, in the absence of active pulmonary disease is rare [21]. In a study by Ricciardiello [8] et al., 0.62% of the sample was found to have this form of TB.

It may result from contact with materials containing bacilli. In the secondary form, it may be due to the contact of sputum containing bacilli from a pulmonary focus. What favors this site being affected are factors such as alcoholism, HIV and infection [22].

Its clinical features are nonspecific; sometimes it can simulate chronic tonsillitis [23]. The oral examination may show hypertrophy of the tonsils, bulging in the oropharynx with edema and erythema, as well as yellow platelets on its surface [24].

4.7. TB in the salivary glands

Primary TB is a relatively common cause of granulomatous disease of the salivary glands. Generally it affects one side, and the usual target is the parotid gland. The primary form can occur in two ways: as an acute inflammatory lesion mimicking an acute suppurative sialadenitis, or as a chronic tumor [25].

As to secondary tuberculosis, unlike the primary form, this more often involves the submandibular and the sublingual glands than it does the parotid one [25].

TB of the salivary gland is more common in immune-depressed patients, and it is difficult to distinguish it clinically from other diffuse diseases of this site [26].

Figure 6 shows a patient who has TB of the submandibular gland [26].

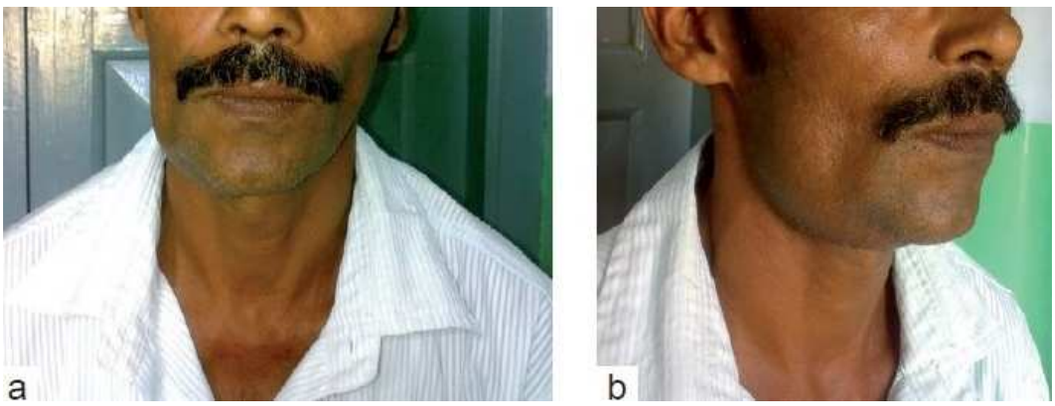


Figure 6. Photograph of the patient showing right submandibular swelling (a) Frontal view. (b) Right lateral view. Source: Tauro, 2011, p.83.

5. Diagnosis

The forms of extrapulmonary TB can be challenging to diagnose because bacteriological confirmation can only be obtained in about a quarter of cases. The reasons for this difficulty include difficult access to some lesions and the fact they are usually paucibacillary. Moreover, the histopathological findings of granulomatous reaction do not rule out the possibility of other diseases. Imaging studies can provide important information, although there are no specific standards for the sites affected [27].

In laryngeal TB, diagnosis may be obtained from the isolation and culture of *Mycobacterium tuberculosis*, but this diagnosis only emerges after about four weeks of cultivation. The best material for culture is obtained by biopsy, but this is positive in only 40% of cases. A biopsy can also be used to check if there is concomitance with cancer of the larynx [28]- [30].

Some authors consider the anatomatopathological exam as the "gold standard" for the diagnosis of laryngeal TB [7]. By using microscopy, we observe inflammatory, granulomatous

reactions. The granulomas consist of giant cells, and central caseous necrosis can occur, which aids a positive diagnosis to be made before receiving a positive culture of *Mycobacterium tuberculosis* [29]. Since most patients have a concomitant pulmonary problem, chest radiography can assist in this diagnosis [7], [12].

The Mantoux or intradermal test is often used. Its positivity is given by a 10mm diameter wheal after up to 48 hours or 5mm in immune-compromised patients. This positive test only indicates infection [7], [12]. The PCR is a test that can amplify amounts of specific segments of deoxyribonucleic acid from microorganisms such as *Mycobacterium tuberculosis* present in a sample [12]. Chest X-ray, the Mantoux test and PCR tests are examinations that are sensitive to the presence of *Mycobacterium tuberculosis.* However, they are not specific to laryngeal disease.

We stress the importance of taking care over recording the patient´s medical history and conducting an ENT examination accurately, with emphasis being given to indirect laryngoscopy and videolaryngoscopy [28].

In the form of TB affecting lymph nodes, diagnosis can be made by aspirative punction. The smear material is positive in 10% to 25% of cases as is culture, in 50% to 85% of them. A biopsy of the lymph node is often inconclusive, showing granuloma with caseous necrosis in 91% to 96% of patients. Usually, the tuberculin test is a strong reactor, except in immumo-suppressed individuals [27].

