



Operationalizing Elimination of Mother-to-Child Transmission of Hepatitis B Virus in the Western Pacific Region

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ABBREVIATIONS

3TC	lamivudine
AASLD	American Association for the Study of Liver Diseases
ALT	alanine aminotransferase
ANC	antenatal care
ART	antiretroviral therapy
AST	aspartate aminotransferase
EASL	European Association for the Study of the Liver
EMTCT	elimination of mother-to-child transmission
EPI	Expanded Programme on Immunization
FTC	emtricitabine
HBeAg	hepatitis B e (envelope) antigen
HBIG	hepatitis B immunoglobulin
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HepB3	hepatitis B vaccine third dose
HepB birth dose	hepatitis B vaccine birth dose
MTCT	mother-to-child transmission
PVST	postvaccination serological testing
RMNCH	reproductive, maternal, newborn and child health
TDF	tenofovir disoproxil fumarate
UHC	universal health coverage
WHO	World Health Organization

GLOSSARY OF TERMS

Antiviral prophylaxis	Anti-HBV drugs given to pregnant women with chronic HBV infection to lower HBV DNA levels and reduce the risk of MTCT of HBV.
Chronic HBV infection	Persistence of HBsAg for six months or more after initial infection with HBV.
Cirrhosis	An advanced stage of liver disease characterized by extensive hepatic fibrosis.
Decompensated cirrhosis	Cirrhosis with clinical complications including jaundice, ascites, spontaneous bacterial peritonitis, oesophageal varices and bleeding, hepatic encephalopathy, sepsis and renal failure.
HBV DNA	HBV viral genomes that can be detected and quantified in serum. ¹
Hepatocellular carcinoma (HCC)	Primary liver cancer arising in hepatocytes.
Hepatitis B surface antigen (HBsAg)	HBV envelope protein and excess coat particles detectable in the blood in acute and chronic hepatitis B infection.
Hepatitis B e antigen (HBeAg)	Viral protein found in the high replicative phase of HBV. HBeAg is usually a marker of high levels of replication with wild-type virus but is not essential for viral replication.
Hepatitis B core antibody (anti-HBc)	Antibody to hepatitis B core (capsid) protein; anti-HBc antibodies are not neutralizing antibodies but are detected in both acute and chronic infection.
Hepatitis B surface antibody (anti-HBs)	Antibody to HBsAg; develops in response to hepatitis B vaccination and during recovery from acute hepatitis B, denoting past infection and immunity.

¹ HBV DNA correlates with levels of circulating viral particles. HBV DNA is measured as IU/mL or copies/mL, with 1 IU/mL ~ 5.3 copies/mL (i.e. 10 000 copies/mL = 2000 IU/mL; 100 000 copies/mL = 20 000 IU/mL; 1 million copies/mL = 200 000 IU/mL).

EXECUTIVE SUMMARY

The *Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific, 2018–2030* (1) proposes a coordinated approach towards achieving the triple elimination of mother-to-child transmission (EMTCT) of HIV, hepatitis B and syphilis through access to quality reproductive, maternal, newborn and child health (RMNCH) services for all women, their children and families, in the context of universal health coverage (UHC).

Prevalence of chronic hepatitis B virus (HBV) infection in the general population is particularly high in the Western Pacific Region, with 115 million people estimated to be living with HBV in the Region in 2015 (2). But progress towards HBV control through immunization in the Region has been significant over the past two decades. There was an estimated regional hepatitis B surface antigen (HBsAg) prevalence of > 8% among children aged 5 years in 1990. Strengthened national immunization programmes then led to the achievement of regional targets to decrease HBV prevalence among children aged 5 years to < 2% by 2012 and to < 1% by 2017.

EMTCT of HBV is one component of the broader hepatitis B control response presented in the *Global Health Sector Strategy on Viral Hepatitis 2016–2021* (3). The Regional Framework presents an approach to introducing additional interventions for preventing mother-to-child transmission (MTCT) of HBV infection. This builds upon high coverage of newborn and infant hepatitis B vaccination programmes, to reduce MTCT of HBV infection even further and achieve the global target of < 0.1% prevalence rate of hepatitis B surface antigen (HBsAg)² among children aged 5 years by 2030 (3).

