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Review

Zoonotic tuberculosis: A review of epidemiology, clinical presentation, prevention and control

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The current increasing incidence of tuberculosis in humans, particularly in immunocompromised persons, has given a renewed interest in the zoonotic importance of *Mycobacterium bovis*, especially in developing countries. The roles of meat and milk, the commonest source of protein to man, in the transmission of the disease remain significant. Due to the grave consequences of *M. bovis* infection on animal and human health, it is necessary to introduce rigorous control measures to reduce the risk of the disease in human and animal populations. The institution of proper food hygiene practices and stronger intersectoral collaboration between the medical and veterinary professions is vital to the control of the disease.

Key words: Tuberculosis, *Mycobacterium bovis*, cattle, human, developing countries, control.

INTRODUCTION

The link between animal and human tuberculosis has long always been known to be strong, as shown by the works of Villemin in 1865 (Davies, 2006) and Koch in 1882 (Calmette, 1923), which demonstrated the cross-adaptability of the tubercle bacilli from one species to another to cause disease; pointing out the danger that tuberculosis could be transmitted from animals to humans (Davies, 2006). This was corroborated in 1902 by Ravenel (1902), who demonstrated *Mycobacterium bovis* in a child with tuberculous meningitis.

Bovine tuberculosis is becoming increasingly important due to the susceptibility of humans to the disease caused by *M. bovis* (Kleeberg, 1984) and there is increasing evidence that *M. bovis* infections may be much more significant than generally considered (Shitaye et al., 2007). The current increasing incidence of tuberculosis in humans, particularly in immunocompromised persons, has given rise to a renewed interest in the zoonotic importance of *M. bovis*, especially in developing countries (Radostits et al., 2000). The direct correlation between *M. bovis* infection in cattle and the disease in the human population has been well documented in developed countries, whereas scanty information is available from developing countries (Cosivi et al., 1995). This lack of data according to Bolognesi (2007), relates to its perception as an animal disease, with the health problems relating to the HIV/AIDS and human tuberculosis given a greater priority.

Zoonotic tuberculosis is one of the many sequels of the adaptability of *Mycobacterium* species in different hosts. Infection due to *M. bovis,* which is the principal agent of zoonotic tuberculosis, was once a major problem in developed countries but following eradication programmes involving test and slaughter policy and milk pasteurization, the incidence drastically reduced (Caffery, 1994). However, the infection currently poses a major concern in the human population in developing countries, as humans and animals are sharing the same microenvironment and dwelling premises, especially in rural areas (Shitaye et al., 2007) and as seen in nomadic Fulani settlements in Nigeria. It is estimated that approximately

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85% of the cattle population and 82% of the human population of Africa are in areas where bovine tuberculosis surveillance and control activities are often inadequate or unavailable, therefore, many epidemiologic and public health aspects of the infection remain largely unknown (Cosivi et al., 1998). The emergence of drug-resistant strains of *Mycobacterium* species, the rise and synergism of HIV/AIDS infection with tuberculosis, poverty, and neglect of tuberculosis control programmes have further complicated this disease current situation in Africa (WHO, 2002; Ofukwu, 2008).

Reports have shown that tuberculosis is a major health problem with over eight million new cases reported annually in the world and three million deaths (WHO, 1994). A varying portion of pulmonary tuberculosis cases are considered to occur, however, almost all cases of the non-pulmonary type of tuberculosis in humans has been caused due to *M. bovis* infection (Schwabe, 1984). It is noteworthy to quote Collins et al. (1985), “Every 15 s one person dies of tuberculosis in the world”. Even though *M. tuberculosis* may be mainly responsible for this mortality; some are caused by infection with *M. bovis* (Teshome, 1995).

Tuberculosis in cattle is a human health issue. The knowledge about the implication of bovine tuberculosis in the human cases has to be developed and disseminated for effective control. The role of the different commodity chains (milk and meat) has to be evaluated. Wildlife, farm animals, pets, food and milk all pose a potential threat to our health. This therefore called for a review which included literature search in books, journals and the internet to highlight the public health implication of zoonotic tuberculosis.

