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The BCG world atlas: a new, open-access resource for clinicians and researchers

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TB & the BCG vaccine

While many in the developed world consider TB a disease of the past, it continues to claim millions of lives every year [1]. With over 9 million new cases reported annually, the global incidence of TB is falling at less than 1% per year, and the prospect of TB elimination by 2050 appears to be a difficult goal to reach [1]. There is widespread acknowledgement that TB elimination will be impossible without novel diagnostics, drugs and vaccines.

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TB is an ancient disease with a diverse and complex history. The only licensed vaccine for TB, the BCG vaccine, was first used in humans in 1921, and continues to be widely used today, almost a century later [2]. However, the efficacy of this vaccine is uncertain, with trials producing highly variable efficacy estimates [3]. This uncertainty, coupled with variation in TB burden across the world, has led to the development of a range of different BCG policies and practices. Furthermore, decline in TB incidence rates in the developed world has led many countries to modify BCG policies over the years [4]. Finally, genomic research has shown that BCG vaccine strains have evolved and differ from each other and from the original BCG first used in 1921, adding more confusion to an already complicated situation [5].

To better interpret existing tools, and to develop novel tools, it is important to document and understand current and previous policies and practices. As described in a recent publication in *PLoS Medicine*, the World BCG Atlas was created to serve as a useful resource for clinicians, researchers and public health practitioners to find information on a country's past and present BCG policy [4]. **FIGURE 1** shows the homepage of the Atlas. The website is a free, searchable, online resource that provides information that may be used to make diagnostic decisions on latent TB infection (LTBI), and to decide which populations will benefit from novel diagnostics and vaccines, and to inform and promote future research.

Improving the selection & interpretation of latent TB diagnostics

The tuberculin skin test (TST) continues to be the most widely used diagnostic for LTBI in the world [6]. It has been used for almost a century, and is well studied; however, previous BCG vaccination can complicate the interpretation of the TST and may cause false-positive reactions [7]. While BCG given at birth does not appear to cause false-positive TST reactions, receiving the vaccination later in life (i.e., childhood to adolescence) or multiple times (i.e., booster shots) may lead to more frequent, pronounced and larger TST reactions [7].

Newer LTBI diagnostics, the *in vitro* IFN- γ release assays (IGRAs), are not affected by prior BCG vaccination, and are an attractive alternative in countries

Figure 1. Homepage for The BCG World Atlas.

Taken from [101].

where BCG may have a big impact on accuracy of the TST [8]. Clinicians cannot be expected to know the BCG policies (past and current) for all of their foreign born patients, and adult patients often do not remember their vaccination histories. This is particularly relevant in low TB incidence settings where screening for LTBI is commonly carried out among recent immigrants. The Atlas can help clinicians by providing the BCG history relevant to a particular patient's country, thus allowing the clinician to assess whether TST is an appropriate diagnostic or whether IGRAs may be preferable.

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For example, in Japan, until 2003, BCG vaccination was repeated every year from the ages of 6–13 if the child was TST negative. This policy resulted in a very high prevalence of TST positivity among the Japanese population and IGRAs may therefore be the preferred diagnostic for adults in this setting. Conversely, in India where the absolute number of TB cases is the largest worldwide, BCG vaccination has been administered at birth since 1948, and at no time were booster BCG vaccines recommended. Therefore, TST would be an adequate diagnostic in the Indian population, because the BCG was administered

at birth, and only once. **FIGURE 2** highlights the countries where IGRAs may be more specific than the TST for diagnosing LTBI.

Development of novel TB vaccines

Finding an effective vaccine against TB would be critical for achieving TB elimination [9]. In recent years, substantial efforts have been made to develop novel TB vaccines, and six candidate vaccines are now in human trials [10]. While some are designed to replace the BCG, others are intended to enhance the immunity conferred by the original BCG vaccine using a ‘prime–boost’ strategy. Thus, BCG policies and practices may play a big role in roll-out of successful prime–boost vaccination strategies. When the time comes to introduce a novel vaccine it may be critical to know in what populations the BCG vaccine was given routinely, what strains were used, at what age the vaccine was initially administered, whether boosters were given, how often and so on.

To this end, The BCG World Atlas can be a helpful resource for vaccine developers and TB controllers tackling this issue.

The Atlas also provides helpful information concerning BCG strain type and manufacturers used by each country, including changes that a country may have experienced over time.

