Difäm Health Community (DHC)

DIFÄM
German Institute
for Medical Mission

Podcast: Vaccines against tuberculosis

My name is xxx, I am a member of the health team of the German Institute for Medical Mission, also called Difäm. With me is my colleague, xxx.

Today, we will present you information about vaccines against tuberculosis. Xxx can you explain the most important facts of tuberculosis for us, please?

Tuberculosis, in short TB, is caused by Mycobacterium tuberculosis, and it most often affects the lungs. TB is spread when people with lung-TB cough, sneeze or spit. Bacteria remain in the air, in the so-called aerosol. A person needs to inhale only a few germs to become infected.

TB is currently the world's second leading cause of death from a single infectious agent, after COVID-19. Every year, 10 million people fall ill with TB and 1.5 million people die. TB is the leading cause of death of people with HIV and also a major contributor to resistance to antibiotics.

About one fourth of the world's population is infected with tuberculosis bacteria, of whom around 10% will develop TB disease during their lifetime. The rest have TB infection but are not ill and cannot transmit the disease.[1]

Is that what we call latent TB?

Yes, exactly. When a person becomes infected with TB, the bacteria can remain inactive in the body without causing symptoms. But this infection can develop into TB disease when the immune system is compromised, for example when a person additionally contracts HIV, or develops diabetes or cancer. People with latent TB do not show any signs or symptoms. To identify TB infection, healthcare providers will screen at-risk patients and may use a skin or blood test.

TB seems to be like a time bomb that can but does not have to detonate during the life of an infected person. Which symptoms characterize TB disease?

When an infected person develops TB disease, common symptoms include prolonged cough, fatigue, weight loss, fever and night sweats. These symptoms can be mild for many months, thus leading to delays in seeking care and increasing the risk of spreading TB to others.

If healthcare providers suspect a patient to have TB disease, they will send the patient for a sputum test that looks for TB bacteria, or acid fast bacilli, AFB. In the case of a suspected non-lung TB disease, we can screen the samples of affected body fluids and tissue for the bacteria. WHO recommends

rapid molecular diagnostic tests, like PCR-tests, as initial tests for people showing signs and symptoms of TB. However, in the case that this is not available, we can use other diagnostic tools include sputum smear microscopy, sputum cultures and chest X-rays.

Despite significant advances in reducing mortality in recent decades, TB still causes enormous human suffering, and is a major economic burden all over the world.[2]

So, we would all benefit from a vaccination against tuberculosis?

Yes. However, vaccination has the greatest impact in countries where the incidence of TB is high, as is the case in many low- and middle-Income countries.

What kind of vaccines are on the market against TB?

To date, there is only one licensed vaccine available against TB: the BCG vaccine which stands for the bacteria Bacillus Calmette-Guérin. It was discovered over 100 years ago in 1921 and it has unfortunately only modest benefits. The BCG vaccineprotects young children against TB, but efficacy against pulmonary TB, particularly in adults, varies. It is an attenuated living bacteria vaccine, which uses a strain of the bacteria that causes TB in cows and humans.

Several factors may explain the variable efficacy of BCG. Over many decades, strains of the BCG bacteria were sent to different laboratories worldwide for vaccine production. Over time, the laboratories used different protocols to grow BCG. It may be due to these variable practices in vaccine production that different BCG charges contain bacteria that slightly differ in terms of their genetics.

But there are new hopes for vaccines against TB.

New hopes? That sounds like a positive perspective. Why did it take more than 100 years?

In the past, TB vaccine development was seriously underfunded compared to other infectious diseases. An example: The US government gave 1.5 billion dollars to Moderna for testing and manufacturing its COVID-19 vaccine. This is exceeding the amount of money spent for TB vaccine research in the past 15 years globally.[4]

In addition, vaccine development against the TB bacteria also faces immunological challenges. The bacteria live in the human cells, are very resistant and can evade several mechanisms of the host's immune response. Basically, every component of the body's immune response takes part in fighting a TB infection, but the TB bacteria display "a complex artillery of immune-escaping mechanisms" as one researcher formulated.[1]

Globally, there are now more efforts to understand better the immune response to TB bacteria, and to identify TB antigens. The first Global Ministerial Conference on ending TB took place in 2017 and agreed to take resolute actions and to invest in TB research.[5]

Has this investment already produced fruits in form of new vaccine candidates ?

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[1] De Martino, M, Lodi, L, Galli, L. Chiappini, E : 2019, Immune response to Mycobacterium tuberculosis : A narrative review, in Frontier in Pediatric, 27.08.2019 available at: https://www.frontiersin.org/articles/10.3389/fped.2019.00350/full

The pipeline for vaccine candidates is full with various types of vaccines and various schemes of application: Vaccines for prevention of TB disease in people with latent TB infection, for early life immunization as BCG replacement, as BCG boosters, for vaccination of TB patients after treatment to prevent disease recurrence, or as supplements to drug therapy intended to reduce treatment duration.

Wow, we seem to be working on a completely new array of weapons against TB. How realistic is it that some of them become ready for use in the near future?

Well, over a dozen candidates have completed successfully phase 2 studies and are now prepared for phase 3 trials.[6]

The most promising vaccine candidate seems to be M72 of GlaxoSmithKline. It protected half of more than 3500 HIV-negative adults with latent TB infection against active TB disease after three years of follow-up. This would meet the WHO's expectations that a TB vaccine should demonstrate at least 50% efficacy in preventing confirmed pulmonary TB.

Honestly, 50% efficacy does not sound so much. I am a bit disappointed.

You should not be disappointed. A rough calculation will show you why. In 2021, 10 million people were newly infected with TB. One million of them will go from latent to active TB and 15% or 150.000 people will die. With 50% efficacy, the M72 vaccine would therefore prevent the development of active TB in half a million newly infected people and prevent the death of 75.000 persons. Leave alone all those who have been living with latent TB for years now.

Ok. So, given the huge numbers of people newly infected with TB per year, vaccination efforts would really make sense. What about people living with HIV who are highly susceptible of contracting TB? Is there any vaccine in the pipeline for them?

For M72 more research is needed on the effect in special at risk groups like children and persons living with HIV .[7]

Other vaccine candidates are in the pipeline. One is an inactivated whole cell vaccine. Another one is a recombinant version of the BCG vaccine. It is in late-stage development and also tested against COVID-19. In addition, there are attempts to revaccinate adolescents with BCG.

Despite all those candidates, it will probably take several years before a new and safe vaccine surfaces. Unfortunately, the COVID-19 pandemic has interrupted or delayed clinical trials.[8]

Thank you very much xxx for this interesting information. So, we can hope for new vaccines against TB even though we have to be patient. We hope that you could gain new information from our podcast and invite you to listen to the other audible professional updates on vaccines and vaccination.

Until we hear each other again, be blessed and stay safe.

Internet sources as of 11.08.2022

1 www.who.int/publications/digital/global-tuberculosis-report-2021/

2 www.who.int/news-room/fact-sheets/detail/tuberculosis

3 www.who.int/publications/i/item/who-wer9308-73-96

4 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4950406/

5 https://www.who.int/teams/global-tuberculosis-programme/research-innovation/development-of-a-global-strategy-for-tb-research-and-innovation

6 https://www.treatmentactiongroup.org/resources/pipeline-report/2020-pipeline-report

7 www.who.int/publications/i/item/9789240037021

8 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4950406/