Tuberculosis, a disease caused by *M. tuberculosis*, has been recorded in history since the Greco-Roman and Egyptian civilizations, with evidence of spinal tuberculosis being recorded as long ago as 3400 BC. Ancient Indian scriptures also mention this disease (1), with the first known description of tuberculous spondylitis being written in Sanskrit sometime between 1500 and 700 BC. However, the modern name of the disease has been attributed to Laennec in the 1800s (2).

It has been postulated that *M. tuberculosis* existed as an unimportant pathogen to man until the coming of the industrial revolution (3). With resulting urbanisation and propinquity of living, a new epidemic, described as ‘a great white plague’, evolved. In the newly industrialised countries, the incidence of tuberculosis probably increased sharply from the mid 1700s with subsequent pandemic spread throughout Western Europe over the next century and a peak incidence around 1800 (4). Migration probably resulted in spread to the United States, central Africa and also to South and South-east Asia. As recently as 1950 tuberculosis has affected previously completely uninfected, and, therefore, non-immune populations, such as the Inuit Eskimos of Northern Canada and the natives of the highlands of Papua New Guinea (5, 6).

It has been stated that as tuberculosis moves through a nonimmune population, natural selection would eventually result in a resistant population and subsequent gradual decline of the disease pandemic. In most persons, infection with *M. tuberculosis* is initially contained by host defences, and the infection remains latent. However, latent tuberculosis infection has the potential to develop into tuberculosis at any time, and persons with active tuberculosis become sources of new infections (7).

Today, tuberculosis remains endemic in most of the developing countries. In common with many other developed countries, Belgium faces a resurgence of tuberculosis. After declining for more than a century, notification rates began to increase in the mid 1980s and the long-term downward trend in mortality also shows signs of levelling off (8). Several factors may have contributed to these trends, including immigration from countries with a high prevalence and the epidemic of HIV and AIDS. In addition, other underlying diseases (diabetes mellitus, chronic renal failure, chronic obstructive pulmonary disease, liver cirrhosis, leukemias and lymphomas) and numerous sociological factors contributed to the re-emergence of tuberculosis: a growing elderly population; overcrowded prisons; poor living facilities; poor nutrition status, alcohol and drug abuse; persons in long-term care facilities and homelessness (9, 10).

Among health care workers, the risk of occupational tuberculosis varies among and within institutions, but workers involved in autopsies and cough-inducing procedures seem to be at higher risk (11). Finally, it is known that immigrants visiting their country of origin can “bring back” tuberculosis on their return (12).

Tuberculosis may arise in two different ways: either from a recent infection with *M. tuberculosis* or from the reactivation of dormant bacilli years or decades after initial infection. Extrapulmonary tuberculosis mainly results from reactivation of a tuberculous focus after hematogenous dissemination or lymphogenous spread from a primary, usually pulmonary focus. Tuberculosis may demonstrate a variety of radiological features depending on the organ site involved and may mimic other pathologies. The final diagnosis of tuberculous disease mainly depends on the detection of the causative organism on histopathological examination, culture and polymerase chain reaction-based assay for mycobacterial DNA on material obtained during bronchoscopic washings, fine needle aspiration cytology (FNAC) or biopsy.

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people having lived through a period of high tuberculosis incidence are very likely to have been infected with *M. tuberculosis* and now comprise a growing population group. In contrast, younger people who have acquired primary infections have done so during a period of much lower incidence and consequently comprise a smaller subgroup. Therefore, it has been stated that disease in the elderly largely consists of endogenous reactivation whilst most tuberculosis in younger people is the result of new exogenous infection (12).

**HIV/AIDS and tuberculosis**

It is well established that the impairment of the immune system as a result of human immunodeficiency virus (HIV) infection predisposes to the development of tuberculosis and the disease is now regarded as a “sentinel” manifestation of the progression from HIV to AIDS (14-16). The specific targeting of the CD4 helper cells by the HIV carries a greater risk of endogenous reactivation of any latent tuberculosis infection. However, in patients infected with HIV, opportunistic infection with *M. tuberculosis* most commonly occurs as a result of exogenous infection (15). The risk of developing progressive primary tuberculosis within the first year in HIV-infected persons is almost 30% in contrast with the 3% risk of the non-HIV-infected persons (17). Infection with *M. tuberculosis* has been reported as one of the most pathogenic of the HIV/AIDS opportunistic infections (15). Foley et al. (18) described an increase in the proportion of tuberculous patients infected with HIV whilst the total number of TB notifications remains largely unchanged and suggested a direction of causality from the wider population to the AIDS group. Tuberculosis as the primary cause of death has also been reported in patients suffering from AIDS and tuberculosis (19, 20). It is unlikely that HIV will directly cause a rise in tuberculous rates in the indigenous population of the developed world because the incidence of infection with tuberculosis amongst the younger population, which is the one most at risk of acquiring HIV, is low. However, in the developing world with a high prevalence of infection with tuberculosis in the young adult population, AIDS-related tuberculosis may increase dramatically over the next decade (21). It is likely that the high and rising rates of tuberculosis in many developing countries with a high HIV prevalence will indirectly make an impact on developing countries as long as rates of tuberculosis amongst migrants to the developed world remain high or increase further (3). During the past 15 years, alongside the dramatic rise in HIV, Africa has experienced a concomitant increase in the tuberculosis rate (18). In the United states, HIV infection has also been implicated in the rapid increase in tuberculosis notifications or young men (18). The extent to which HIV is implicated in the resurgence of tuberculosis in Belgium will depend on the overlap between the populations infected with these two conditions. However, this overlap seems to be small.

