TB in Zoo Elephants and the Transmission of Infection into Zookeepers due to Extended Proximity during COVID-19 Pandemic

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Tuberculosis in captive Asian elephants has been a subject of interest among the experts and practitioners for the past few decades. During COVID -19 pandemic, the zoos remained closed and the caregivers had to spend extended hours in the enclosures to help the elephants get rid of boredom and depression. Such proximity enhanced the chance of TB transmission from elephants to human bodies. Hence, effective measures are needed for early detection of TB infection in captive elephants to curb further transmission.

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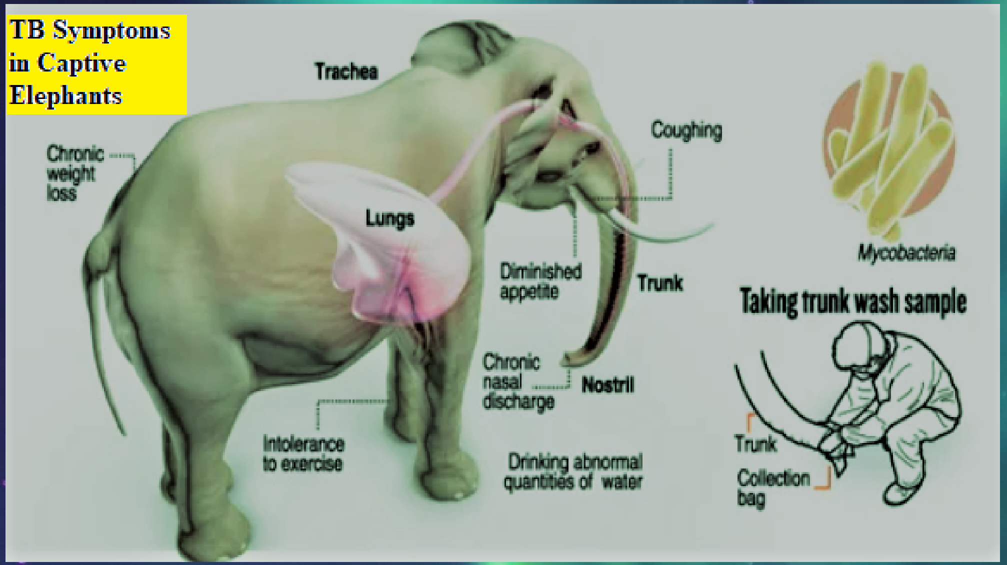

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Introduction

Tuberculosis (TB) caused by *Mycobacterium tuberculosis,*and similar organisms (e.g., *M. bovis*, *M. pinnipedii etc.*) has been observed in a wide range of species encompassing non-human primates, elephants, several wild ungulates (e.g., wild boar, red deer etc.), carnivores, marine mammals (e.g., the sea-lions and the seals) and psittacine birds (especially, the parrot family) [1-5]. The extent of infection and the intra-species transmission from one individual to another depend on the population dynamics, as well as, on several geographical and climatological factors [2]. The infection can even get transmitted from one species to another (especially, in case of the wild ungulates) based on the foraging patterns. Experts and practitioners associated with the TB have mentioned that principally '*Animal TB*' is caused by the archetypical zoonotic pathogen named *M. bovis,* which can be transmitted from animals to the human bodies and *vice versa* [6, 7].

From a conceptual perspective, mere discovery of TB in wild animals in any particular environment is not sufficient to conclude whether the affected group (or species) is a self-sustaining maintenance host or a dead-end spill-over host. Moreover, based on the basic findings it is often difficult to label those groups of wild individuals as significant source of TB infection for livestock, companion animals or humans. Such distinction is critical for the development of strategies to curb the large-scale spreading of the dangerous zoonotic infection [6].

