Editorial

BCG: The waning of a vaccine

Over a hundred years ago, Léon Charles Albert Calmette, Director of the Pasteur Institute at Saigon, gave up his post and joined hands with veterinarian and immunologist, Camille Guérin, to begin one of the most fascinating journeys in medicine. For over 11 long years, surviving the ravages of World War I, Guérin and Calmette systematically weakened the bovine TB bacillus by serially culturing it over 230 times. The result of their exertions was the BCG vaccine, which to date has been the only TB vaccine used for mass immunization against a disease that kills over two million people each year.

The BCG vaccine has been regarded as being safe in immunocompetent individuals (there are serious safety concerns in HIV-infected individuals and others with depressed immunity). But the key question that that begs an answer is: does it work? In 1968, an entire district in South India was vaccinated, in a “trial to end all trials.” The results were deeply disappointing: the protection rate in children was a modest 17%, but the efficacy in adults was zero. Large meta-analyses carried out in several parts of the world have been more encouraging. In the year 2000 alone, the vaccine is estimated to have prevented about 30,000 cases of childhood meningitis and 12,000 cases of disseminated TB. Although these figures appear impressive at first sight, consider this: it takes 3400 vaccinations to prevent one case of meningeval TB, and 9300 vaccinations to prevent one case of disseminated TB. Overall, the vaccine seems not to have a success rate over 50%.

Unsurprisingly therefore, countries the world over have evolved their own BCG vaccination policies. For instance, the United Kingdom has a universal BCG vaccination program while the United States, Sweden, the Czech Republic and Slovakia recommend vaccination only in specific high-risk individuals. In Canada, BCG vaccination policies differ between provinces. Countries disagree as to the age at which the BCG should be given (the WHO recommends vaccinating children either at birth, or in young childhood), in the number of doses, and sometimes even as to the methods used for vaccine delivery. Nonetheless, over 90% of the world’s children, and four billion of the 9-billion odd inhabitants on this planet now stand ‘vaccinated’—but not necessarily protected—with a preparation of dubious efficacy.

Modeling studies predict that TB cannot be eliminated without an effective vaccine that encompasses all age groups, and is inclusive of populations living with HIV. As for the lethal multidrug-resistant (MDR-TB) and extensively drug resistant (XDR-TB) forms of TB—where cure is uncertain at best—prevention holds the key. Without a superior vaccine, a TB-free planet by 2050—as envisaged by the WHO—will continue to be a pipe dream.

Finally, the good news: with the mapping of the Mycobacterium-TB genome, several new Mycobacterial targets are on offer. According to Stop-TB Partnership figures, as many as 16 candidate vaccines are now in clinical trials, of which a dozen are undergoing field testing; a new (and hopefully, much more effective vaccine) now seems a matter of time.

In its desperation, the world spends 70–100 million US$ each year in the quest for an effective vaccine against TB: clearly, this is not enough. We have arrived at what must certainly be the defining moment for TB research. With the promise of success so close at hand, it is time to inject more capital into the vaccine of tomorrow.

Today, a nearly century-old vaccine remains the only licensed vaccine against TB. It is time to move on.

References

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