**Manifestations of tuberculosis**

Inhalation is the predominant route of *M. tuberculosis* infection, making pulmonary tuberculosis the commonest form of tuberculous infection (22). The organism gains access to the blood stream via the lymphohematogenous route and may then affect any organ. The incidence of extrapulmonary tuberculosis is increasing, especially because of HIV (23). In patients infected with HIV *M. tuberculosis* usually involves multiple extrapulmonary sites including the skeleton, abdominal organs, and central nervous system. Tuberculosis may demonstrate a variety of clinical and radiological features depending on the organ site involved and as a consequence may mimic other pathologies. It is important to be familiar with the various radiological features of tuberculosis to obtain a presumptive diagnosis as early as possible (24).

**Pulmonary tuberculosis**

Pulmonary tuberculosis is classically divided into primary and post-primary (reactivation) tuberculosis. However, a considerable overlap in the radiological presentations of these entities may be seen. Although primary tuberculosis is the most common form of pulmonary tuberculosis in infants and children, it has also been increasing-ly encountered in adult patients.

**Primary tuberculosis**

Primary disease accounts now for 23%-34% of all adult cases of tuberculosis (25). Primary pulmonary infection occurs when an uninfected person inhales an infectious droplet, which successfully establishes infection in a terminal airway or alveolus (22). The resultant primary parenchymal (Ghon) focus usually drains via local lymphatics to the regional lymph nodes. The combination of the Ghon focus, local lymphangitis and regional lymph node involvement is known as the Ranke complex. Sometimes, associated pleural reaction overlying a peripheral Ghon focus may be present. The formation of the Ghon complex is often subclinical and a random chest radiography following primary infection is often normal or reveals only a single component, mostly hilar adenopathy (Fig. 1) (22).

Disease progression may occur at the site of the Ghon focus, within the regional lymph node, or as a result of lymphatic drainage with hematogenous dissemination or after local penetration across anatomical boundaries (26). Pneumonia may occur into an adjacent anatomical space or structure, into an airway with additional intra-bronchial spread or into a blood vessel with hematogenous dissemination. Two main types of hematogenous spread of *M. tuberculosis* are differentiated, but dissemination via the hematogenous route represents a condition of infinite gradation. Following dissemination, bacilli lodge in small capillaries where they may progress locally and give rise to further hematogenous spread. In the other type, disease progression may result in a caseous focus eroding into a blood or lymph vessel (Fig. 2). Except for immunocompromised patients, the first type, contrary to the second one, rarely progresses to disseminated disease (27).

Primary tuberculosis typically manifests radiologically as parenchymal disease, lymphadenopathy, pleural effusion, miliary disease, or atelectasis, which may be either lobar or segmental. Parenchymal disease in primary tuberculosis affects the areas of greatest ventilation. Most commonly, the middle lobe, the lower lobes, and the anterior segment of the upper lobes are involved (11). Atelectasis is usually the consequence of bronchial obstruction by an enlarged hilar adenopathy.

**Postprimary tuberculosis**

Postprimary tuberculosis usually results from reactivation of a previ
ously dormant primary infection in 90% of cases. In a minority of cases, it may result from the continuation of primary disease (28). Reinfection is very rare. Reactivation of mycobacterial disease is almost exclusively seen in adolescence and adulthood. Reactivation occurs as the result from numerous causes such as poor nutrition status, neoplasm, infection or increasing age. Post-primary tuberculous lesions show a slow progressive course resulting in high morbidity and mortality if not adequately treated (29).

The radiologic features as seen in postprimary tuberculosis are the result from a continuous interaction between the individual patient, with his own immune status, and M. tuberculosis (30). The radiologic features may be classified as parenchymal disease with cavitation, airway involvement, and pleural extension.

