

## **‘POOR’ VACCINE RULED OUT IN TB PUZZLE**

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TB experts have come a step closer to solving one of the great mysteries in global public health: why the BCG vaccine often fails to protect against the disease in developing countries.

BCG is a weakened, live bacterium known as Bacille Calmette-Guerin, a relative of *Mycobacterium tuberculosis*, the organism that causes TB. BCG is supposed to stimulate immune responses that protect against *M. tuberculosis*. Numerous different strains of BCG are used around the world. In trials in developed countries, the vaccine has been shown to protect more than two-thirds of those who receive it.

For years, researchers have puzzled over why BCG fails in developing countries. Some argue that the vaccines used are of poor quality. Others say that children in tropical countries are exposed to numerous other mycobacteria- relatives of both TB and BCG- and that these somehow interfere with the BCG vaccine's ability to stimulate immunity to Tb.

Now, in the biggest vaccine trial ever undertaken in Africa, researchers from the London School of Hygiene and Tropical Medicine and colleagues in Malawi have ruled out the first explanation, and found strong support for the second.

In a trial involving 120 000 children, they found that the strain of BCG vaccine that protects 10 per cent of British children offered absolutely no protection in Malawi against the lung form of TB, which is responsible for most deaths (*The Lancet*, vol 348, p17). This crushes the idea that inferior vaccines are to blame says Paul Fine, who led the trial.

"This result is really interesting," says Mark Carrington, a molecular biologist at the University of Cambridge. "It shows that the vaccine we use in the UK simply does not work there." Now, says Fine, the finger points to the effects of other mycobacteria. Scientists have long speculated that the presence of other mycobacteria - such as *M. avium* and *M. fortuitum* - may block the effect of the BCG vaccine. These mycobacteria are ubiquitous in soil and even tap water, not only in the tropics but also in temperate countries such as Britain. But in hotter, damper climates these bacteria are much more abundant.

Fine says there are several possible ways in which the bacteria could interfere with the vaccine. If a child's immune system has already been exposed to numerous infections with mycobacteria, it may hardly react to BCG because the antigens on the surface of the bacterium are similar to those of the other mycobacteria. As a result, the child's immune system is not primed to respond to *M. tuberculosis*.

Another possibility, says Fine, is that the child's immune responses to other mycobacteria may offer some natural protection against *M. tuberculosis*. This would mean that the vaccine's effect in trials would be masked: since even the unvaccinated children have some protection against TB, the relative difference between vaccinated and unvaccinated children would be smaller than in countries with fewer mycobacteria. *M. Day*