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Review on Mycobacterium Tuberculosis

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Review Article

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ABSTRACT

Tuberculosis is a bacterial infection, which is the dominant cause of death all over the world. It is the chronic infectious disease caused by the tubercle bacillus. It is regarded as oldest disease. Tuberculosis is the infection occurs by inhaling the droplet nuclei containing Mycobacterium tuberculosis organisms by susceptible person. New methods have been evolved in diagnosing, treatment and prevention.

INTRODUCTION

Tuberculosis (TB) is known to be recorded as one of the oldest form of human disease. Accordingly it's known to be the major reason for mortality of nearly two million people each year [1-3]. In spite of the effective treatment strategies, the disease still remains to be the major cause of death among the different curable infectious diseases [4-8]. TB could be seen through different instances like it can affect the bones, the nervous system or many other organ systems, but basically it's characterized as pulmonary disease which occurs due to accumulation of *Mycobacterium tuberculosis* (MTB) onto the lungs alveolar surfaces [1]. *Mycobacterium tuberculosis* is a constrained pathogenic bacterial species which belong to the family of mycobacteriaceae first discovered by Robert Koch in 1882 [9-13]. It is the chronic infectious disease caused by the tubercle bacillus [14-18]. It can form acid stable complexes made up of peptidoglycan. It mainly infects the lungs of humans. There are many methods to diagnose the tuberculosis among them tuberculin skin test, acid-fast stain, and chest radiographs are commonly used to detect the mycobacterium pathogen [19-22].

EVOLUTION

MTB complexes are mainly evolved from Africa [23,24]. This group includes a number of members like *Mycobacterium africanum*, *Mycobacterium bovis* (Dassie's bacillus), *Mycobacterium caprae*, *Mycobacterium microti*, *Mycobacterium mungi*, *Mycobacterium orygis*, and *Mycobacterium pinnipedii* [25-28]. Another set of *Mycobacterium canettii* which includes *Mycobacterium prototuberculosis* are smooth colony forming species which form recombinations with other species. *Mycobacterium canettii* appears to be the acenstor of MTB [28-31]. There are evidences that proof that MTB have co-evolved, migrated and expanded along with the human host to the different strains which are geographically defined to a particular region [32,33]. Mycobacterium tuberculosis is the pathogenic agent in the humans. Mycobacterium bovis is the pathogenic agent in the animals like cows and rarely in humans [34-37].

PATHOPHYSIOLOGY

MTB are non-motile, rod shaped bacterial of nearly 2-4 micro meters in length and 0.2-0.5 micro meters in width, so have a resemblance to Actinomycetes. Many non-pathogenic mycobacterium's are a part of the normal flora in humans [38].

MTB are obligating aerobic in nature which is the sole reason they are usually found on the well aerated upper lobes of the alveolar surfaces [38].

MTB is not classified as a Gram negative or Gram positive bacteria because of a particular characteristic exhibited by its cell wall [39-42]. It poses a waxy coating on its cell surface which is due to the presence of mycolic acid, which makes it insensitive to Gram staining [43-45]. As it is not able to withstand any of the Bacteriological strains, Ziehl-Neelsen staining is used instead [46].

MTB is a facultative intracellular parasite and has low generation time of about 15-20 hours which aids to its virulence factor [38]. There are many new diagnostic tests are evolved to detect the antibody and antigen at low cost at very much flexible to adopt in laboratories in the developing countries to detect the Growth of Mycobacterium tuberculosis

CLINICAL MANIFESTATION

Pulmonary TB is considered to be the most severe and phthisis disease because it leads to wasting and coughing of the blood at different stages of the disease [47-50]. Tb can also be caused at different areas in the human body like the pot disease or spinal TB (it causes spinal deformities and fewer bone defects), cervical TB, urogenital track, digestive track etc. these are all categorised as Extra-pulmonary TB (EPTB) [51-54]. The incidence of EPTB disease varies with country and also according to the origin of the particular individuals. In a study it was found that out of the 20000 cases registered for TB in US, 20% was cases were reported as EPTB cases. On the other hand nearly 2-5% of cases of the 2 million cases were registered as EPTB cases [55]. Yet in another study proved that carried out in England it was found that 20% of the cases with European origin had EPTB in lymph nodes, bones and joints etc [56-59], while in those individuals with their origin from Indian continents constituted nearly 45% of the total cases [60]. In modern times, the TB infection is spread mainly through respiratory routs because milk is being pasteurised by everyone nowadays at least in all developed countries. A small note about the types of TB is given below [61]:

- Skeletal TB (termed Pott's disease): Possible Symptoms are spinal pain and back stiffness, at times paralysis is possible
- TB meningitis: headaches (variable in length but persistent), mental changes, coma
- TB arthritis: usually pain in a single joint (hips and knees most common)
- Genitourinary TB: dysuria, flank pain, increased frequency, masses or lumps (granulomas)
- Gastrointestinal TB: difficulty swallowing, nonhealing ulcers, abdominal pain, malabsorption, diarrhea (may be bloody)
- Miliary TB: many small nodules widespread in organs that resemble millet seeds (hence its name)
- Pleural TB: empyema and pleural effusions
- MDR TB: patients infected with TB bacteria that are resistant to multiple drugs
- XDR TB: patients infected with TB bacteria that are resistant to some of the most effective anti-TB medications; XDR stands for extensively drug resistant.