This document has been developed at the request of Western Pacific Member States following several regional consultations. The aim of the document is to compile and summarize information and existing WHO guidance of relevance to countries in the Region on EMTCT of HBV, based on available evidence, experiences and regional consultations. The target audience is primarily national programme managers and policy-makers in countries and areas in the Region who are planning to integrate EMTCT of HBV into their national hepatitis control programmes and EMTCT strategies.

Where WHO recommendations exist, they are stated. If no WHO recommendations exist but there are other professional guidelines, this is indicated.

Summary of WHO recommendations related to EMTCT of HBV

Hepatitis B vaccination (4,5)

WHO recommends that all infants receive monovalent hepatitis B vaccine as soon as possible after birth, preferably within 24 hours. The birth dose should be followed by two or three doses, with a minimum of four weeks between successive doses to complete the primary hepatitis B vaccine series.

Recommended schedules include:

- a three-dose schedule of hepatitis B vaccine, with the first dose (monovalent) being given at birth and the second and third (monovalent or combined vaccine) given at the same time as the first and third doses of diphtheria, tetanus and pertussis (whooping cough), or DTP, vaccine; or
- a four-dose schedule, in which a monovalent birth dose is followed by three monovalent or combined vaccine doses, usually given with other routine infant vaccines.

² Chronic hepatitis B infection is defined as the persistence of HBsAg for six months or more after acute infection with HBV.

WHO does not recommend booster vaccination for persons who have completed the three- or four-dose vaccination schedule.

Hepatitis B immunoglobulin (HBIG) (5)

- HBIG prophylaxis in conjunction with hepatitis B vaccination (that is, active immunization) may be of additional benefit for newborn infants whose mothers are HBsAg-positive, particularly if they are also HBeAg-positive.
- Improved protection has been demonstrated in neonates immunized with hepatitis B vaccine and HBIG when compared with hepatitis B vaccine alone.
- In full-term neonates born to mothers who are HBsAg-positive but HBeAg-negative, the addition of HBIG may not significantly improve the protection against perinatally acquired infection achieved by immediate hepatitis B vaccination (timely birth dose, given within 24 hours).
- Additionally, owing to concerns related to supply, safety and cost, the use of HBIG is not feasible in some settings.

Antenatal (ANC) testing (6,7)

WHO recommends that all pregnant women be tested for **HIV, syphilis and hepatitis B surface antigen (HBsAg)** at least once and as early as possible during their pregnancy (6).

In settings with a $\geq 2\%$ or $\geq 5\%$ seroprevalence in the general population,³ **HBsAg serological testing** should be routinely offered to all pregnant women in antenatal clinics, with linkage to prevention, care and treatment services. Couples and partners in antenatal care settings should be offered HBV testing services (7).

WHO also recommends offering **serological testing for hepatitis C virus (HCV) antibody** to individuals who are either part of a population with high HCV seroprevalence or who have a history of exposure and/or high-risk behaviours for HCV infection. In settings with a $\geq 2\%$ or $\geq 5\%$ HCV antibody seroprevalence in the general population,³ it is recommended that all adults have access to and be offered HCV serological testing with linkage to prevention, care and treatment services (7).

Prevention for non-immune groups (7,8,9)

- In countries where there is low or intermediate endemicity of chronic HBV infection, people in high-risk groups may acquire the infection and should also be vaccinated. High-risk groups include household and sexual contacts of people with chronic HBV infection, people with multiple sexual partners, sex workers, transgender people, men who have sex with men, prisoners, people who inject drugs, health-care workers, mobile or migrant populations, indigenous populations, people exposed in health-care settings and through other invasive procedures (including tattooing, body piercing, scarification and circumcision), people living with HIV, and travellers (7,8).
- Individuals who are HBsAg-positive should: adopt correct and consistent condom use during sexual intercourse if the partner is neither HBV immune nor has been vaccinated; not share razors, toothbrushes or other personal care items; not donate blood, organs or sperm; and follow standard universal precautions with open cuts or bleeding (9).

