patients previously infected with another serotype. Preexisting nonneutralizing heterotypic antibodies bind to DENV and facilitate infection of monocytes, which triggers an inflammatory cascade that is eventually responsible for enhanced disease severity.¹ Recently, Katzelnick et al. found that patients with anti-DENV titers of 1:21 to 1:80 were at the highest risk for severe dengue.² The importance of antibody concentration is particularly relevant, because postvaccination anti-DENV titers wane with time in patients without natural reexposure.^{3,4}

Consequently, children who were seronegative before vaccination and whose postvaccination antibody titers wane are most at risk for severe disease. Studies should therefore evaluate whether booster doses could protect these patients from subsequent severe disease.

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H4:IC31 Vaccine or BCG Revaccination for Tuberculosis

TO THE EDITOR: Nemes and colleagues (July 12 issue)¹ examined the effects of bacille Calmette-Guérin (BCG) revaccination on reducing the rate of sustained QuantiFERON-TB Gold In-tube assay (QFT) conversion among adolescents in a high-risk setting. One aspect that received relatively little attention in the trial regards the immunologic mechanisms responsible for these effects, which were assessed only by measurement of interferon- γ and interleukin-2 T-cell responses. Studies have shown a combination of improved long-term innate or trained immunity (through epigenetic reprogramming of myeloid cells) and adaptive responses after BCG vaccination, which leads to more effective control of mycobacterial and unrelated infections.²⁻⁴ These mechanisms can also explain the decrease in unrelated respiratory tract infections after BCG revaccination that was observed by the authors. This decrease is consistent with the nonspecific beneficial effects after BCG vaccination that have been observed repeatedly in persons included in epidemiologic studies,⁵ especially in infants, and warrants sustained attention in future investigations.

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