Inclusion of wildlife disease management as an integrated part of the TB eradication programme is a complicated process, as ethical perspectives of the stakeholders and the level of engagement are directly linked with the identification of beneficiaries of the programme. These aspects lead to a certain level of difficulty in continued surveillance and systematic study of the wild species (or populations) for possible tuberculosis infection. However, representative studies conducted on the livestock, as well as the specimens living in the menageries can unearth important information about the transmission of tuberculosis infection from the captive animals to the human bodies and vice versa.

TB in Captive Animals and the Need for Adaptive Diagnostic Tools

It is important to mention that the pathogenesis of tuberculosis bacteria, the receptivity and immune responses to the infection are found to vary widely in the captive wild species living in the zoos. The variation is even more prominent when the comparisons are made between the zoo species and the domestic animals. The diagnostic tools usually used for the domestic animals tend to show limited performance for the zoo species. This necessitates the development of customized, adaptive diagnostic tools for detection of tuberculosis infection in different species [8]. Recently, diagnostic tools based on the investigation of humoral immunity have paved a promising way towards detecting antibodies directed against certain immunogenic mycobacterial antigens in various zoo species [8].

The tuberculosis in the captive elephants (Elephant TB) has emerged as a serious infectious zoonotic disease in the past few decades [9, 10].Three elephants succumbed to the pulmonary complications caused by M. tuberculosis in an exotic animal farm located in Illinois (USA) between 1994 and 1996. In October 1996, a fourth living elephant tested culture-positive for M. tuberculosis [11]. A Swedish zoo witnessed an outbreak of TB during 2001-2003, that involved five elephants and several other species viz. giraffes, rhinoceroses, and buffaloes. Four different strains of M. tuberculosis could be separated from those infected animals [9]. Studies indicate that about 3% of captive elephants in the United States were infected with M. tuberculosis in 2000 [12, 13]. More recent estimates by Mikota indicate that the infected elephants may account for ~ 6% of the total captive elephant population housed in various US zoos [14]. It is also noteworthy that amongst the captive elephants in the zoos and the circuses, the Asian elephants (*Elephas maximus*) are more frequently detected to be infected with TB, as compared to the African elephants (*Loxodonta africana*) [14].

Elephant TB: Diagnosis, Monitoring of Treatment and Limitations

Following the untimely deaths of several high-profile captive elephants in the United States in the mid-1990s, veterinarians discovered that those animals were infected with the human strain of tuberculosis (TB) [15]. Although awareness about the TB infection in captive elephants has been gradually increasing over the past few decades, unfortunately anti-tuberculosis therapy for these animals has not been standardized yet. Currently, the most reliable diagnostic method for TB in captive elephants in the USA is based on the culture of respiratory secretions obtained by washing trunks [12]. However, the trunk wash culture method has serious limitations, as it does not facilitate rapid identification of infected individuals. Therefore, innovative and more efficient diagnostic methods are needed for early diagnosis. Early diagnosis results in timely initiation of chemotherapy leading to more effective control of TB. Although the key mycobacterial antigens responsible for elephant TB are yet to be understood completely and the optimal immunoassay formats are still not established, serological methodology has shown ample promise as a diagnostic tool towards characterizing the humoral responses associated with elephant TB [14]. In quite a few cases, *anti-tubercular* therapeutic doses based on the humoral responses have resulted in gradual decrease in the antibody levels to certain antigens, which hint at the possibility that the serological methodology can be effectively used for monitoring the treatment.

Usually, treatment of active TB in captive elephants involves administering combinations of Isoniazid (INH), Rifampin (RIF), and/or Pyrazinamide (PZA) orally or rectally, daily or every 48 hours for 6 months. Reported indicative daily drug dose limits are 2.5 -7.5 mg/kg for INH, 8 -10 mg/kg for RIF, and 25- 35 mg/kg for PZA. Moreover, for treating multidrug-resistant (MDR) TB, a combination of PZA, ethambutol (EMB), enrofloxacin (ENRO), and amikacin (AMK) is also used. The dosage and the duration of treatment vary from one elephant to another [14]. The preventive therapy usually continues for 6 months.