EPIDEMIOLOGY

Bovine tuberculosis caused by *M. bovis* is another zoonosis in which both natural and anthropogenic movement of animals has influenced the epidemiology (Kruse et al., 2004). In many parts of the world, badgers, brush-tail opossums, wild boars, deer and other wildlife species constitute a wildlife reservoir of the pathogen. Thus, the natural movement of these reservoir animals increases the spread of the disease to domestic animals and thereby, its public health impact.

Transmission of *M. bovis* can occur between animals, from animals to humans and vice versa and rarely, between humans (HPA, 2009). *M. bovis* infection is transmissible from cattle to humans directly by aerogenous route (WHO, 1994) and through direct contact with material contaminated with nose and mouth secretions from an infected herd of cattle (Beals, 2007). Research findings revealed that at risk, individuals are persons in contact with potentially infected animals such as veterinarians, abattoir workers, meat inspectors, autopsy personnel, farmers, milkers, animal keepers (as well as those in the zoo), animal dealers, laboratory personnel and owners of potential tuberculous pets (e.g. monkeys) (O’Donahue et al., 1985; Ofukwu, 2006; Yumi et al., 2007). Indirectly, man acquires the disease from animal sources by ingestion of meat and meat products from slaughtered infected cattle and consumption of unpasteurised infected milk (Cosivi et al., 1998; Radostits et al., 2000; Thoen et al., 2006). Ingestion of unpasteurized contaminated milk products poses a greater risk than ingestion of infected meat products because badly infected carcasses are condemned; parts of carcasses that are processed as meat products are inspected and thoroughly cooked (Konhya et al., 1980). Thorough cooking [170°F (76.7°C) for 30 min] removes virtually all risk of infection (Hubbert and Hagstad, 1991; EUFIC, 2006). People suffering from *M. bovis* tuberculosis can retransmit the infection to cattle; however, this is not common (Kirk, 2003) (Figure 1)

According to Shitaye et al. (2008), the burden of tuberculosis cuts across all age groups of susceptible host. However, various authors (Kirk, 2003; Davies, 2006; Ofukwu, 2006; HPA, 2009) have argued on the age distribution of human tuberculosis caused by *M. bovis.* Kirk (2003), Bikom (2005) and Ofukwu (2006) are of the view that children are most often affected. This was supported by Myers and Steele (1969), who stated in his review that, in the early 20th century in the United States, a significant percentage of tuberculosis in humans, occurred in children and was caused by ingesting dairy products contaminated with *M. bovis*. In contrast, Davies (2006) and HPA (2009) argue that most cases of the disease is in the older age groups and it is likely that infection had occurred sometime, perhaps decades, in the past.

The number of reported cases of human tuberculosis caused by *M. bovis* is very low, but nevertheless, it is worthy of public concern giving the global upsurge in the prevalence of tuberculosis especially in developing countries. From a review of a number of zoonotic tuberculosis studies, published between 1954 and 1970 and carried out in various countries around the world, it was estimated that the proportion of human cases due to *M. bovis* acccounted for 3.1% of all forms of tuberculosis; 2.1% of pulmonary forms and 9.4% of extrapulmonary forms (Gervois et al., 1972; Cosivi et al., 1998). In Latin America, a conservative estimate would be that 2% of the total pulmonary tuberculosis cases and 8% of extrapulmonary tuberculosis cases are caused by *M. bovis* (Cosivi et al., 1998). During the period of 1990 - 2003, in the United Kingdom, an average of 7,000 cases of human tuberculosis were reported per annum and between 0.5 - 1.5% of those cases which were confirmed by culture were caused by *M. bovis*. These cases were found mostly to be either reactivation of old lesions or infections contracted in other countries which lacked aggressive animal control measures (Del la Rua-Domenech, 2006). In this 13-year study, only one case of

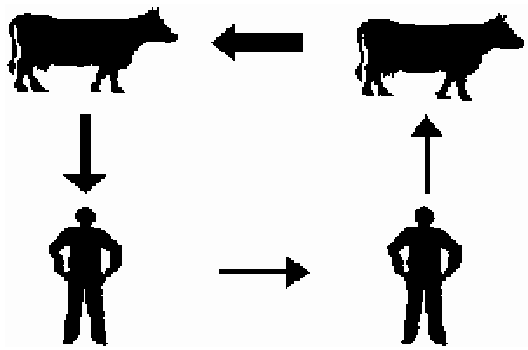

Figure 1. Cycle of *M. bovis* transmission between cattle and humans. The thickness of the arrows suggests level of probability (Grange and Collins, 1987).

human *M. bovis* was determined to be acquired from an animal source in the United Kingdom (Del la Rua-Domenech, 2006). Also, in the United Kingdom, disease in humans from *M. bovis* has occurred in no more than 25 cases a year for the last 5 years (Davies, 2006).