Treatment of persons with chronic hepatitis B infection (9)

As a priority, all adults, adolescents and children with chronic hepatitis B and clinical evidence of compensated or decompensated cirrhosis (or cirrhosis based on an aspartate aminotransferase to platelet ratio index – APRI – score of > 2 in adults) should be treated, regardless of alanine aminotransferase (ALT) levels, HBeAg status or HBV DNA levels.

³ A threshold of $\geq 2\%$ or $\geq 5\%$ seroprevalence was based on several published thresholds of intermediate and high seroprevalence. The threshold used will depend on other country considerations and epidemiological context.

Treatment is recommended for adults with chronic hepatitis B who do not have clinical evidence of cirrhosis (or based on an APRI score of ≤ 2 in adults) but are aged over 30 years (in particular) and have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA $> 20\,000$ IU/mL), regardless of HBeAg status.

Where HBV DNA testing is not available, treatment may be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status.

Antiviral prophylaxis in pregnancy for prevention of MTCT of HBV (10)

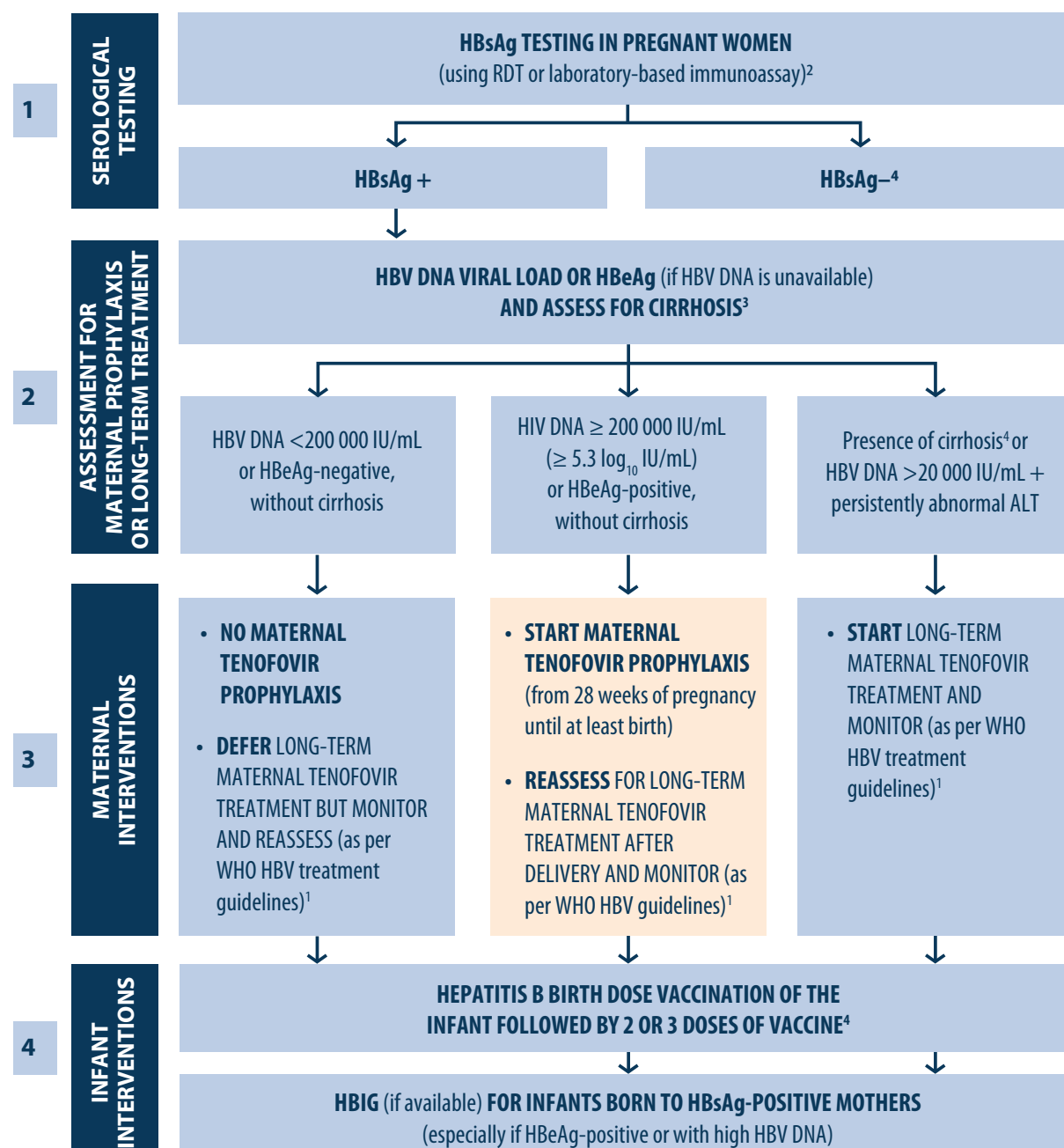
WHO recommends that pregnant women testing positive for HBV infection (HBsAg-positive) with an HBV DNA $\geq 200\,000$ IU/mL ($5.3 \log_{10}$ IU/mL) receive tenofovir prophylaxis from the 28th week of pregnancy until at least birth, to prevent mother-to-child transmission of HBV. This is in addition to three-dose hepatitis B vaccination, including timely birth dose.

