Eliminating Tuberculosis

Rishendra Verma

DID TB appear first in humans or animals, or did it appear in humans and animals both simultaneously or did TB appear first in humans in India and later in animals in the context of mention of TB in ancient India? In contrast to the earlier hypothesis that tuberculosis first emerged in humans and it was subsequently transmitted to animals, recent studies suggest that the common ancestor of the *M. tuberculosis* complex emerged from its progenitor perhaps 40,000 years ago in East Africa.

Some 10,000-20,000 years later, two independent clades evolved, one resulting into *M. tuberculosis* lineages in human while the other spread from humans to animals resulting in the diversification of its host spectrum and formation of *M. bovis*. This adaptation to animal hosts probably coincided with the domestication of livestock approximately 13,000 years ago.

Recent comparative genomic analyses show that animal Mycobacterium Tuberculosis Complex (MTBC) strains nest within the genetically more diverse human MTBC strains. These results not only contradict the hypothesis of an animal origin for human MTBC but also promote an alternative scenario for a human origin of animal MTBC.

However, little is known about MTBC diversity in domestic animals, and even less about MTBC diversity in wildlife, including our phylogenetically closest relatives, the great apes. There is a hypothesis hinting at co-evolution between humans and certain MTBC lineages. Humans differ in their genetic susceptibility to TB, and the genetic diversity in MTBC is also increasingly recognised as a factor influencing the outcome of TB infection and disease.

Cattle is the principal reservoir of *M. bovis* and hence it is known as bovine tuberculosis**.** There are a number of wild animals who act as reservoirs. Cattle also act as a reservoir of the tubercle bacillus.

In India, *M. tuberculosis* and *M. bovis* have been reported from humans and animals and sometimes from both. *M. tuberculosis* is primarily a human pathogen and does not cause progressive disease in animals. However, *M. bovis*, the principal pathogen of cattle, has been isolated also from several other domestic and wildlife species including goat, sheep, dog, cat, horse, camelids, wild boar, red deer, fallow deer, badger, bison, brushtail possum and many others including humans.

Badger, UK

Possum, New Zealand

Tailed Deer, USA

TB in India

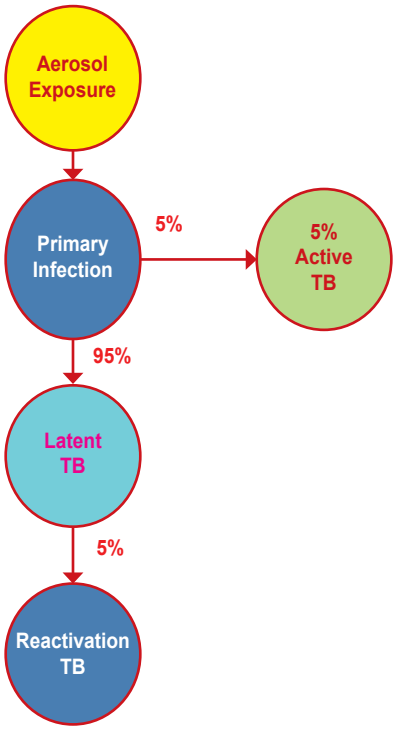
At the beginning of the 19th century, it was generally believed that there was hardly any TB occurring in India. However, by the middle of the 19th century, TB was reported in some districts particularly among the English troops, and it was often found in some areas "among natives as well", such as in the district of Madras. It was also believed that TB in India was of "an extremely pernicious type".

However, TB is now considered to be a global priority. As per the *Global TB Report 2017*, the estimated incidence of TB in India was approximately 28,00,000 accounting for about a quarter of the world's TB cases. As per the report, 10 million people had TB in 2018, while 26,90,000 people had TB in India, out of which 19,90,000 were notified.

According to the report, TB kills 1.5 million every year and is the leading killer of people living with HIV/AIDS and a major cause of deaths due to anti-microbial resistance. When a person with infectious TB coughs or sneezes, droplet nuclei containing *M. tuberculosis* are expelled into the air. If another person inhales the air containing these droplet nuclei, he or she may become infected.

However, not everyone infected with TB bacteria becomes sick. Two TB-related conditions exist: latent TB infection and TB disease. Persons with latent TB infection are not infectious and cannot spread TB infection. Overall, without treatment, about 5 to 10% of infected persons will spread TB disease at some time in their lives to others.

