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PERSPECTIVE

Call to Action: Prevention of Mother-to-Child Transmission of Hepatitis B in Africa

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Hepatitis B virus (HBV) is a significant public health issue that has not been adequately addressed, especially in the high-prevalence region of Africa. Despite the incorporation of HBV vaccines into the Expanded Program on Immunization, children continue to be infected with HBV through maternal-to-child transmission (MTCT). The addition of a birth dose of HBV vaccine would be a cost-effective method to reduce MTCT. Birth-dose HBV vaccine policies have been adopted in the Western Pacific region but not yet in Africa. Even better protection against HBV MTCT can be achieved by treatment of pregnant women with high HBV viral loads with tenofovir. Tenofovir is already widely used in prevention of HIV MTCT (PMTCT) programs. We suggest that existing HIV PMTCT programs could be expanded to deliver care for HBV-infected pregnant women. With appropriate adoption of birth-dose vaccination policies and expansion of PMTCT programs, elimination of HBV MTCT in Africa is achievable.

Keywords. Hepatitis B virus; pregnancy; mother-to-child transmission; hepatitis B vaccine; sub-Saharan Africa.

Hepatitis B virus (HBV) represents a major, ongoing threat to public health. Worldwide, over 257 million people are living with chronic HBV infection, which results in complications such as cirrhosis, hepatocellular carcinoma, and death [1]. Global estimates suggest that 3.6% of the world's population are infected with HBV, with the greatest burden of disease among those living in the African region [2]. Morbidity and mortality rates remain high because public health systems have not implemented effective prevention of HBV transmission nor have they made effective drug therapy available to those who need it. In 2015 alone, 887 000 deaths were attributable to HBV [1]. These rates are unacceptable in light of the existence of an effective vaccine against HBV and suggest an underlying disparity in resources allocated to this important public health problem. The medical and public health communities should prioritize the hepatitis B epidemic in order to provide equitable care for all affected patients, regardless of country of origin.

A common route of acquisition of HBV, a blood-borne pathogen, is through maternal-to-child transmission (MTCT). Unfortunately, up to 90% of infants infected via MTCT will go on to develop chronic infection by adulthood [3]. In contrast, fewer than 5% of adults progress to chronic HBV when acutely infected in adulthood [1]. What's more, HBV infection oftentimes goes undetected in childhood, as those infected are typically asymptomatic until they present with liver complications later in life. However, if HBV is detected during pregnancy, effective preventive measures can be undertaken to avert MTCT.

The HBV vaccine, first introduced in 1982 [4], can provide >95% protection for recipients of the 3-dose vaccine series [5]. Because of its protective effect, the World Health Organization (WHO) recommended universal HBV vaccination beginning in 1992. Upon adoption of this policy, many countries experienced drastic reductions in rates of chronic HBV infection [6–8]. In The Gambia, for instance, rates of chronic HBV among 9-year-old children plummeted from 10.0% to 0.6% after introduction of the HBV vaccine series [6]. However, the 3-dose series typically begins at 6 weeks of age and provides little protection against HBV MTCT.

Administration of HBV vaccine and immunoglobulin (HBIG) within 12 hours of life, the standard-of-care for HBV-exposed infants in the United States and other developed nations, reduces the rate of HBV MTCT by 85%–95% [9, 10]. HBIG is not available in many developing nations because of cost and storage issues. However, there is evidence to suggest that the efficacy of HBV vaccine alone approaches that of HBV vaccine plus HBIG when a 3-dose series is initiated at birth [11].

Timely HBV birth dose vaccination is one of the key interventions identified by the WHO in its Global Health Sector Strategy on Viral Hepatitis, with the target coverage rate of 90% by 2030. The goal is to eliminate viral hepatitis by the year 2030 [12]. Despite high HBV vaccination rates among children (84% in 2016), only 39% received birth doses of the vaccine [13]. Vaccination outside of the critical 24-hour period after birth may not protect exposed infants against infection [14].

The success story of the Western Pacific region points to the power of birth

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dose vaccination against HBV MTCT in high-burden countries. Rates of chronic HBV infection were estimated to be greater than 8% in many countries in this region in the 1990s [15]. In response to these alarmingly high rates, leaders in the region agreed upon a goal to reduce chronic HBV infection among children to less than 1% by 2017 [15]. The implementation strategy, founded upon the introduction of the birth dose of HBV vaccine throughout the region, was designed and carried out starting in 2005, with assistance from the WHO and the Global Alliance for Vaccines and Immunizations (GAVI), among others. The execution of this plan also relied on political commitments of the individual countries within the region to prioritize administration of the HBV birth dose [16]. By 2014 in 24 of the 36 countries in the Western Pacific region, the prevalence of chronic HBV infection among children under the age of 5 decreased to 0.9% [15]. An estimated 7 167 128 deaths were averted over a 25-year period (from 1990 to 2014) [15]. This remarkable and effective method for prevention should serve as an example to other high-burden areas.