Conclusion

Despite nearly a century of use, the BCG vaccine continues to be poorly understood, with highly variable vaccine efficacy and heterogeneous global policies and practices. Within countries, policies have changed substantially over the last 20 years, and these changes can have real impacts on the interpretation of LTBI diagnostics and the introduction of novel vaccines. The World BCG Atlas: A Database of Global BCG Vaccination Policy and Practices provides a free, interactive resource that attempts to supply the researcher, clinician or public health administrator with critical BCG information to aid in diagnosis, vaccine development or to further TB research. Since its launch, the Atlas has been viewed over 26,000 times and continues to get several hits each day. Efforts are underway to improve the Atlas and add newer content.

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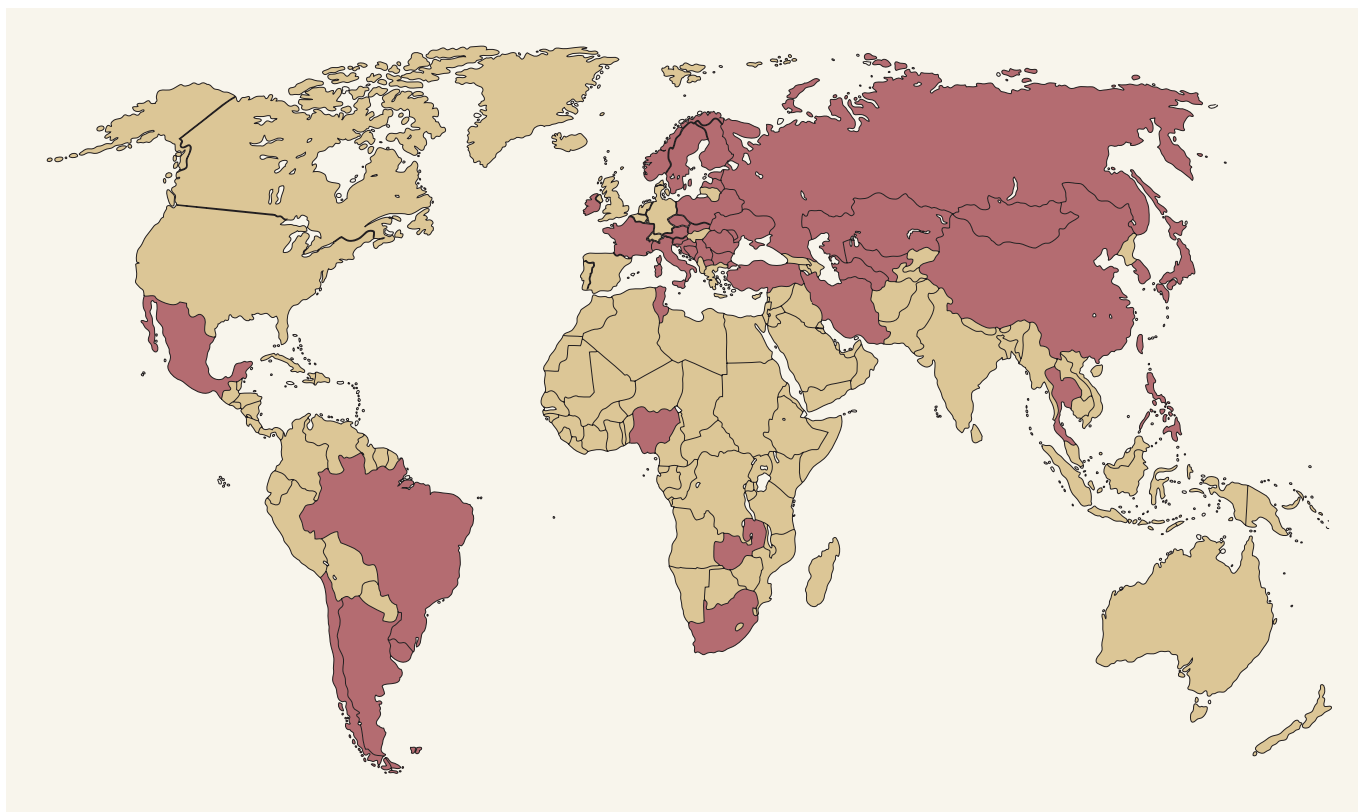


Figure 2. Countries likely to benefit from IFN- γ release assays for latent TB infection diagnosis (shaded).

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Website

- 101 The BCG World Atlas
www.bcgatlas.org

