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Ponto de vista

Care and Precautions for Immunization with Bacillus Calmette-Guérin

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In 1921, French bacteriologists Léon Charles Albert Calmette and Jean-Marie Camille Guérin administered, for the first time in humans, a vaccine capable of preventing tuberculosis (TB), a highly transmissible infectious disease associated with high mortality rates, particularly in socially vulnerable populations. This vaccine, called Bacillus Calmette-Guérin (BCG), was developed from an attenuated strain of *Mycobacterium bovis*, a mycobacterial species known to cause bovine TB [1].

With over a century of use, the BCG vaccine remains widely utilized worldwide for the prevention of severe forms of TB. In Brazil, it is part of the National Immunization Program and is provided by the Unified Health System (Sistema Único de Saúde [SUS]) in multidose vials in a lyophilized form for vaccination of all newborns. After reconstitution with 0.9% saline solution, the vials must be stored refrigerated (2°C to 8°C) and protected from light to maintain stability for up to six hours. The BCG vaccine is

indicated for children under five years of age and is preferably administered within the first hours after birth, as the risk of tuberculous meningitis and miliary TB, severe forms of the disease, is highest in early childhood, while vaccination at older ages does not offer effective immunological protection [1,2].

The BCG vaccine is administered intradermally in the right upper arm (deltoid region), often resulting in a scar up to 1 cm in diameter, referred to as the vaccination scar. The healing process, which may take up to six months, begins with a nodule that evolves into a pustule, followed by the development of an ulcer that gradually heals, leaving a characteristic mark at the injection site. The absence of a vaccination scar, however, does not indicate immunization failure, and revaccination with another BCG dose is unnecessary [2].

Unlike other bacterial vaccines included in the National Immunization Program, such as DTPa, Hib, meningococcal, and pneumococcal vaccines, which are made from inactivated bacterial components, the BCG vaccine contains live attenuated bacilli. Consequently, specific precautions are required during its administration: i) Infants under 2 kg in weight, who should only be vaccinated once they reach 2 kg or more, ensuring sufficient skin tissue for proper vaccine administration; ii) Children in contact with patients with active TB, who can be vaccinated following primary chemoprophylaxis and medical evaluation; iii) For children undergoing high-dose corticosteroid therapy or immunosuppressants for more than two weeks, vaccination is possible three months after treatment ends; iv) For infants born to mothers who used immunomodulators during the last two trimesters of pregnancy, vaccination is recommended from the second semester of life; v) Children with severe skin lesions: who should only be vaccinated after complete healing. The BCG vaccine is definitively contraindicated for children with permanent severe immunodeficiencies and pregnant women [2].

Nonetheless, BCG vaccination can lead to adverse reactions, either local or

systemic, which should always be reported and monitored. Local adverse reactions, known as BCGitis, commonly include subcutaneous abscesses and lymphadenopathy. In rare cases, systemic dissemination of *M. bovis* bacilli can occur, leading to disseminated BCG disease, a potentially fatal condition that affects multiple organs [3]. These adverse reactions may result from factors such as the bacillary load administered, vaccination technique, or the presence of immunodeficiencies disorders. Therefore, vaccination should always be performed by trained healthcare professionals, adhering strictly to the Ministry of Health's guidelines for vaccine preparation, storage, and administration. Proper handling minimizes risks of vaccine inefficacy or exacerbation of adverse reactions. For suspected primary (congenital) or secondary (acquired) immunodeficiencies, a prior diagnostic evaluation before BCG vaccination can prevent cases of BCGitis/disseminated BCG disease, particularly in conditions frequently associated with bacillus dissemination, such as severe combined immunodeficiency, chronic granulomatous disease, and Mendelian susceptibility to mycobacterial disease (MSMD) [1,2,3].

