BIZCOMMUNITY

TB vaccine: WHO expert explains why it's taken 100 years for a scientific breakthrough, and why it's such a big deal

By Charles Shey Wiysonge

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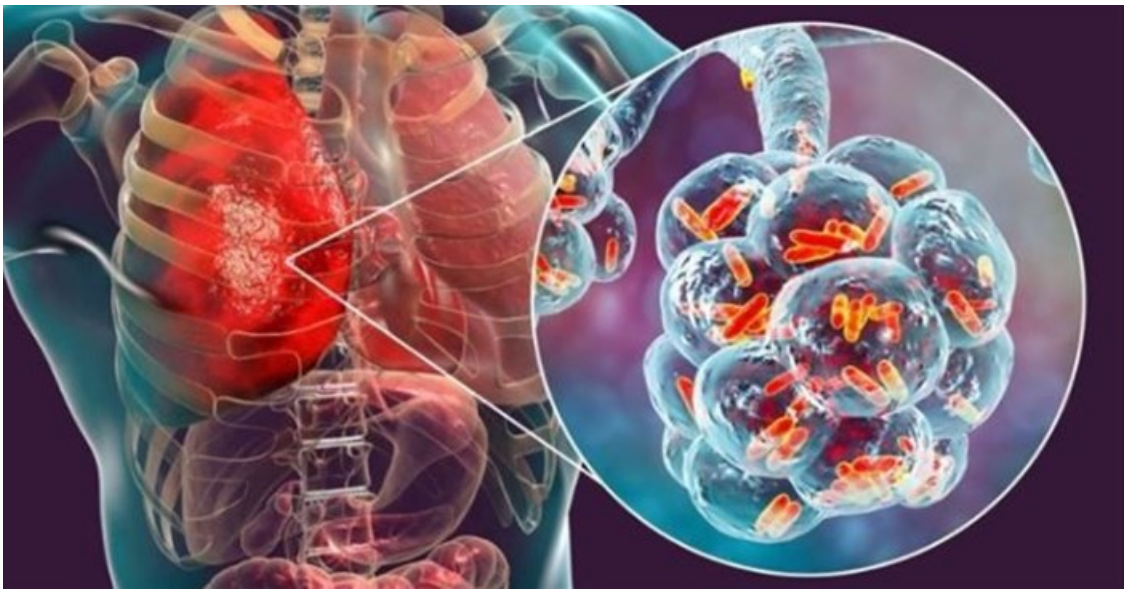
The BCG vaccine for TB has been used for 100 years. It is largely effective for children under five, but less so in older people and can't be used on patients who have certain medical conditions. Today we're the closest we've ever been to discovering a vaccine that might replace or complement it.



Source: Advin Healthcare.

But, why has it taken so long?

We do not yet have a new vaccine for TB. But, for the first time, there are several vaccine candidates that are at advanced stages of clinical development.

Vaccine development usually takes decades and unfolds step by step. Experimental vaccine candidates are created in the laboratory and tested in animals before moving into progressively larger human clinical trials.

Clinical trials are research studies that test an intervention such as a vaccine in human beings and occur in phases, from phase 1 to phase 3. We say vaccines are in clinical development when they reach the clinical trial stage.

- A phase 1 trial is a first-in-human study which recruits a small number of healthy people (usually fewer than 100), to assess whether a candidate vaccine is safe.

- Phase 2 trials are typically conducted among several hundred participants, to assess whether the candidate vaccine produces an immune response.

- For phase 3 trials, thousands of people are enrolled to assess whether the vaccine is efficacious and safe. Phase 3 TB vaccine trials are currently going on in Gabon, Kenya, Russia, South Africa, Tanzania and Uganda.

Even though we are still, at best, three years away from broad regulatory approval of a new TB vaccine, the scientific community can do a lot now to prepare for its use, and to inform the public so that the vaccine may be accepted when it becomes available.

TB vaccines are very challenging to develop. The bacterium that causes the disease is complex, and is proficient at evading the human immune system. We don't yet have a full understanding of how to appropriately target the bacterium or what kind of immune responses are needed to induce immunity. But there are some interesting approaches in the pipeline and there have been some encouraging data from clinical trials that are providing clues.

Why do we need a new TB vaccine?

TB is a global health emergency. About 2 billion people are currently infected with *Mycobacterium tuberculosis*, and of those, 5% to 10% may become ill with TB and will potentially transmit the bacterium.

In 2021, nearly 10.6 million people developed TB disease and 1.6 million died. We urgently need new tools to fight TB, including new and improved vaccines.

The Bacille Calmette-Guérin (BCG) vaccine has saved tens of millions of lives and is effective in children under the age of five in preventing TB deaths and severe forms of the disease.

The vaccine has variable efficacy for protection against pulmonary TB (TB affecting the lungs) in adolescents and adults – and it is pulmonary TB that's responsible for the majority of TB transmission. So new and improved vaccines that are effective in preventing pulmonary TB in adolescents and adults are essential to control TB, and to reduce transmission to all, including newborn babies.

> *"The South African HIV Clinicians Society is meeting in Cape Town this week. Day 1 sees two of our own, @LindaGailBekker and @sheetalkassim, presenting on the advances of HIV treatment and on the latest on the HIV vaccine front.#HIVtreatment #HIVprevention #HIVvaccines pic.twitter.com/QKxJwjRnjq— Desmond Tutu Health Foundation (@DTHF_SA) November 7, 2023"*

TB is the leading cause of death among people living with HIV. People living with HIV have up to 20 times higher risk of developing TB disease compared to those without HIV infection. The current BCG vaccine is not recommended for use in people living with HIV, for safety reasons. Although BCG is a safe vaccine in immunocompetent infants (those whose immune systems are working properly), severe adverse events can occur in HIV-infected infants following vaccination with BCG.

These adverse events include a rare but life threatening condition known as disseminated BCG disease. However, new TB vaccine candidates are being developed and evaluated to offer clinical benefit in people living with HIV.

How effective has the BCG vaccine been?

BCG vaccines are given to more than 100 million children every year worldwide, at birth or soon after. The effectiveness of

BCG can vary depending on several factors, including the prevalence of TB in a given area, the strain of the BCG vaccine used, and the age at which BCG was administered.

Several studies have shown that the effect of the BCG wanes as children approach adolescence. People may become infected with TB but not be aware of it.

What will happen to the BCG vaccine?

The BCG vaccine will not be replaced by another TB vaccine until and unless there is compelling data on the safety and efficacy of an alternative. Most of the current vaccines in advanced stages of clinical trials are tested in adolescents and adults. Their safety and efficacy would need to be proven in newborn infants to be able to replace BCG.

In addition, BCG vaccination has nonspecific beneficial effects on overall mortality and leads to more reductions in child mortality than would be expected by just protecting against tuberculosis. There is thus a great possibility that BCG would remain in use.

What will a new vaccine mean for the fight against TB?

This depends on what the clinical trial data for the new vaccine candidates show. Most importantly, any new vaccine will need to be safe, and it will need to offer clear clinical benefit to populations at risk. We hope that the TB vaccine candidates that are in the pipeline will be effective at reducing TB infection, TB disease and TB transmission and can become part of a combination of tools in the fight against TB.

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