TB: NATURAL EVOLUTION



The economic burden of TB is extremely high. Between 2006 and 2014, TB cost the Indian economy a massive USD 340 billion. [http://www.tbfacts.org/tbindia/#sthash.kuL1UPY7.dpuf]. *M. bovis* infection in several countries inflicts annual losses to agriculture of $ 3 billion.

The major risk factors for tuberculosis include human immunodeficiency virus infection, diabetes, malnutrition, smoking, alcohol abuse, poverty, and overcrowding.

According to the *India TB Report 2019*, in 2018, in India was able to majority of the TB burden is among the working-age group; 89% of TB cases come from the age group of 15-69 years. About 2/3rd of the TB cases are males. Uttar Pradesh, with 17% of the population of the country, is the largest contributor to the TB cases with about 4.2 lakh cases.

The Prime Minister of India has reiterated the target for ending TB by 2025. Union Health and Family Welfare Ministry has launched the National Strategic Plan (NSP) for Tuberculosis (TB) Elimination (2017-2025). The NSP (2017-2025) is based on DETECT-TREAT-PREVENT-BUILD approach. This approach focuses on early diagnosis followed by the prompt treatment which is backed by proper financial and nutritional support.

Prevention strategies such as active case finding, Latent TB Infection (LTBI) management in the high-risk population, contact tracing and airborne infection control are adopted. NSP has great potential because of the latest discoveries of drugs and regimes.

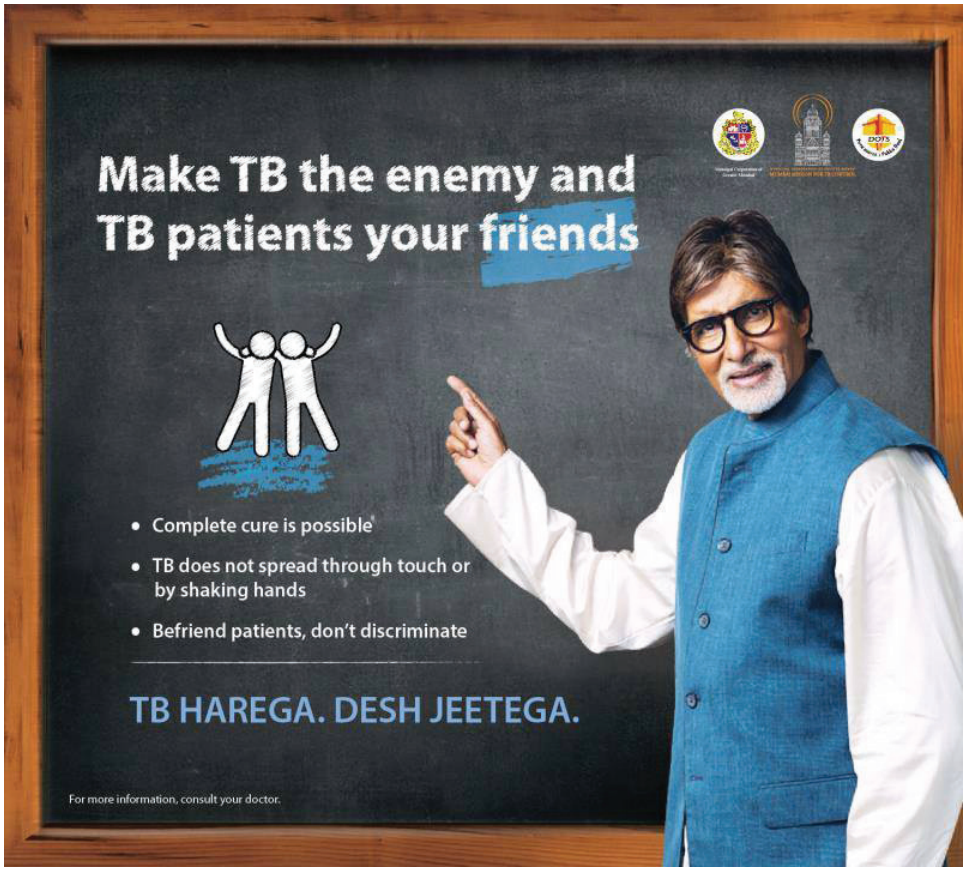
For a successful TB elimination programme, we need to take lessons from the Polio Campaign which was a huge success because the major stakeholders such as hospitals, government, NGOs, social workers and many more came together to make India Polio-free. A holistic approach was adopted in the eradication of the disease. The same needs to be done in the case of TB.

