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### EFFECTS OF BACILLE CALMETTE-GUÉRIN AFTER THE FIRST DEMYELINATING EVENT IN THE CNS

**Nitin K. Sethi, New York:** Ristori et al.<sup>1</sup> reported the benefits of Bacille Calmette-Guérin (BCG) vaccination after clinically isolated syndrome (CIS). BCG vaccination may prevent progression to clinically definite multiple sclerosis in these patients. In countries like India where tuberculosis is endemic, BCG vaccination is administered to all children any time from birth to 15 days. If administered after 6 months, a Mantoux test is carried out, and if it is positive, the vaccine is withheld. Widespread BCG vaccination at birth may explain the low incidence of multiple sclerosis in the Indian subcontinent along with other hypotheses: distance from the equator, Epstein-Barr virus association vs causation, genetics, and hygiene. A well-designed study could clarify this vaccination hypothesis.

**Author Response: Giovanni Ristori, Silvia Romano, Giulia Coarelli, Maria Chiara Buscarinu, Marco Salvetti, Rome:** We thank Dr. Sethi for his comments on our article.<sup>1</sup> His hypothesis is plausible. Studies have been carried out regarding the association of early BCG vaccination and type 1 diabetes. Protective

effects of repetitive vaccinations have been shown in Turkey,<sup>2</sup> and an association between BCG vaccine and reduced production of GAD65 and IA-2 autoantibodies was demonstrated in Southern India.<sup>3</sup> It is unclear how early administration of the BCG vaccine may work over time and how it may affect autoimmunity prevalence in children and young adults. It is possible that early priming with BCG sensitizes this population to environmental nonpathogenic mycobacteria that exert long-term immunomodulatory effects, especially in developing countries. This may represent a sort of benign exposure to microbes that lacks or is deficient in the context of Westernization.<sup>4</sup> Another possibility is that BCG vaccination could provide protection from mycobacterial triggers and dysregulated immune response to mycobacterial antigens that have been associated with multiple sclerosis.<sup>5,6</sup>

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## Effects of Bacille Calmette-GuÉrin after the first demyelinating event in the CNS

Nitin K. Sethi, Giovanni Ristori, Silvia Romano, et al.

*Neurology* 2014;83;293

DOI 10.1212/01.wnl.0000452303.37990.ff

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