Parenchymal pulmonary disease may show caseous and liquefaction necrosis and communicate with the tracheobronchial tree to form cavities (Fig. 3). A predilection for the apical or posterior segment of the upper lobes or the superior segment of the lower lobes has been reported (28). Mostly, two or more segments are involved, and bilateral upper lobe involvement may also be noted (11). Most commonly, cavities occur within areas of consolidation, are multiple, and show thick irregular walls. However, thin and smooth cavity walls may also be seen. An air-fluid level within the cavity is an uncommon finding, and may reflect superimposed bacterial or fungal infection (31).

Bronchogenic spread is a common complication in postprimary tuberculosis and represents a chronic granulomatous infection in which active organisms spread via airways after caseous necrosis of bronchial walls. Endobronchogenic spread is characterized by multiple, ill-defined micronodules, distributed in a segmental or lobar distribution, distant from the site of the cavity formation and typically involving the lower lung zones (30) (Fig. 4). If untreated, end stage disease may lead to lobar or complete lung opacification and destruction (Fig. 5). However, with chronic disease, fibroproliferative lesions composed of nodular opacities and clearly defined, medium to coarse reticular areas, may develop. Most often associated poorly margined areas of increased density may be present (Fig. 6).

A marked fibrotic response is a common finding after postprimary tuberculosis and may result in atelectasis of the upper lobe, retraction of hilum, compensatory lower lobe hyperinflation, mediastinal shift towards the fibrotic lung and...
Central airway involvement in tuberculosis may be the result of direct extension from tuberculous lymph nodes, endobronchial spread of infection, or lymphatic dissemination to the airway (32). Bronchial stenosis may result in segmental or lobar collapse, lobar hyperinflation, obstructive pneumonia, or mucoid impaction. A common complication of endobronchial tuberculosis consists of bronchiectasis resulting from pulmonary destruction and fibrosis, and central bronchostenosis.

Pleural effusions in postprimary tuberculosis are usually small and associated with parenchymal disease. A loculated pleural fluid collection with parenchymal disease and cavitation may indicate tuberculous empyema and air-fluid levels in the pleural space indicate bronchopleural fistula.

Occasionally, pericardial involvement may be seen with mediastinal and pulmonary tuberculosis and may cause calcific pericarditis (Fig. 8) (33).

Imaging findings of pulmonary tuberculosis

Chest X-rays

Chest X-rays are effective in demonstrating airspace disease, the parenchymal nodule that represents the Ghon focus, diffuse interstitial disease and pleural effusions (Fig. 9A). Revealing the presence of lymphadenopathy is an important diagnostic sign. However, chest X-

Fig. 4. — Endobronchial spread of tuberculosis (same patient as Fig. 3). CT obtained with lung windowing shows severe changes of bronchiolar dilatation and impaction. Bronchiolar wall thickening (curved arrow) and mucoid impaction of contiguous branching bronchioles produce a tree-in-bud appearance (straight arrow).

Fig. 5. — Endobronchial spread of tuberculosis with end stage disease. CT obtained with mediastinal windowing shows extensive abnormalities of both lungs with distortion of lung parenchyma, confluent consolidations, multiple cavities, pleural thickening and effusions.

Fig. 6. — Chronic tuberculous disease characterized by fibroproliferative lesions. Nodular opacities, coarse reticular areas and poorly margined areas of increased density are present.

Fig. 7. — Lung destruction in postprimary tuberculosis. CT demonstrates a fibrotic, shrunken left lung with compensatory overexpansion of the right lung. Bronchiectasis is noted in the left lung with areas of emphysema and atelectasis. Bilateral symmetrical interstitial nodules, typical of miliary tuberculosis, are also present.
Rays have been shown to be insensitive for the detection of lymphadenopathy (34). On frontal view, lymphadenopathy is seen as a lobulated density occupying the hilum and obliterating the hilar point.

CT

Despite a high radiation dose and the need for intravenous contrast administration, CT has evolved to the modality of choice for the evaluation of primary and postprimary pulmonary tuberculosis (11, 30). Compared to chest X-ray, CT shows a higher sensitivity for the demonstration of tuberculous lymphadenopathy (34). On contrast-enhanced CT, lymphadenopathy may appear as circular or ovoid lesions showing peripheral enhancement pattern with low-density centres, heterogeneous, and homogeneous enhancement. Calcifications may be present within these nodes (35). High-resolution CT is the imaging technique of choice for demonstration early parenchymal disease and early endobronchial spread of disease. Primary tuberculosis typically manifests as air-space consolidation that is dense, homogeneous, and well defined (22). Typical findings in early bronchogenic spread of disease are 2- to 4-mm centrilobular nodules and sharply margined linear branching opacities representing severe bronchiolar impaction, with clubbing of distal bronchioles ("tree-in-bud" appearance) (Fig. 4).