According to Cosivi et al. (1998), preliminary studies conducted in Africa indicate that a proportion (approximately 5 - 7%) of human tuberculosis cases is caused by *M. bovis.* A study in Egypt revealed that nine of twenty randomly selected patients with tuberculous peritonitis were infected with *M. bovis,* and the remaining with *M. tuberculosis* (Nafeh et al., 1992). In Tanzania, 10.5% of people with stomach or lymph gland tuberculosis were infected with *M. bovis* (Bolognesi, 2007). Also, in Tanzania, the proportion of extrapulmonary tuberculosis among all forms of tuberculosis stands at nearly 16% (WHO, 2006). In Zaire (Congo Democratic Republic), *M. bovis* was isolated from gastric secretions in two of five patients with pulmonary tuberculosis (Mphosy et al., 1983), with the prevalence of the disease in local cattle determined to be approximately 8% by tuberculin testing and isolation of *M. bovis* (Cosivi et al., 1998). In Ethiopia, *M. bovis* was found to be a cause for tuberculous lymphadenitis in 17.1% of 29 human tuberculosis cases (Kidane et al., 2002). Also in Ethiopia, Shitaye et al. (2007) reported that 16.7% of 42 human isolates were identified as *M. bovis.* These findings show that the role of *M. bovis* in causing human tuberculosis seemed to be significantly important.

In a study in Nigeria, it was reported that one of the ten mycobacteria isolated from sputum-positive cultures was *M. bovis* (Idrisu et al., 1977). Also, in Nigeria, zoonotic tuberculosis due to *M. bovis* is said to account for 5% of all cases of tuberculosis in humans and up to 3% of cases in children less than 5 years of age (Ofukwu, 2006). Alhaji (1976) found the presence of *M. bovis* in the sputum of market milk (“nono”) sellers in Zaria. Kolo (1991) in his study at the Ahmadu Bello University Teaching Hospital, Zaria, revealed that out of 300 samples of urine, pus, peritoneal and pleural fluid, bone marrow and lymph nodes collected from patients, 75% of the isolates were *M. tuberculosis* while 3% was *M. bovis*. A reported case in 1999 of tuberculosis of the sternum caused by *M. bovis* in a 3-year old Nigerian (Fadiran et al., 1999) supported the earlier findings of other authors. More recently, Abubakar et al. (2005) in his work showed that there is a high prevalence of both bovine and human tuberculosis amongst herders in the Federal Capital Territory, Abuja. Ofukwu (2006) in his study covering hospitals in Benue State reported that 2.4% of 124 samples of pus, urine and sputum collected from patients were characterised as *M. bovis* while *M. tuberculosis* accounted for 82.3%. Another study by Ofukwu et al. (2008) revealed the presence of *M. bovis* in samples of milk (*‘nono’*) collected from a market in Makurdi, Benue State. These findings evoke serious public health concern taking into consideration the large proportion of the Nigerian population exposed to beef, milk and their products. There is every likelihood that many out there are infected with *M. bovis.*

The existing eating culture (eating of raw meat and drinking of raw milk), the very common close contact of animals with humans (most common in rural areas), inadequate meat inspection and the prevailing low standard of hygienic practices are potential risk factors that favours the spreading of zoonotic tuberculosis (Shitaye et al., 2007). Development and spread of multidrug resistant strains and increased immigrant population from infected area to free zone or communities have been reported to increase the risk of infection (WHO, 1992).

People with HIV/AIDS, other forms of immmuno-suppression and debilitating disorders such as chronic renal disease, cancer, diabetes, etc are reported to be at risk of being infected on exposure to tuberculosis (Harries, 1990; Hamburg and Frieden, 1994). If the apparent difference in virulence of *M. bovis* and *M. tuberculosis* in humans is the result of differences in responsiveness of the host defense mechanisms, HIV-induced immunosuppression could well lower host defences leading to overt disease after infection (Cosivi et al., 1998). In France (Dupon et al., 1992), the USA (Dankner, 1993) and England (Daborn et al., 1993), there have been reported cases of HIV related human tuberculosis due to *M. bovis.* This lends credence to the fact that the possibility that HIV infection may lead to a perpetuating cycle of tuberculosis transmission from animal-to-animal, human-to-human and human-to-animal and therefore requires careful consideration.