The WHO African region suffers from an undue burden of HBV, with an estimated 8.8% of the population affected by acute or chronic HBV [2]. Only 11 of 47 countries in Africa include the HBV birth dose as part of the routine infant immunization schedule [16, 17]. Instead, according to the routine infant vaccination schedule in the DRC [18], infants receive a pentavalent vaccine that cannot be administered until 6 weeks of age. This vaccine schedule has been adopted by GAVI for many of the least-developed countries and does not incorporate the vital birth dose of HBV vaccine. The failure to administer HBV vaccine within 24 hours of life leaves exposed infants vulnerable to acquiring infection from their mothers. A recent systematic review suggests that 1% (or 367 250) of newborns in sub-Saharan Africa are infected each year through MTCT of HBV [19]. Some of the barriers to administration of a birth dose in this region include "poor knowledge of or lack of national [HBV birth dose] vaccination guidelines, high prevalence of home births, and an unreliable vaccine supply" [17]. These implementation challenges can be overcome, as they were in The Gambia [6]. Additionally, recent studies have proven that the vaccine can be stored at room temperature and maintains potency after exposure to heat, negating the cold-chain requirement [20]. Furthermore, the addition of a birth dose to the current GAVI vaccine schedule has been proven to be cost-effective in sub-Saharan Africa [21, 22]. Only with allocation of appropriate resources, adoption of clear vaccination guidelines, and strong political commitments can the African Region meet its goal of reducing HBV prevalence to <2% by 2020 [17].

While HBV birth dose administration is a cost-effective strategy to reduce MTCT of the disease, treatment of HBV-infected pregnant women with antivirals is another key intervention measure. Even with timely infant vaccination, breakthrough transmission can occur among mothers who have high-risk HBV infection (ie, positive "e" antigen [HBeAg] and/or high viral loads) [23–25]. If high-risk disease is identified among pregnant women, effective antiviral treatment can be provided to them in order to reduce the risk of MTCT [25, 26]. To avoid negative side effects of tenofovir [26–28], antiviral treatment is only recommended for women with high-risk HBV rather than for all HBV-positive women. Based on evidence that vertical transmission does not occur at levels <200 000 IU/mL but does occur at levels above this, antiviral treatment is currently only recommended for pregnant women with an HBV viral load ≥200 000 IU/mL [28]. Treatment of pregnant women with high-risk HBV is now the standard-of-care in the USA and Europe [28, 29] but has yet to be implemented in many low- and middle-income countries with high burdens of disease.

This treatment approach has not been adopted in low-resource countries, often due to limited HBV diagnostic testing capacity, inadequate access to antivirals, and a lack of dedicated HBV programs. Rapid HBV testing is available with the advent of point-of-care tests for HBV surface antigen (HBsAg), but viral load testing is not yet routinely available. However, the use of dried blood spots for hepatitis testing is a promising technique in low-resource settings [30–32]. Tenofovir, an antiviral that is approved for the treatment of HBV in pregnant women, is also effective against HIV. Existing prevention of HIV maternal-to-child transmission (PMTCT) programs throughout Africa already provide treatment with tenofovir to pregnant women, so the supply chains are well established. HIV-HBV coinfected women in these programs receive effective treatment for both diseases in order to reduce MTCT. But HBV-infected pregnant women who test HIV-negative by PMTCT programs do not currently receive the drug.

The prevention of HBV vertical transmission in sub-Saharan Africa could be achieved by taking advantage of existing HIV PMTCT programs. Studies in several African countries have proven the effectiveness of combining HIV and HBV care for coinfected pregnant women [33–36]. In these programs, mothers receive effective treatment for HBV through tenofovir and other components of their HIV regimen. However, current HIV PMTCT testing programs only identify and treat HBV-HIV coinfected pregnant women. By expanding existing HIV PMTCT programs to include HBV screening for all pregnant women, HBV monoinfected pregnant women can be linked to care. HBV-positive, HIV-negative pregnant women with high viral loads could then be identified and offered antiviral prophylaxis or treatment during pregnancy. The addition of a birth dose of HBV vaccine for infants of all HBV-positive women to PMTCT programs is a key component of efforts to protect this vulnerable population of infants. Formal cost

analysis studies are needed to prove that this approach would be cost-effective and to assess its impact on HBV-associated chronic liver disease. However, we propose that the existing HIV PMTCT infrastructure could provide effective HBV PMTCT with relatively modest investment, reducing costs and achieving "horizontal" health systems strengthening. The success of these strategies would require buy-in from many stakeholders, including political leaders, nongovernmental organizations, GAVI, and the WHO.

Note

Potential conflicts of interest. All authors report no potential conflicts of interest related to this work. All authors have submitted the ICJME Form for Disclosure of Potential Conflicts of Interest.

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