In 2023, Brazil recorded 80,012 new cases of TB, of which 1,248 occurred in children under five years old, including 44 cases of miliary TB or tuberculous meningitis. This age group has exhibited a growing proportion of TB diagnoses, with a 5.4% increase in new cases from 2021 to 2023. Interestingly, this period also coincided with a significant decline in BCG vaccination coverage, influenced by the COVID-19 pandemic. Public hesitation regarding potential exposure to the virus in healthcare settings, combined with the spread of misinformation about vaccines efficacy and safety, are associated with reduced adherence to vaccination. These factors contributed to vaccination coverage during this period falling below the goal established by the Brazilian Ministry of Health of 90% of the population immunized. Therefore, BCG vaccination remains an essential public health strategy in Brazil, playing a crucial role in preventing severe forms of TB

and reducing childhood morbidity and mortality caused by the disease. Ensuring high vaccination coverage underscores its importance in safeguarding this vulnerable population, even with the possibility of adverse reactions in rare situations [4,5].

Despite recent advances in genomic and biotechnological tools, BCG remains the only approved vaccine for TB prevention. There is a pressing need for safer vaccines for infants and children, as well as immunizations offering effective protection for adolescents and adults. Another global goal is the development of a vaccine consistently preventing pulmonary TB, the most prevalent and transmissible form of the disease.

Recently developed strategies include vaccines based on nucleic acids or bacterial vectors, offering greater safety and production efficiency compared to the current whole-organism approach derived from mycobacterial cultures. Innovative approaches also explore the use of nanoparticles, microneedle patches, antivirulence therapies, and phages, paving the way for promising alternatives in TB prevention. These novel approaches hold the potential to improve global TB control and reduce the significant burden of the disease[6].

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Conflicts of interest

The author reports no conflicts of interest.

References

1. Lange C, Aaby P, Behr MA, Donald PR, Kaufmann SH, Netea MG, Mandalakas AM. 100 years of *Mycobacterium bovis* bacille Calmette-Guérin. The Lancet Infectious Diseases. 2022; 22(1): e2-e12. Doi: https://doi.org/10.1016/S1473-3099(21)00403-5

2. Ministério da Saúde. Secretaria de Vigilância em Saúde e Ambiente. Departamento do Programa Nacional de Imunizações. Manual de normas e procedimentos para vacinação [versão eletrônica]. 2. ed. rev. Brasília: Ministério da Saúde, 2024. 294 p.

https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/guias-e-manuais/2024/manual-de-normas-e-procedimentos-para-vacinacao.pdf/view. Accessed December 07, 2024.

3. Kourime M, Akpalu ENK, Ouair H, Jeddane L, Benhsaien I, Ailal F, Bousfiha AA. Bécégites de l'enfant: diagnostic, classification et exploration. Archives de Pédiatrie. 2016; 23(7): 754-759. Doi: https://doi.org/10.1016/j.arcped.2016.04.003

4. Ministério da Saúde. Boletim Epidemiológico Especial – Tuberculose 2024 [versão eletrônica]. Brasília: Ministério da Saúde, 2024. 67 p. https://www.gov.br/aids/pt-br/central-de-conteudo/boletins-epidemiologicos/2024/boletim-epidemiologico-tuberculose-2024/view. Accessed December 07, 2024.

5. de Souza BVM, Franco ALAG, Barros ALM, Freire SP, Rodrigues HM, dos Santos Souza ARF, Oliveira RMC, Lôbo IMO. Considerações acerca da cobertura vacinal da BCG nas regiões brasileiras dos anos de 2019 a 2023. Studies in Health Sciences. 2024; 5(3): e7363-e7363. Doi: https://doi.org/10.54022/shsv5n3-045

6. Mohamad F, Alzahrani RR, Alsaadi A, Alrfaei BM, Yassin AEB, Alkhulaifi MM, Halwani M. An explorative review on advanced approaches to overcome bacterial resistance by curbing bacterial biofilm formation. Infection and Drug Resistance. 2023; 16:19-49. Doi: https://doi.org/10.2147/IDR.S380883