Transmission of Elephant TB infection into the Zookeepers: Following the deaths of the captive elephants in the US-based exotic farm in Illinois in the mid-1990s, twenty-two elephant handlers at the farm were screened for tuberculosis (TB) [11]. Eleven of the tested handlers showed positive reactions to purified protein derivative that was introduced through intradermal injection. One handler exhibited smear-negative, culture-positive active TB. Comparison of DNA fingerprint using IS6110 and TBN12 typing further unearthed the fact that the isolates from the four elephants and the handler with active TB belonged to the same strain.

This investigation formally brought forth the evidence of transmission of M. tuberculosis between humans and the elephants [11]. In July 2009,the routine screening conducted among the elephant handlers and caregivers at a non-profit elephant refuge in south central Tennessee, USA exhibited conversion of tuberculin skin test (TST) results from negative to positive. Further, from the records of the facility it was revealed that the trunk wash collected in December 2008 from a quarantined elephant contained M. tuberculosis[16].Results also showed that the susceptibility of the employees to the latent M. tuberculosis increased by more than 20 times upon working for more than 4 hours in the quarantine facility during 2009. A study conducted in 2012 on 600 captive Asian elephants in Kerala, Tamil Nadu and Karnataka exhibited high prevalence of asymptomatic TB infection of elephants in the captive Indian settings [17]. In 2019, eight caregivers dedicated to the pachyderms of Point Defiance Zoo in Tacoma, Washington tested positive for latent TB infection [18]. These observations further stresses on the need for early diagnosis in order to reduce the risk of exposure and subsequent TB transmission to the elephant handlers, other zoo inmates, as well as the visitors.

Impact of COVID-19 on TB Transmission between Captive Elephants and Caregivers

According to Adam Langer, branch chief of surveillance, epidemiology, and outbreak investigations for the CDC, depending on the environmental conditions TB bacteria can remain suspended in the air for several hours. The key deciding factors behind the exposure risk include the concentration of pathogenic load in the air, the duration of exposure, the size, and the ventilation system of the room [15]. Owing to the large lung size of the elephants, a relatively large number of bacteria are released into the surrounding air from the infected individuals during the breathing process. Therefore, sharing air space with a TB-infected elephant poses a higher risk of transmission than the same exposure to an infected person. Therefore, the handlers and caregivers, who spend substantial amount of time with the captive elephants in the indoor environment of the zoo enclosures, are highly susceptible to the TB infections. During the ongoing COVID-19 pandemic, all the zoos and the menageries with exotic collection of wild species have remained closed in order to protect the zoo inmates from the novel coronavirus SARS-COV-2. However, during this period, many captive animals have exhibited symptoms of depression that are owed to the sudden change in their respective lifestyles. Although lesser crowd during the extended lockdown period has helped some species to behave in a more stress-free manner (e.g., the deer, giraffes, kangaroos, lesser carnivores) leading to better health and reproductive behaviours; the species like the elephants that are more attached to the human beings, intelligent and responsive to the visitors, have suffered heavily in terms of the emotional health due to the extended loneliness. In order to ensure emotional wellbeing of the captive elephants, the zookeepers and caregivers have spent extended hours in the enclosures during the lockdown period. This has posed a greater risk for the zookeepers, as they have become more prone to the TB infection from the elephants.

In 2015, the United States Department of Agriculture (USDA) withdrew its policy mandating the TB testing for captive elephants in the USA, which earlier was an integral part of the standard veterinary cares for elephants. Subsequently, it has now been left to the individual facilities (private, public, or non-profit) and veterinarians to decide on the testing. The regulations for the TB testing of the elephants vary in terms of strictness and requirements from one state to another [15].

Clearly, the seriousness of the TB infection is being ignored. The COVID-19 pandemic, and the morbidity associated with it have shown the world the level of price that we have to pay due to our collective negligence. If attention is not immediately paid to the finer details associated with the critical diseases, such as the various forms of TB, it would not take a long time before another catastrophe is witnessed.

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