

DEFINITIONS

1. **Tuberculosis** is an infectious disease caused by the bacillus **Mycobacterium tuberculosis** (tubercle bacillus). It can affect many parts of the body, but most commonly involves the lungs, when it is known as **pulmonary tuberculosis**.
2. Of a number of strains of tubercle bacillus (usually named after the animals which they most often infect), the **bovine** and **human** strains cause nearly all human tuberculosis.
3. **Primary** tuberculosis is the name given to the disease caused by tubercle bacilli in a subject who has never before been infected.
4. **Post-primary** pulmonary tuberculosis is the name given to the disease which results from reactivation of a healed primary focus following a quiescent period, which may vary from months to many years, or from a further exogenous infection.

CLINICAL MANIFESTATIONS

PRIMARY TUBERCULOSIS

5. This consists of a focus of infection, usually in a lung (the primary focus), together with direct involvement of the lymph nodes which drain the focus of infection. It is termed the **primary complex**.
6. The majority of primary infections do not cause any symptoms and become dormant, without the individual concerned being aware of any problem. Healing occurs in the majority of cases - such healing being by fibrosis, with or without calcification - and the infection becomes quiescent within a period of about 3 years. Calcification, if it occurs, is rarely detectable radiologically until more than a year after the initial infection. The healed focus remains permanently but does not cause any clinical disability, although it may continue to harbour viable tubercle bacilli.
7. Coincident with development of the primary focus, the patient becomes hypersensitive to a protein fraction of the tubercle bacillus. This hypersensitivity can be shown by a positive reaction to a skin test, the **tuberculin test**. The tuberculin test usually becomes positive within 4 to 8 weeks of the initial infection.
8. Bacilli may be disseminated directly from the primary infection via lymphatics and blood vessels, leading to generalised (**miliary**) tuberculosis or tuberculous meningitis. These forms have become rare in Britain, and are seen mainly in Asian and West Indian immigrants. They occur usually within 6 months of the primary infection, most commonly in children under 5 years.
9. In adolescents and young adults, tuberculous pleural effusion may occur, usually within a year of infection. Such effusions often clear without any residual disability, but may be accompanied by overt pulmonary tuberculosis.

10. Extra-pulmonary disease may occur in bones, kidneys or other sites, usually within 3 years of the primary infection.
11. Sometimes, the primary disease may continue to be active and progress directly to post-primary pulmonary tuberculosis.

POST-PRIMARY PULMONARY TUBERCULOSIS

12. This most frequently produces clinically recognisable disease. It is by far the most important type of tuberculosis because of its frequency and, because of the resulting sputum, is the main source of the persistence of infection in the community. It may occur from reactivation of a quiescent primary focus or from exogenous re-infection.
13. Post-primary pulmonary tuberculosis may, as stated at Paragraph 11 above, progress directly from a primary focus (this being particularly likely if the primary infection occurs after puberty). More commonly, it develops insidiously after a period of dormancy, which may vary from a few months to many years, due to **reactivation of the original primary focus**. It is held that, in the majority of patients, the primary lesion results in such considerable enhancement of the patient's defences as to prevent the development of disease if there is later introduction of further tubercle bacilli.
14. In economically advanced communities **exogenous reinfection** is probably uncommon. However, in less developed areas of the world, which have a high incidence of tuberculosis; it appears to be a major cause of post-primary disease. Recent clinical studies suggest that the relative contribution of exogenous reinfection increases in parallel with the incidence of the disease in a community. Analysis and comparison of "fingerprints" from various strains of tubercle bacilli have suggested that up to a third of cases of active TB in United States inner-city communities are due to recent reinfection.
15. The earliest symptoms of post-primary TB are likely to be malaise, weight loss and pyrexia. Cough is common but may have been present for years as a "smoker's cough" or "bronchitis". Haemoptysis (blood-stained sputum) may be a feature. Reactivation usually occurs in the upper lobes of the lungs, and extensive caseous necrosis occurs in the lesions, with the development of cavitation. The patient is then highly infectious. Destruction of lung tissue and fibrosis occurring during healing will cause permanent loss of pulmonary function.
16. Dissemination of bacilli to regional lymph nodes and more distant organs is uncommon in post-primary disease, but there may be direct spread to other parts of the lungs and to the larynx.
17. Not uncommonly, cases are discovered in the early stages by routine chest X-ray.

AETIOLOGY

18. Primary tuberculosis is caused by the tubercle bacillus. The bacillus has no natural reservoir other than infected persons, from whom it is transmitted in the respiratory secretions. In order to give rise to a primary focus the bacillus has to reach the lung alveoli. The mode of spread is by very fine particles, called droplet nuclei, suspended in the air and inhaled. Coughing, sneezing and spitting are especially liable to transmit infected droplets into the air. The disease is not spread by direct contact, and spread in milk from infected cattle is now rare.
19. Factors which influence the development of the disease once the bacillus has gained entry are:-
 - 19.1. The size of the infecting dose.
 - 19.2. The virulence of the particular bacilli.
 - 19.3. The defences of the individual or the “**resistance complex**”, which may be affected by:-
 - 19.3.1. **Genetic** differences.
 - 19.3.2. **Physiological** differences, including the effects of age, sex and pregnancy. Unmarried elderly males are a high risk group for reactivation of infection in Great Britain at the present time.
 - 19.3.2. **Environmental influences**, including nutrition, occupation and living conditions; in most instances more than one of these factors is relevant. Poor hygiene and overcrowding may lead to greater spread of tuberculous infection; the inhabitants of lodging houses, prisons and mental institutions have a relatively high prevalence of TB. The disease is commoner among health service workers, especially medical laboratory staff, due to an increased risk of exposure to the bacillus.
 - 19.3.3. **Immigration**. In the United Kingdom immigrants from Asia have particularly high TB notification rates. Rates are highest in those who have recently arrived in the UK.
 - 19.3.4. **Toxic influences**, including the effects of alcohol and tobacco, which produce lowered resistance. TB is common in alcoholics, contributory factors probably being malnutrition and poor social circumstances.
 - 19.3.5. **Immunological effects**. Reactivation of tuberculosis may occur in patients receiving corticosteroid or other immunosuppressant drugs for the treatment of disease. Artificial immunity induced by BCG vaccination has a protective effect, as does a previous primary infection.

19.3.6. **The Acquired Immuno-Deficiency Syndrome (AIDS).** At the present time the most potent risk factor for TB patients is co-infection with the human immunodeficiency virus (HIV), which suppresses cellular immunity. The risk of developing TB is several times higher among HIV-positive than among HIV-negative hosts.

19.3.7. **The presence of other diseases.** A variety of other diseases favour the development of TB. These are type 1 diabetes mellitus, silicosis, lymphoma, leukaemia and other malignant neoplasms, haemophilia, and renal failure and haemodialysis. The debilitating effect of procedures such as gastrectomy also predisposes.

20. The mechanism by which latent infection (from a healed primary focus) may be reactivated is not completely understood, but is generally held to result from waning of the individual's defences, which may occur at any time in life. Factors which affect those defences have been listed at Paragraph 19 above.

CONCLUSION

21. Pulmonary tuberculosis results from infection of the lung by the tubercle bacillus. This produces primary tuberculosis which may settle and become dormant, or which may progress to become overt post-primary tuberculosis. The latter may also arise after a lengthy period of quiescence following primary tuberculosis, or less commonly from a fresh infection with the bacillus. Factors which influence both initial infection and recrudescence have been listed.

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