

# Experimental vaccine shows promise against TB meningitis

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A team of Johns Hopkins researchers working with animals has developed a vaccine that prevents the virulent TB bacterium from invading the brain and causing the highly lethal condition TB meningitis, a disease that disproportionately occurs in TB-infected children and in adults with compromised immune system.

A report on the federally funded research is published online June 11 in the journal *PLOS ONE*.

TB [brain](#) infections often cause serious [brain damage](#) and death even when recognized and treated promptly, researchers say. This is so because many drugs currently used to treat resistant [TB strains](#) cannot cross the so-called brain-blood barrier, which stops pathogens from entering the brain, but also keeps most medicines woefully out of the brain's reach.

"Once TB infects the brain, our treatment options have modest effect at best, so preventing [brain infection](#) in the first place is the only fool-proof way to avert neurologic damage and death," said lead investigator Sanjay Jain, M.D., an infectious disease specialist at the Johns Hopkins Children's Center. "Unfortunately, our sole preventive weapon, the traditional BCG [vaccine](#), has a spotty track record in terms of efficacy."

The new Johns Hopkins vaccine, tested in [guinea pigs](#), could eventually add a much-needed weapon to a largely depleted therapeutic and preventive arsenal. TB currently affects nearly 9 million people

worldwide and is growing increasingly resistant to many powerful antibiotics, according to the [World Health Organization](#) (WHO).

The [experimental vaccine](#) works against certain lethal strains of TB that are marked by the presence of a protein known as PknD, which helps the [TB bacterium](#) sneak past the [blood-brain barrier](#). Specifically, PknD makes TB virulent by allowing it to attach to, damage and penetrate the protective cells that line the small blood vessels of the brain and prevent toxins and bugs traversing the blood from invading the organ.

If proven effective in people, the vaccine also could be used to boost the brain-protective effects of the traditional BCG vaccine, the only currently available anti-TB vaccine, the efficacy of which varies greatly, Jain says. In addition, BCG contains live bacteria and therefore cannot be given to immune-compromised people, such as HIV patients, who are at greater risk of developing widespread TB. About one-third of the 34 million HIV-infected people worldwide have TB, according to the WHO.

By contrast, the experimental vaccine is made with PknD protein chunks, which by themselves cannot cause full-blown disease even in people with weakened immune systems.

In their experiments, the Johns Hopkins researchers compared the effectiveness of the new vaccine with the traditional [BCG vaccine](#). Animals were injected with placebo, BCG or the new vaccine and then exposed to airborne TB. The researchers measured TB loads in the lungs and brains of all three groups, as well as in those of non-vaccinated animals.

Animals given either active vaccine had far fewer TB cells in their brains compared with their non-vaccinated or placebo-vaccinated counterparts. Both vaccines were equally effective in preventing invasive TB

infections of the brain and spinal cord, even though the new vaccine fared worse at reducing TB cell loads in the lungs. Notably, animals injected with the new vaccine had TB cell counts in their lungs similar to those of placebo-injected or non-vaccinated animals, yet far fewer TB cells in their brains.

"What this tells us is that even in the presence of full-blown lung infection, the new vaccine somehow blunted TB's ability to infect and damage the brain," said investigator Ciaran Skerry, Ph.D., of the Johns Hopkins Center for Tuberculosis Research.

Animals that got the new vaccine also had higher levels of protective TB-specific antibodies and higher levels of interferons, the cry-for-help chemicals released by virus-infected or bacterium-infected cells that summon the body's immune defenses against pathogens.

To determine whether the new vaccine could also render the TB bacterium less virulent in human cells, the researchers soaked TB bacteria in blood obtained from BCG-vaccinated, non-vaccinated and experimentally vaccinated animals, then mixed the pre-soaked TB bacteria with human endothelial cells that line the small blood vessels of the brain and guard it against invasive pathogens. Bacteria treated with blood from the experimentally vaccinated animals showed far less virulence and were far less capable of damaging the human cells than were the TB bacteria soaked in blood from BCG-vaccinated or non-vaccinated animals.

**More information:** [dx.plos.org/10.1371/journal.pone.0066310](https://doi.org/10.1371/journal.pone.0066310)

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