CLINICAL PRESENTATION

It is not clear whether progression from infection to overt disease occurs readily with *M. bovis* as in the case of *M. tuberculosis* (Bikom, 2005). Epidemiological studies indicate that people infected by *M. bovis* are less likely to develop post-primary disease later in life than those infected by *M. tuberculosis*, but it is not clear whether this is the result of differences in the predominant route of infection or to differences in host susceptibility (WHO, 1994).

The human form of *M. bovis* infection has similar clinical forms as that caused by *M. tuberculosis* (Kirk, 2003; Ofukwu, 2006; HPA, 2009). As with human infection by *M. tuberculosis,* access of *M. bovis* to the tissues is followed by an initial macrophage response that is not, however, sufficient to prevent proliferation of the microorganism. Most contemporary studies (Myers and Steele, 1969; WHO, 1994; Cosivi et al., 1998; Kirk, 2003) agree that the most common clinical manifestation of *M. bovis* infection in man is associated with the extra-pulmonary form of the disease, but about half the cases of post-primary (reactivation) disease involve the lung and this raises the possibility of human-to-human transmission of tuberculosis due to *M. bovis* (WHO, 1994). Following ingestion of the organism, the primary infection in the intestine may heal, it may progress in the intestines, or it may disseminate to other organs (Grange and Collins, 1987).

Cervical lymphadenopathy (which primarily affects the tonsilar and pre-auricular lymph nodes), intestinal lesions, chronic skin tuberculosis (lupus vulgaris), and other non-pulmonary forms are particularly common (Cosivi et al., 1998). Bolognesi (2007) reported that young children infected with *M. bovis* typically have abdominal infections and older patients suffer from swollen and sometimes ulcerated lymph glands in the neck. Pulmonary disease is more common in people with reactivated infections (Shitaye et al., 2006) and this would occur only when some of the animals had active tuberculosis (Beals, 2007). The symptoms may include fever, cough, chest pain, cavitation and hemoptysis (Shitaye et al., 2006). The pulmonary form of tuberculosis occurs less frequently and is usually occupationally related (Kirk, 2003). Farm workers, zookeepers, veterinarians, slaughterhouse workers, and laboratory personnel may be in contact with infected animals or their tissues in situations that produce aerosols of organisms. People in these occupations may develop pulmonary tuberculosis from *M. bovis* and in turn put other humans and susceptible animals at risk (Kleeberg, 1984; Dankner et al., 1993).

PREVENTION AND CONTROL

The basic strategies required for control and elimination of bovine tuberculosis are well known and well defined. However, because of financial constraints, scarcity of trained professionals, lack of political will, as well as the underestimation of the importance of zoonotic tuberculosis in both the animal and public health sectors by national governments and donor agencies, control measures are not applied or are applied inadequately in most developing countries (Cosivi et al., 1998).

M. bovis is resistant to pyrazinamide, which is widely used in the treatment of infections caused by *M. tuberculosis* Complex in humans (Krauss et al., 2003). Cattle should not be treated at all and as such farm animals with tuberculosis must be slaughtered (culled) (Krauss et al., 2003; CFSPH, 2007). This is because the risk of shedding the organisms, hazards to humans and potential for drug resistance make treatment controversial.

In order to reduce the risk associated with consumption of contaminated milk and meat, it is necessary that specific hygiene rules for food of animal origin be laid down to prevent infected animals from entering the food chain. Meat inspection system should be strengthened and designed to prevent the consumption of contaminated products by people. All animals entering the food chain should be subjected to ante-mortem and post-mortem inspection. The tuberculin test is valuable in the control of zoonotic tuberculosis because early recognition of preclinical infection in animals intended for food production and early removal of infected animals from the herd eliminates a future source of infection for other animals and for humans. In the case of cattle, a tuberculin test should be performed in the course of the twelve months prior to presentation for slaughter (FSAI, 2008). Milk should be pasteurized or effectively treated with heat prior to human consumption or further processing, as this is the generally agreed critical and effective control measure to prevent transmission of zoonotic tuberculosis through milk (FSAI, 2008). The tuberculosis bacteria are killed when meat is cooked and when milk is pasteurized, hence these products are safe to eat in the unlikely event that products inadvertently gained access to the food chain (Figure 2).