WHO recommends that, in settings in which antenatal HBV DNA testing is not available, HBeAg testing can be used as an alternative to HBV DNA testing to determine eligibility for tenofovir prophylaxis to prevent MTCT of HBV.

Postvaccination serological testing (PVST) (5)

- Routine postvaccination serological testing for immunity is not necessary, but it is recommended for high-risk individuals whose subsequent clinical management depends on knowledge of their immune status, including infants born to HBsAg-positive mothers.
- HBsAg testing should be performed 1–2 months after administration of the last dose of the hepatitis B vaccine series.
- Anti-HBs testing should use a method that allows for a quantitative determination of the anti-HBs antibody level with a detection limit of < 10 mIU/mL.

Algorithm on maternal and infant interventions for prevention of MTCT of HBV (10)



ALT: alanine aminotransferase; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HBeAg: hepatitis B e antigen; HBIG: hepatitis B immunoglobulin; HBsAg: hepatitis B surface antigen; RDT: rapid diagnostic test.

¹ Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection (<https://www.who.int/hepatitis/publications/hepatitis-b-guidelines/en/>).

² At least once and as early as possible in the pregnancy.

³ Using clinical criteria and non-invasive tests (APRI score > 2 in adults, or FibroScan).

⁴ Hepatitis B timely (within 24 hours) birth dose vaccination of the infant followed by two or three doses of hepatitis B vaccine should be given regardless of HBsAg status of the pregnant mother.

1. BACKGROUND



The *Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific, 2018–2030* (1) proposes a coordinated approach to achieving triple elimination of mother-to-child transmission (EMTCT) of HIV, hepatitis B and syphilis through access to quality reproductive, maternal, newborn and child health (RMNCH) services for all women, their children and families, in the context of universal health coverage (UHC). It also presents an approach to introducing additional interventions for preventing mother-to-child transmission (MTCT) of hepatitis B virus (HBV) infection, building upon high coverage of newborn and infant hepatitis B vaccination programmes, to reduce MTCT of HBV infection even further and achieve the global target of < 0.1% prevalence rate of hepatitis B surface antigen (HBsAg)⁴ among children aged 5 years by 2030 (3).

