New research points to elderly as growing contributor to tuberculosis in China

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A major contributor to the number of tuberculosis infections and cases in China will likely be the elderly over the next few decades, requiring a refocus in efforts to control a disease affecting millions of people in the country, according to preliminary new research presented today at the Fourth Global Forum on TB Vaccines in Shanghai. The researchers from the London School of Hygiene & Tropical Medicine found that developing a "post-infection" vaccine could reduce overall TB rates in China by almost a third by 2050.

Globally, 2050 is the target year for eliminating TB as a public health problem. China is acknowledged to have made a great deal of progress in controlling the disease over the last 20 years, but it is still hard hit by the TB epidemic. According to the World Health Organization, China has an estimated 980,000 new cases of TB every year, second only to India, and 41,000 deaths each year result from the infectious, airborne disease. More troublingly, a third of the world's drug-resistant TB cases are found in China.

"We chose to study TB trends in China given the magnitude of the disease burden present and the anticipated increase in the number and proportion of elderly people within the population. We wanted to understand how these factors would affect the attempt to eliminate TB in the country," said Rebecca Claire Harris, an epidemiologist with the London School of Hygiene & Tropical Medicine in the UK, who presented the results.

"This is the first time the possible impact of giving new TB vaccines to older adults has been considered in any setting, and could inform how future clinical trials and vaccine deployment plans are developed," said Harris.

Preliminary study results predict that the elderly (those aged 65 years and above) contribution to TB infection transmission in China may increase from 18 percent to 53 percent, and their burden of TB disease may increase from 13 percent to 71 percent of all new TB cases.

"Our preliminary findings suggest that in China it may be useful to increase TB control efforts for preventing disease in older adults and the elderly, and that development of new TB vaccines aiming to protect this population could have substantial impact," Harris said. "Targeting older adults is a departure from the current thinking in the field, which mostly focuses on developing vaccines for children and adolescents. This also may be different from other parts of the world, such as sub-Saharan Africa, where there is much more disease in young adults."

According to the researchers, a combination of the success in China in bringing down TB transmission and the increasing size of the elderly population are contributors to this expected trend. The population that will be elderly during 2025 to 2050 may have been infected back in the pre-1990 era when transmission was still very high. As they get older, their risk of reactivation of infection increases, so they are more likely to develop disease and contribute to disease figures. Whereas because disease transmission has declined so much in recent years, younger people are now infected in relatively lower numbers, so the number of younger people developing disease will also become lower since most disease in this group is due to recent infection.

The researchers used mathematical models to explore the potential impact of new TB vaccines and found that some types could reduce the

rate of TB in China by up to nearly a third by 2050. An effective vaccine option of those explored for China was found to be one that could be given to older adults, including those who have already been infected by the bacteria that cause TB but who haven't yet developed TB disease. Such a vaccine, if it had 80 percent efficacy, 20 years duration of protection, and covered 70 percent of people aged 55-64 in 2025-27 and then 55 year olds as part of a routine program, could reduce the rate of new TB cases in China by 31 percent by 2050, avoiding up to 3.7 million cases between 2025-50, the results suggest. Even at lower efficacy and coverage, such a vaccine given to older adults could prevent hundreds of thousands of TB cases.

"If our research continues to validate results to date, it would highlight the importance of ensuring TB vaccine trials include these older age groups and that China begins to plan how a vaccine or other interventions to prevent infected people developing TB could be delivered to people of this age group," said Harris. "However, these early results suggest that even the most effective older adult vaccine will need to be part of a wider control package to reach the WHO 2050 TB elimination goal in China."

The global quest for new vaccines

BCG, the nearly 100-year-old existing TB vaccine, works most consistently in infants and is largely ineffective against the most common and contagious form of the disease, that is, TB in the lungs. Decades of widespread use of this vaccine has failed to control the global TB epidemic, leading researchers globally to work on development of new, more effective TB vaccines.

The two nonprofit organizations at the forefront of this vaccine development work, the U.S.-based Aeras and the Netherlands-based TuBerculosis Vaccine Initiative (TBVI), helped organize the

international gathering of TB and TB vaccine experts in Shanghai this week.

"Tuberculosis is a major public health threat, tied with HIV as the leading cause of death globally among infectious diseases, with antibiotic resistance a major treatment challenge, yet we are years behind where we should be in vaccine development due to lack of acknowledgement of the TB health threat and the resultant lack of investment in new tools," said Tom Evans, CEO of Aeras. "One of the reasons the global TB vaccine community is excited to meet in China is the level of commitment we've seen from the authorities here to innovative research, including developing the world's only TB vaccine candidate currently in a Phase 3 trial."

The Phase 3 trial of the Chinese vaccine, called VaccaeTM, is sponsored by Anhui Zhifei Longcom Biologic Pharmacy Co., Ltd. Scientists running the trial of this vaccine, are providing an update on progress at the TB vaccine Forum. According to Aeras, aside from VaccaeTM, there currently are 14 vaccine candidates in various stages of clinical testing, including GSK's M72+AS01E candidate, which is currently in Phase 2b testing at sites in Africa.

"The global clinical trial pipeline for TB vaccines is more robust than ever before, yet at the same time there is still much we need to learn about how TB exactly attacks the body and manages to evade the natural immune response," said Tom Ottenhoff, member of the scientific team of TBVI. "Fortunately, the TB vaccine community has managed to come together at these forums in order to coordinate joint research efforts so that the relatively little funding available for our efforts is used in the most effective manner possible."

TB can affect anyone but often strikes those who live in poverty, have poor nutrition, limited access to healthcare, and live in overcrowded

conditions. In China, out-of-pocket TB treatment costs account for more than half of the average annual household income for the rural poor, according to Aeras. And because each individual with active TB typically infects between 10 and 15 others, entire families and communities are at risk.

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