There should be an increased enlightenment of at-risk individuals and the public on the possible risks of *M. bovis* infection in man. Farmers and other occupationally at-risk individuals should be required to adopt appropriate measures to minimise exposure of employees and farm visitors to infections that can be transmitted to humans from animals (HPA, 2009). Efforts should continue in the control or elimination of tuberculosis in cattle and other animals used for food production as this may be expected to reduce or eliminate the ultimate source of *M. bovis* infection. The test-and-slaughter policy, which is the mainstay of bovine tuberculosis control programme in any given country, can be modified to accommodate a step-wise basis involving segregation and phased slaughter of reactor animals (WHO, 1994). This will make control of tuberculosis in cattle more practicable, especially in developing countries. Also, the role of wild fauna in the epidemiology of tuberculosis in livestock and humans need not be ignored, as they have been reported to serve as a reservoir of the pathogen (CFSPH, 2007). Animal husbandry practices should be improved upon to reduce contact between domestic livestock and wild ruminants especially during grazing.

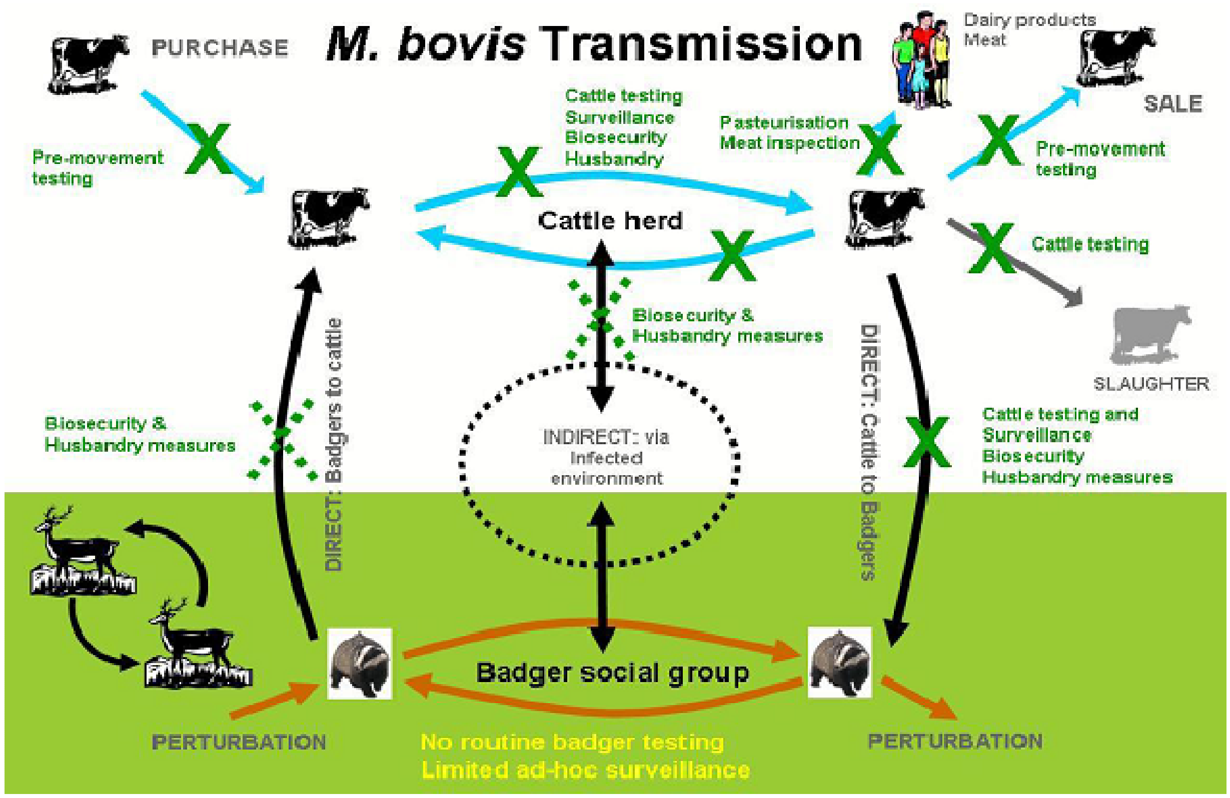

Figure 2. Bovine TB transmission routes and available control measures. Note: The solid crosses indicate those areas where current controls are likely to be highly effective in mitigating against that route of transmission of *M. bovis*. The dotted crosses indicate those routes of transmission where current measures are likely to be less effective. Source: Anon (2008) Badgers and Bovine TB: Government response to the EFRA Select Committee's Tenth Report of 2007 - 2008.

In view of the recent increasing health problems due to tuberculosis in the population at large, the world over; there is the need to promote intersectoral cooperation between medical, public health, veterinary, agricultural, environmental, food safety, nature conservation, anthropological, and many other related sectors in the fight against tuberculosis in humans and animals, particularly in Africa (WHO, 1994). This helps and simplifies the designing of feasible control programme against bovine tuberculosis infection and to minimize zoonotic threat of tuberculosis. The medical and veterinary professionals have traditionally focused respectively on the improvement of human and animal health and production as their primary objectives. This compartmentalisation of the roles of medical and veterinary sectors is undesirable for effective control of zoonotic tuberculosis, especially in developing countries where the burden of the disease is highest. Bovine tuberculosis being a zoonotic disease, has a direct impact on public health and livestock production and therefore should be a point of convergence for the two sectors for an effective management and control of the disease. The effect of this non-collaboration is most pronounced in the developing countries, where the scarcity of fund and inadequate external financial aids have also affected the control of zoonoses.