The world has pledged to end the Tuberculosis (TB) epidemic by 2030. The important question, therefore, is why a higher decline in global TB incidence is not happening now. Two key multi-component actions need to happen on the ground. First, every person who develops active TB (approximately 10 million each year) must be diagnosed and effectively treated as quickly as possible and also the transmission of *Mycobacterium tuberculosis* (Mtb) be prevented. Second, every person latently infected with Mtb and at risk of reactivation (Houben and Dodd, 2016) needs to be identified and treated to prevent progression to active disease.

The recent Lancet Commission outlines the two main strategies for achieving the ambitious UNHLM targets and ending TB by 2030: scaling-up proven interventions and investing in new products, such as point-of-care diagnostics, shorter treatment/prevention regimens, and a more effective TB vaccine. Empirical evidence from the recent proof-of-concept study in Vietnam (Marks et al., 2019), together with historical evidence from the period of TB elimination in high-income countries, suggests that intensive active case finding alone may be sufficient to end TB if sustained for a sufficient period and accompanied by concrete measures to address TB

social determinants and health system failures.

In May 2012, India declared TB to be a notifiable disease. This was done with the aim of improving the collection of patient care information. It meant that in future all private doctors, caregivers and clinics treating a TB patient had to report every case of TB to the government. But TB in animals is not notifiable in India.



The National Strategic Plan (NSP 2012–2017) period included mandatory notification of all TB cases, integration of the program with the general health services (National Health Mission), national drug resistance surveillance, etc. The NSP for TB elimination made provision of digital X-ray preferably with Computer-Aided Diagnosis (CAD), teleradiology services across the health sector, Universal Drug Susceptibility Testing (DST) to at least Rifampicin for all diagnosed TB patients through the offer of Cartridge-based nucleic acid amplification test (CBNAAT), a sentinel surveillance system in the country, the establishment of two additional National Reference Laboratories (NRLs) (West and North-East), National TB Policy and TB Bill, National TB Elimination Board (apex body to facilitate policy development, implementation, etc.), Nutritional support to TB patients and families, financial incentives to patients and providers, health system strengthening, and linking patients with existing social and financial support systems of the government, etc.

India is one of the twenty countries listed by WHO with the highest estimated numbers of incident Multi-Drug Resistant-TB (MDR-TB) cases. India accounts for a quarter of the global TB burden with an estimated 27 lakh new cases in 2018. Under the Revised National Tuberculosis Control Programme (RNTCP), 14.4 crore vulnerable people were screened, resulting in reporting of additional 49,733 cases. The efforts to improve diagnostics has led to a 52 per cent increase in drug-resistant TB detection, along with decentralization of Drug-resistant Treatment Centres (DR-TB) centres from 197 to 509 in the past year. The largest-ever National Drug Resistance Survey in the world for 13 anti-TB drugs has been completed and it has indicated about 6.2 per cent prevalence of drug-resistant TB in India among all TB patients.

Vaccination

The BCG vaccine strain named after scientist Bacillus Calmette Guerín was developed from *M. bovis* in 1921. A BCG Vaccine Production Center in Guindy, Madras was set up in 1948. In India, as per the vaccination policy BCG is recommended to be given at an early age preferably before the end of the first year after birth (childhood) as a part of Universal Immunization Programme (UIP). Currently, there is no vaccine against adult pulmonary TB. There is no vaccine for bovine or animal tuberculosis. BCG vaccine is also not administered into bovine or animals.

Social Awareness

TB is an international problem. Although preventable and curable, erratic treatment dose or untimely detection of TB in humans leads to problems. Raising awareness about TB, what it is, and how to prevent its spread can help lower tuberculosis rates around the globe. Eradicating tuberculosis infection would require setting up an organized system for recognizing the infection, treating it, and reducing transmission from person to person. "TB Mukt Bharat" (the national "sweep out TB") campaigns need to be massive, repetitive, intensive and persuasive, for case-finding and community commitment at panchayat, district and state level.

Elimination as defined by the WHO means that there should be less than one case of TB for a population of a million people. In view of the current TB burden in India, a lot needs to be done if elimination is to be achieved by 2025.

Prof. (Dr) Rishendra Verma is ICAR-Emeritus Professor, ICAR-Indian Veterinary Research Institute, Izatnagar-243122 (UP). Email: rishendra_verma@yahoo.com