DISEASE STAGES

As discussed in the earlier section most of the TB infection is pulmonary. This could be because of the use of the use of pasteurized milk in the modern times. In record to the studies carried out in 1978, 85% of the registered TB cases are diagnosed to be pulmonary [62]. Since mostly all the cases of TB follows a general pattern, it was divided into four different stages by Wallgren

Stage 1: This stage is dated to be after 3-8 weeks of the inhaled MTB infected aerosol which becomes implanted on the alveoli surface [63-66]. This occurs when the bacteria dissimilates from the lymphatic circulation system to regional lymph nodes which leads to the formation of the Ghon-complex. This aids to the conversion of tuberculin reactivity [67-70].

Stage 2: During this stage the hematogenesis of bacteria to different organs and also different areas of the lungs occurs [71-73]. During this time some acute or fatal diseases like tuberculosis meningitis or military tuberculosis occurs to some individuals. This stage nearly lasts for a period of about 3 months [74,75].

Stage 3: The identification of this stage is characterized by the onset of Pleurisy or inflammation of the pleural surfaces along with severe chest pains [76-79]. These stage last for a period of about 3-7 months but can also be

prolonged to about 2 years. The inflammation is thought to be due to the dissipation of bacteria to the pleural surfaces from subpleural areas [80-83]. These free circulating bacteria interact with the sensitized CD4 T lymphocytes, thus leading to its proliferation and release of inflammatory cytokines [84].

Stage 4: The last stage is the liquefaction of the primary complex which is accompanied with the slow development of the extra pulmonary lesions like those on bones and joints [85-88].

In most cases the individuals infected with the TB do not exhibit disease progression. This indicates that normally an individual infected with TB will have MTB in the body but the immune system of the individual keeps the bacteria under control by the production macrophages against these bacteria [38].

TREATMENT

Mycobacterium tuberculosis has developed resistance over the drugs hence drug resistance has become a serious problem around the world [89-92]. The effective treatment regime for TB must contain multiple drugs to which the organism is susceptible to this is because using a single particular drug for its treatment may lead to the development of drug resistant bacterial populations [93-96]. Using two or more drugs simultaneously will help each other in order to counter the problem of resistance towards a particular drug [97-100]. During the initial stages of TB it is difficult to select the particular drug to which the patients isolate would be susceptible [101-104]. This selection criterion is important because improperly selected drug would subsequently lead to the development of additional drug resistant organism [38].

The antibiotics commonly used for TB treatment include isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) or streptomycin (SM) [105-108]. The course of the drug therapy normally last for at least 6-9 months [109-112]. It is important to take the medication as per the guidance of the instructor and also complete the full course of the medication. This helps in totally removing the types of TB which are drug resistant [113].

PREVENTION

BCG (*Bacillus of Calmette and Guerin*) is the commonly available vaccine for tuberculosis till date [114-117]. It consists of live attenuated strains being derived from *Mycobacterium bovis* which were supposed to be among the avirulent strains for about 60 years [38]. The vaccine was developed in 1921 and remains to be the effective prevention vaccines yet available for TB [117-120].

But the vaccines is only partially effective because it only provides a moderate protection against the paediatric TB and totally unreliable against adult pulmonary TB [121-124]. BCG is normally not administered to HIV-infected newborn's because it can cause fatal disseminated infection in immunosuppressed patients [125]. Administration of the BCG vaccine at times can cause a positive tuberculin skin test; this indicates the successful take of the immunization [126-129]. Depending on the persons age the long term persistence of tuberculin positivity varies [130-133]. Earlier the vaccine is administered less durable would be the skin test positivity [134-137]. Since this induced positivity decreases the possibility to diagnose new infections it is mostly not used in United States [138].

In support with an international venture, a range of vaccines which capable of replacing BCG with primary immunogens and also as boosters for BCG are being studied thus aiding in development of nearly 30 vaccines [139-142]. Among these 30, 12 vaccines have entered clinical trial [113,143-146]. In a research on polyantigenic inactivated whole-cell vaccine was tested on HIV-infected adults who had previously received BCG immunization showed 39% of efficacy for prevention against tuberculosis in phase 3 trails [147-150].

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