



## FACTSHEET: Tuberculosis Vaccines

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The badger tuberculosis (TB) vaccine has recently been in the news, but how was it produced? This fact sheet explains how it was necessary to use animals to develop and test TB vaccines, as well as ways of administering it to animals without the need for anaesthetic.

### Vaccinating animals

Animals are vaccinated mainly to protect cattle. TB vaccines have been developed for cattle, but these can cause false positives in TB skin tests making it difficult to detect infected animals. It is not possible to vaccinate cattle in the field under EU legislation so research is done using experimentally infected cattle<sup>1</sup>.

The UK government maintains that the vaccination of cattle against bovine TB, used in conjunction with existing TB control measures, could have benefits in reducing the prevalence, incidence and spread of TB in the cattle population. Vaccination could also reduce the severity of a herd infection regardless of whether infection is introduced by wildlife or cattle. There is some evidence to suggest that cattle-to-cattle TB transmission is a greater risk than badger-to-cattle, and that cattle-to-badger infection also occurs. Badgers infected with TB will be debilitated but rarely die. The disease attacks their lungs and kidneys leading to weight loss, a general loss of condition and breathing difficulties. They represent a risk to other wildlife as they become infectious in later stages, shedding live bacteria.

However, badger vaccination could help reduce the prevalence and severity of bovine TB in a badger population, benefitting badgers, cattle and other animals.

### Vaccinating humans

The BCG vaccine was developed using a weakened form of bacterium *Mycobacterium bovis* (cattle TB), which humans can be exposed to through unpasteurised milk. After extensive testing in animals to identify a suitable strain of the bacteria, the vaccine was first given to humans in 1921. Today, the human form of TB is more usually caused by *Mycobacterium tuberculosis*. While very safe, the *M. tuberculosis* vaccine is a relatively ineffective with limited protection against adult forms of the disease. However the disease is almost always fatal if left untreated. The vaccine is now only administered routinely in countries that are highly endemic for TB.

## Developing the vaccines

French physician and bacteriologist Albert Calmette, and his assistant and later colleague, veterinarian Camille Guérin, were working at the Institut Pasteur de Lille in 1908. Their work included subculturing virulent strains of TB and testing different culture media. They noted that a glycerin-bile-potato mixture grew strains that seemed less virulent. They changed the course of their research to see if repeated subculturing would produce a strain that was attenuated enough to be considered for use as a vaccine. The weakened strain was carefully subcultured every three weeks for many years, throughout World War 1, until 1919 when the now avirulent bacteria were unable to cause TB in research animals.

The BCG vaccine is in fact several vaccines, as it became apparent that the subculture Calmette and Guérin distributed to labs around the world were evolving in different ways. It is now produced from samples emanating from 7 sites around the world, each with subtly different molecular and genetic characteristics. Different strains are named after these sites: BCG (Paris), BCG (Copenhagen) etc.

The BCG 'vaccine' has since been tested in brushtail possums<sup>2</sup>, cattle<sup>3</sup> and badgers<sup>4</sup> to determine its ability to prevent infection in some cases, rather than just reducing the severity of symptoms. This research has helped scientists to realise that BCG can be used to prevent infection rather than being limited to restricting the extent of the disease.

Initial tests to determine the safety of the badgerBCG vaccine required collaboration with researchers in the Republic of Ireland where a facility to house badgers under appropriate biological containment was built. This allowed the determination of a suitable dose of the vaccine<sup>5</sup>.

Tests on badgers deliberately infected with TB were used to show that intramuscular administration was safe and as effective as subcutaneous delivery<sup>6</sup>. This has the advantage of being more easily administered, without requiring the use of anaesthesia. Field trials and experimental infection studies were used to demonstrate that the intramuscular BCG vaccination reduces the progression, severity and excretion of *M. bovis* infection in badgers<sup>7</sup>.

Oral vaccines are currently in trials for use in badgers. The formulations used in these trials were developed for possums by researchers in New Zealand<sup>8</sup>.

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