In suspected cases of tuberculosis of the middle ear, the following tests are important: Gram stain and culture of the middle ear secretion, specific for AFB (acid fast bacilli); biopsy of polyp or mucosa of the middle ear and histopathological studies with tissue culture; tuberculin skin test (Mantoux); chest X-ray. Other tests may clarify some details: a radiological and tomographic study of the mastoids; audiogram [31].

In TB of the middle ear, the histopathological examination of the granulation tissue (when it is abundant), is still the most reliable diagnostic method, but very often the biopsy needs to be repeated for confirmation. The method is used to demonstrate caseous necrosis and specific granulation with epithelioid and giant Langerhans cells [10].

Audiometric tests detect precocious hipoacusia and out of proportion to the apparent degree of development of the disease seen at otoscopy. Radiographic studies of the middle ear and mastoid do not reveal specific features, but the detection of well-pneumatized mastoid in patients with chronic otorrhea may suggest the possibility of hypocausia [31].

The diagnosis of nasal TB can be established by smear (using nasal exudate) and the biopsy of the lesion [14]. The diagnosis of tonsillar TB is also based on histopathological findings and on identifying the bacillus [21].

6. Differential diagnosis

In laryngeal TB, differential diagnosis with inflammatory diseases and with laryngeal carcinoma should be conducted [7]. Similarly, in TB which affects the ear, differential diagnosis may reveal other diseases with chronic suppuration which do not improve with conventional

treatment, such as cholesteatoma, syphilis, Wegener's granulomatosis, fungal infection, eosinophilic granulomatosis and sarcoidosis [9].

Traumatic ulcers, aphthous ulcers, blood disorders, actinomycosis, syphilis, midline granuloma, Wegener's disease and cancer are differential diagnoses of oral tuberculosis [21]. In nasal TB, differential diagnosis should include looking for inflammatory processes, as well as other diseases that can manifest themselves with similar lesions, such as herpes simplex, leishmaniasis, syphilis and some fungal infections [16].

TB of lymph nodes can be determined by making a differential diagnosis with diseases such as lymphomas and atypical mycobacterioses [13].

7. Tuberculosis and HIV

Individuals who live with HIV and who are also infected with TB are more likely to develop the disease of TB than those who are HIV negative. From the 80s, the HIV epidemic has led to a large increase in TB cases and TB mortality in several countries [4].

In 2011, 1.1 million (13%) of the 8.7 million people who had developed tuberculosis worldwide were HIV positive. In the same year, there were an estimated 0.4 million deaths from HIV-associated tuberculosis in the world [4].

HIV has been pointed out as being one of the factors for the resurgence of TB, as well as having an impact on its epidemiology, natural history and clinical evolution. This is also related to the reactivation of latent infections of TB [32]. HIV infection also modifies the clinical presentation of TB, the duration of treatment, tolerance to antituberculosis and resistance to the drugs available [33].

8. Treatment

TB is a serious but curable disease in almost 100% of new cases, as long as the principles of chemotherapy are followed [34]. However, in the absence of beginning treatment, it is estimated that 60-70% of patients with pulmonary TB without co-infection by HIV progress to death [35].

Treatment of active baciliferous TB is the priority activity of TB control, since this allows the greatest sources of infection to be annulled. Tubercle bacilli practically lose their virulence, a few days after the start of chemotherapy [34].

The drugs used are: isoniazid, rifampicin, pyrazinamide and ethambutol. The inclusion of ethambutol in Brazil, was authorized in 2008 and is indicated for adults and adolescents (> 10 years old), in the first-line treatment of TB in Brazil. Thus, the use of rifampicin, isoniazid, pyrazinamide and ethambutol in the first phase of treatment is recommended for two months followed by rifampicin and isoniazid for four months, thus maintaining the short duration regime of 6 months. For children, this continues with three drugs in the first phase [34].

This scheme is used in Brazil for the treatment of all forms of pulmonary and extrapulmonary TB (except meningoencephalitis) in new cases of patients whether or not they are infected by HIV [34].

9. Prevention

The best way to prevent TB is to diagnose and isolate infectious cases quickly by administering treatment appropriately until the patient is no longer infectious the disease is cured [36].

BCG vaccination and the treatment of individuals with latent TB infection, who are at high risk of developing the disease are other strategies that can be used [36].

10. Final remarks

TB is a disease with a very long history and one which has sprung up again and been affecting various countries. Among the factors responsible for this resurgence, HIV should be mentioned. HIV has been regarded as responsible for changing the characteristics of TB, such as its epidemiology, natural history, clinical presentation, and resistance to drugs.

The manifestations of TB in cervico-cephalic regions are frequent and have aroused interest, mainly because of changes in the pattern of how the disease is caught. These forms can also be challenging to diagnose.

Provided appropriate treatment is begun promptly, TB is a curable disease, and doing so for infectious cases is moreover a form of prevention.

In this context, public policies are needed that encourage not only the adoption of preventive measures, but also aid early diagnosis and seek to ensure adherence to TB treatment. This is because the earlier that treatment is started and is done so appropriately, the more likely that the patient will suffer from fewer sequelae and deformities.

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