

# IV Administration of TB Vaccine Appears More Effective

Intravenous administration allowed the marginally effective BCG vaccination to work better in monkeys.

January 10, 2020 By [Liz Highleyman](#)

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Administering a widely used tuberculosis (TB) vaccine intravenously rather than injecting it into the skin may offer a greater level of protection against the life-threatening disease, according to a recent study.

“The effects are amazing,” study coauthor JoAnne Flynn, PhD, of the Center for Vaccine Research at the University of Pittsburgh School of Medicine, said in a [university press release](#). “When we compared the lungs of animals given the vaccine intravenously versus the standard route, we saw a 100,000-fold reduction in bacterial burden. Six of the animals had no tuberculosis bacteria in their bodies, and nine out of 10 animals showed no inflammation in their lungs.”

Tuberculosis is one of the most deadly infectious diseases and the leading cause of death for people with HIV worldwide. The only available TB vaccine uses Bacille Calmette-Guérin (BCG), a live but weakened form of bacteria related to *Mycobacterium tuberculosis*, which causes TB.

This vaccine is given by intradermal injection between the layers of the skin. Although still widely used in countries where TB is common, the vaccine is not particularly effective. While it can protect infants against disseminated TB, it is much less effective at preventing pulmonary TB in adolescents and adults—the type most likely to be fatal.

Researchers from [#NIH](#) and [@PittHealthSci](#) saw dramatic improvement in how well the world’s only tuberculosis vaccine works by simply changing the delivery method and dose. Instead of the usual injection into skin, they gave it to animals intravenously.

<https://t.co/cNaNPXbhto>

— Francis S. Collins (@NIHDirector) [January 2, 2020](#)

Robert Seder, MD, of the National Institute of Allergy and Infectious Diseases Vaccine Research Center, and colleagues compared different doses and routes of BCG vaccine administration—including intradermal, intravenous (IV) and aerosol delivery—in rhesus macaque monkeys.

The researchers hypothesized that administering the vaccine directly into the bloodstream or as a mist into the lungs might lead to stronger protective immune responses than the standard intradermal method. Previous work by Seder's group showed that malaria vaccination is more effective when administered intravenously.

As described in [a recent issue of the journal Nature](#), the study authors found that intravenous administration “profoundly alters the protective outcome” when monkeys were challenged with *M. tuberculosis*.

In the months following immunization, IV administration of a high dose of BCG—about 100 times higher than a standard intradermal dose—led to substantially greater CD4 and CD8 T-cell responses as measured in the blood, spleen, lung fluid, lung lymph nodes and lung tissues.

Six months after vaccination, the monkeys were exposed to virulent TB bacteria introduced directly into their lungs.

The researchers saw that nine of the 10 animals that received a single IV injection of the BCG vaccine were highly protected. Six of them had undetectable infection according to lung imaging, mycobacterial growth assays and pathology analysis. The others had only very low levels of *M. tuberculosis* in their lung tissue.

In contrast, infection rates were significantly higher among unvaccinated monkeys and those that received the vaccine via intradermal injection, aerosol mist or both. All animals that received a standard intradermal dose developed persistent lung inflammation and had only slightly less *M. tuberculosis* bacteria in their lungs than unvaccinated monkeys. Among the 10 monkeys given higher intradermal or aerosol doses, only two showed no signs of infection.

The researchers suggested three immune mechanisms by which IV administration might improve protection, including stronger T-cell responses in lung tissue, better antibody responses and modified macrophages with enhanced capacity to protect against infection, dubbed “trained immunity.”

IV vaccination was generally well tolerated, but the researchers cautioned that more research around safety and the durability of response is needed before this method could be widely

implemented. Safety concerns about injecting a live, albeit weakened, virus into the bloodstream are particularly relevant for people living with HIV who have compromised immune function.

[Click here](#) to read the study.

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