In Nigeria, efforts are being made to control and eradicate all forms of tuberculosis. More tuberculosis diagnostic centres are being established to afford people access to effective treatment. However, the public health significance of *M. bovis* infection is yet to receive appropriate attention. Inadequate control programmes for tuberculosis in animal does exist just as poor food hygiene practices. For instance, rather than institute the cattle test and slaughter policy and compensate affected farmers to eliminate the disease at source, the medical sector would continue with the management of human tuberculosis cases while the veterinary sector would concentrate on meat inspection and condemnation of infected carcasses. This development has hampered the efforts towards lowering the present high burden of tuberculosis in human population in the country. Human tuberculosis caused by *M. bovis* and *M. tuberculosis* often present similar clinical pictures, but can require different treatment. However, few hospitals have the diagnostic capacity to distinguish between them. These may lead to underestimation of *M. bovis* tuberculosis cases in humans in Nigeria and other developing countries.

On the international scene, several fora and institutions have stressed on the need to prevent and control tuberculosis in both humans and animals. The Food and Agricultural Organisation (FAO), World Organisation for Animal Health (OIE) and the World Health Organisation (WHO) are some of these institutions and they have jointly or individually formed platforms to combat the disease. Surveillance programmes by these institutions are presently going on, especially in developing countries and they share and verify information generated, all geared towards the eradication of tuberculosis.

CONCLUSION

Animal and human health is inextricably interwoven and food animals, especially cattle serve as a reservoir of diseases of public health importance (Cadmus et al., 2008). The safety of food of animal origin with regard to infection by *M. bovis* is worth giving consideration, taking into cognizance the current tuberculosis crisis ravaging the world. Though animals with tuberculosis pose some risk to humans, this risk is extremely remote in developed countries due to introduction of milk pasteurisation and effective bovine tuberculosis control programmes (Shitaye et al., 2006).

In contrast, spread from animals to humans in developing countries remains a very real danger, mostly from infected milk. This seems to be a danger, which is being entirely ignored (Davies, 2006). The animal and public health consequences of *M. bovis* are grave. Disease surveillance programmes in animals and humans should be considered a priority, especially in areas where risk factors are present. Other recommendations made by the WHO (1994) in its memorandum on zoonotic tuberculosis include: Training of personnel at all levels of control programmes and the urgent need for further research on the diagnosis and control, immunological, epidemiological and socioeconomic aspects of the disease. International cooperation in all aspects of zoonotic tuberculosis remains essential in the fight against this disease.

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