In both primary and postprimary tuberculosis, acute hematogenous dissemination of M. tuberculosis may result in innumerable small tuberculous granulomas in both lungs. This mililiary disease may be visible on CT before it become radiographically apparent (Fig. 9B). At high-resolution CT, a mixture of both sharply and poorly defined, 1- to 4-mm nodules, are seen in a diffuse, random distribution often associated with intra- and interlobular septal thickening (30). On chest X-ray, the classic mililiary pattern consist of innumerable micronodular infiltrates, which are all very similar and diffusely scattered in both lungs, especially the lung apices.
The use of MRI for the evaluation of intrathoracic tuberculous lesions is limited because of technical limitations, as well as the limited availability in countries where tuberculosis is endemic. MRI has been used for the demonstration of intrathoracic lymphadenopathy and pleural effusions (36) (Fig. 10).

Extrapulmonary tuberculosis

Although the predominant form of tuberculosis is pulmonary disease, infection with *M. tuberculosis* may be seen in any organ system. Extrapulmonary tuberculosis mainly results from hematogenous dissemination or lymphogenous spread from a primary, usually a pulmonary, focus. This hematogenous spread may occur years before the onset of progressive tuberculosis, as foci of latent infection may lie dormant before reactivation occurs (37). The precise incidence of extrapulmonary tuberculosis has not been determined, but an increasing incidence has been noted both in developing countries and in developed countries since the mid-1980s (38). Especially in patients infected with HIV an increased prevalence of extrapulmonary tuberculosis has been reported (39).

In these patients multiple extrapulmonary sites are often involved (11). Other factors that have contributed to the increased prevalence of extrapulmonary tuberculosis are the development of drug-resistant strains of *M. tuberculosis*, and aging of the population (11, 40). Finally,
the more widespread use of cross-sectional imaging modalities may also explain why extrapulmonary tuberculosis is more commonly seen.

The most common sites of extrapulmonary tuberculosis consist of lymphatic, genitourinary, bone and joint, and central nervous system involvement followed by peritoneal and other abdominal organ involvement (Fig. 11) (39). Recently, many authors focused on the imaging features of extrapulmonary tuberculosis using cross-sectional imaging methods (11, 27, 41, 42).

**Diagnosis of tuberculosis**

The radiological manifestations of tuberculosis depend largely on whether the host is naïve to the infecting organism, i.e. primary tuberculosis, or whether there has been reactivation or re-exposure, i.e. post-primary tuberculosis. As mentioned previously a broad spectrum of radiographic appearances has been attributed to mycobacterial infections.

Infection with *M. tuberculosis* is indicated by a significant tuberculin skin test. However, the tuberculin skin test is not 100 percent sensitive; therefore, the diagnosis of mycobacterial infection often depends on the detection on the causative organism. Detection of the organism on microscopy provides the most immediate confirmation but requires a relatively high organism load in the tissue or fluid being examined. Detection of *M. tuberculosis* by culture may take up to 6 weeks. A rapid confirmation of the presence, and type, of mycobacterial organisms, with a low organism load, may be achieved using polymerase chain reaction-based assay for mycobacterial DNA (43).

With pulmonary tuberculosis, the use of sputum culture requires a high burden of organisms to confirm diagnosis (44). Identification of infection with a lower burden of organisms may be obtained by other techniques, such as bronchoscopic washings and lung biopsy.

Extrapulmonary tuberculosis, however, produces no pathognomonic imaging signs, and in advanced stages may mimic other disease processes. Although diagnosis depends largely on the clinical context, ultrasound, CT and MRI are valuable tools for early diagnosis and accurate evaluation of extrapulmonary tuberculosis. When a mass lesion is present, fine needle aspiration cytology (FNAC) or biopsy may provide material for histopathological examination, polymerase chain reaction-based assay for mycobacterial DNA and culture. Today, FNAC has become the first-line diagnostic technique that is highly sensitive and specific in endemic areas, where the mere presence of epithelioid cell granuloma indicates tuberculosis until proven otherwise. Furthermore, FNAC provides an easy way for collecting material for bacteriological examination. However, FNAC has several limitations, especially in the absence of demonstrable acid-fast bacilli. The presence of granuloma and/or necrosis in cytology smears could not be regarded as definite, especially in non-endemic areas as they have several other causes. Therefore, the combined use of polymerase chain reaction-based assay for mycobacterial DNA and FNAC has been shown to result in increased sensitivity in FNAC negative, clinically suspicious cases, and as a consequence, results in a reduced need for surgical biopsy (45).

**Conclusion**

The clinical and radiologic features of tuberculosis may mimic those of many pathologic processes. A positive culture, polymerase chain-reaction based assay for mycobacterial DNA or histologic analysis on specimens obtained during bronchoscopic washings for pulmonary lesions and fine needle aspiration cytology or biopsy for mass lesions are still required to reach a firm diagnosis. In the appropriate clinical setting, recognition of the spectrum of imaging features of tuberculosis may guide diagnostic work-up and may result in earlier and adequate treatment.

**References**