

# Prevention of Hepatitis B Virus Vertical Transmission: Time for the Next Step

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Hepatitis B virus (HBV) continues to be a worldwide public health concern. There are more than 240 million people with chronic infection across the globe and 780 000 deaths each year as a result of acute or chronic HBV.<sup>1</sup> Infants born to mothers with chronic HBV infection are at very high risk of acquiring the virus and progressing to chronic infection.<sup>2,3</sup> In the 1970s–1980s, HBV vaccine and high-titer HBV immune globulin (HBIG) were effective in preventing vertical transmission (VT), and the combination was ~90% effective.<sup>4–6</sup> Prevention programs have since focused on universal screening of pregnant women for HBV surface antigen to identify those requiring prophylaxis.

In this issue of *Pediatrics*, Schille and Murphy<sup>7</sup> share data from the Centers for Disease Control and Prevention on efforts to identify HBV-infected pregnant women from selected sites in a public health–funded network. Much of the data they share is good news. Almost 95% of infants born to these HBV-infected mothers are receiving the combined prophylaxis and 99% of infants across the board are receiving all 3 doses of HBV vaccine at and after birth. These results should cause us to stop and recognize the scope and success of the tremendous efforts of everyone involved in preventing HBV VT. This article should also spur us to take the next step in HBV prevention. We have known for many years that infants born to HBV-infected pregnant women with more “active” disease (HBV e-antigen positive or HBV DNA levels  $\geq 10^7$  copies/mL) make up almost all of those infants for whom vaccine and HBIG fail to prevent

transmission.<sup>8,9</sup> The widespread efforts documented in this article reinforce this point.<sup>7</sup> Some studies have shown that using antiviral agents, specifically tenofovir, to suppress HBV DNA in pregnant women with active disease in the third trimester can prevent VT when combined with standard of care.<sup>10,11</sup> Many adult hepatologists already do this routinely for those women with chronic HBV infection with risk factors for VT prophylaxis failure when they become pregnant. To find the women with previously unknown disease, we as a medical community need to broaden, standardize, and implement these practices so they can be used by everyone. The authors suggest additional reflex testing of all women who are HBV surface antigen positive to identify those with e-antigen present or significant HBV DNA levels as an option. Those women who test positive and are defined as being at high risk of prophylaxis failure are systematically referred and started on antiviral therapy. A program like this has already been implemented with some success in northern California.<sup>12</sup> Further studies will need to be performed to optimize this management: How do we ensure that screening and reflex testing occur? Which antiviral agent is best? When should it be started to maximize benefit? How long should it be continued to maximize protection and minimize antiviral resistance?

Further studies are important because there are tangible downstream risks to using antiviral agents during pregnancy. Women in the “immune tolerant” phase of chronic HBV, with

HBV e-antigen positive and high-level HBV DNA in the absence of symptoms or elevated liver enzymes, may transition to a more active phase of hepatitis when treatment is stopped postpartum.<sup>13</sup> Despite the published warning, there is likely little infant drug exposure if a woman breastfeeds while taking tenofovir, but fetal drug exposure before delivery could have some long-term effect that is not yet appreciated.<sup>14</sup>

It is clear that we have come a long way in preventing HBV VT. It is also clear that it is time to take the next step. We have the tools available; we just need to have the will.

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