Tuberculosis: A Brief Overview and Recent Advancements in Clinical Treatment

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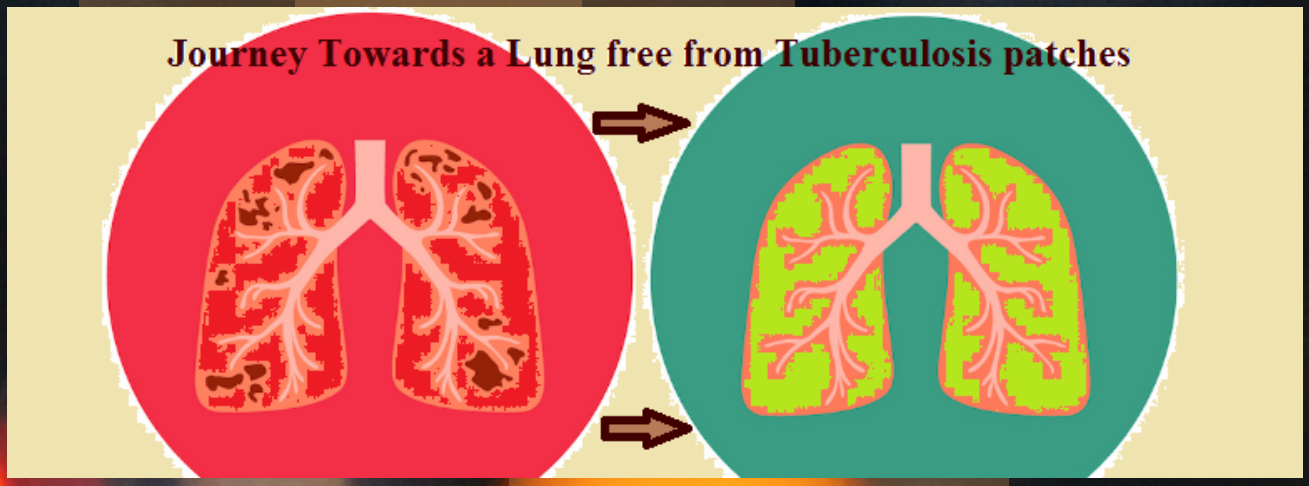

Brief overview about TB infection:

Tuberculosis, which is also popularly called as TB, is one of the most ancient diseases that has stayed and co-evolved continuously with the human beings, with the earliest record being more than 17000 years old**[1, 2]**.TB is caused by the bacterium named *Mycobacterium tuberculosis*. Broadly, TB can be categorized into two different classes: (a) active disease and (b) latent infection. The most common form of active TB is pulmonary TB, but it can manifest in other organs as well, and those instances are termed as "*extra pulmonary TB*"**[3]**. Depending on the degree of infection, a person with active pulmonary TB disease may exhibit the symptoms like chest pain, cough, phlegm, weight loss, weakness, fever, chills and sweating at night; and the active patients are prone to spreading the disease by coughing the infectious particles into the air. An aggressive form of active TB is known as *miliary TB*, which may take place if TB bacteria find their way into the bloodstream. In this rare form, the bacteria quickly spread all over the body in tiny nodules and affect multiple organs, leading to the fatality of the concerned patient**[4]**.

On the other hand, the patients with latent TB do not develop the overt disease, and in many of the cases, even the chest x-ray images may appear to be normal. One proven and effective way to detect latent TB is to look for the reaction to the tuberculin skin test (TST) or interferon-gamma release assay (IGRA). However, the latent TB infection in asymptomatic individuals may escalate to the active disease at any time during their lives due to a compromised immune system arising from other illnesses such as HIV or special medications (e.g. the medication following organ transplants to prevent organ rejection)**[5, 6]**. To curb this TB escalation, the United States devised a preventive therapy for latent TB infection.

Vaccination for TB has always been inadequate, as only one vaccine (Bacille Calmette-Guérin (BCG) TB vaccine) developed way back in 1921 is available for treating the disease. The vaccine usually administered to the infants of the at-risk populations. In some of the advanced countries, like the United States, BCG vaccine is not generally recommended as variable effectiveness of the vaccine has been found against adult pulmonary TB, and there is a chance of the vaccine's potential interference with TST reactivity**[7]**.

The emergence of drug-resistant tuberculosis (DR-TB)

With the advances in the mainstream medical sciences, the number of reported tuberculosis patients experienced a decline. Further, the ability to treat some forms of TB effectively with drugs led to the collective perception amongst the general population, as well as, the medical community that TB is no longer a disease of morbidity and mortality. However, the recent discovery of multidrug-resistant tuberculosis (MDR-TB) in the US-American centres for the HIV patients, as well as, in a few other countries that regularly sees a large influx of migrants with TB syndromes, highlights the importance of continued research and innovation towards curbing the TB outbreak**[6]**. The World Health Organization (WHO) data shows that about 10 million people were infected with TB in 2017, and about 1.6 million succumbed to the disease. Data-based evidence brought forth 558,000 new cases with TB infection that exhibited resistance to the most effective first-line antibiotic. Among the patients with drug-resistant TB, about 82% were resistant to multiple antibiotics**[8]**. Therefore, we should get rid of the sense of complacency and large-scale research should be directed towards the innovation of an effective drug, as well as, an advanced treatment regimen.

Treatment Regimen for TB and Recurrence of Infection:

The prevalent treatment regimen for the infected people is quite lengthy with tuberculosis symptoms lasting for a duration of six months to a year, and sometimes even more for the drug-resistant TB variants**[9]**. Relapse of TB for people undergoing treatment is also very common, as many of the patients fail to stick with the daily schedule of medications that typically comprises of multiple pills**[9]**. Recurrence of TB infection may arise due to multiple reasons. Data show that the trends and signatures are also specific to the geographical locations in this context. For example, in the United States and Canada, most of the recurrent tuberculosis cases were found to be a relapse of the original infection, presumably because of the insufficient treatment; whereas, in a study done in the TB-prone city of Cape Town in South Africa, 18 % of the 612 participants exhibited tuberculosis reinfection and 14 % of those patients were infected again with a different strain of TB following a successful treatment**[9]**.

Latest Advancements in the Research:

Recently, in a clinical trial conducted on the 3,330 participants living in active tuberculosis disease centres in Kenya, South Africa, and Zambia, doses of the Glaxo SmithKline inoculation called M72/AS01E was administered. The vaccine trial was found to have a 50 % efficacy rate. However, William Schaffner, an infectious disease specialist and a professor of preventive medicine and health policy affiliated with the Vanderbilt University School of Medicine in Nashville, Tennessee mentioned that the scaling up of such research activities is required, and the vaccine will not be available to the public for at least a decade or so**[10]**. In another major effort in 2019, a team of researchers at RCSI (Royal College of Surgeons in Ireland), funded by the Health Research Board (HRB) and the Royal City of Dublin Hospital Trust, claimed to have developed small, safe-for-consumption particles packed with all trans-retinoic acid (atRA), a derivative of Vitamin A, so that they can be used in an inhaler. Upon being inhaled by a patient, the atRA-loaded particles would reduce the load of TB bacteria in the lungs and improve the patient's immune system leading to an increased chance of recovery**[8]**. In a further advanced study at the University of Michigan, Artificial Intelligence (AI) is being used to create a software tool to enable prediction of suitable combinations of pharmaceutical drugs, from the pool of both likely, as well as, unlikely candidates, to facilitate more effective treatments without requiring exhaustive clinical trials that are typically time-consuming**[11]**.

Looking at these recent advancements, it would be reasonable to conclude that along with malaria, HIV, and universal flu vaccine, an effective TB vaccine is going to be a major discovery and such a breakthrough innovation could prevent many serious illnesses and reduce the mortality that is owed to the insufficient medical intervention.

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