Prevalence of chronic HBV infection in the general population is particularly high in the Western Pacific Region, estimated as 6.2% in 2015, with 115 million people calculated to be living with HBV in the Region in 2015 (2). The burden of HBV infection varies widely among countries. Prevalence estimates in the general population range from < 2% in a small number of countries (Australia 0.9%, Fiji 1.8%, Japan 1.0% and Malaysia 0.7%) to > 18% in Solomon Islands. Absolute numbers of people living with chronic HBV infection ranged from approximately 10 000 (Samoa) to more than 86 million (China) in 2017 (11). HBV is frequently transmitted perinatally from HBV-infected women to their newborn infants. Data on the prevalence of HBsAg positivity among women attending antenatal clinics are limited, but rates of 0.1%–1.0% in Japan, 3% in the Republic of Korea, 4% in Mongolia to 6% in China have been reported. Every year, an estimated 180 000 infants in the Region are newly infected with HBV through perinatal transmission (12).

Most of the burden of HBV-related disease results from infections acquired in infancy through perinatal or early childhood exposure to HBV. Infection acquired at an early age is more likely to become chronic than infection acquired later in life: 80%–90% of infants infected in the first year of life and 30%–50% of children infected between 1 and 5 years of age go on to develop chronic infection. The risk of chronic infection then stabilizes at around 5% (5,13). The major complications of chronic HBV infection are liver cirrhosis and hepatocellular carcinoma (liver cancer). In the Western Pacific Region, chronic hepatitis B is the most common cause of liver cancer and liver cancer is the second most common cause of cancer deaths.

Progress towards hepatitis B control through immunization in the Region has been significant over the past two decades. With an estimated regional HBsAg prevalence of > 8% among children aged 5 years in 1990, strengthened national immunization programmes led to the achievement of Regional targets to decrease hepatitis B prevalence among children aged 5 years to < 2% by 2012 and to < 1% by 2017. At the end of 2019, 21 of the 37 countries and areas in the Region had been verified as meeting the target of < 1% HBsAg prevalence among children aged 5 years. A further four countries and areas have serosurvey evidence (not yet submitted for verification) of having met the target.⁵ In 2019, the Region achieved 84% coverage of the timely hepatitis B vaccine birth dose (HepB birth dose), defined as given within 24 hours of birth, among newborn infants and 94% coverage of the third dose of hepatitis B vaccine (HepB3) among infants (14). Global timely HepB birth dose and HepB3 coverage in 2019 were 43% and 85%, respectively (15). In 2019, 10 of 22 reporting countries achieved the ≥ 95% coverage target of timely HepB birth dose⁶ and 13 of 25 countries achieved the ≥ 95% coverage target of HepB3.⁷ In 1990–2014, these immunization gains prevented more than 37 million chronic HBV infections, averting more than 7 million deaths (12).

Most cases of perinatal HBV transmission occur during delivery, with rare cases of in utero transmission. Timely HepB birth dose and additional doses of hepatitis B vaccine act as post-exposure prophylaxis against

⁴ Chronic hepatitis B infection is defined as the persistence of HBsAg for six months or more after acute infection with the hepatitis B virus.

⁵ Japan, Philippines (preliminary findings), Samoa, Wallis and Futuna.

⁶ China, Cook Islands, Kiribati, Malaysia, Mongolia, Nauru, Niue, Palau, Tonga, Tuvalu. It should be noted that Japan and New Zealand selectively administer HepB birth dose to infants of HBsAg-positive mothers.

⁷ Australia, Brunei Darussalam, Cambodia, China, Cook Islands, Kiribati, Malaysia, Mongolia, Niue, Palau, Republic of Korea, Singapore, Tonga.

HBV infection, preventing an estimated 70%–95% of cases of perinatal, or vertical, transmission (13,16). They also protect against horizontal transmission. Epidemiological and modelling data, however, indicate that infant hepatitis B vaccination alone (modelled at 90% coverage), including timely HepB birth dose (modelled at 80% coverage), may not be sufficient to reach the 2030 incidence target of < 0.1% prevalence rate of HBsAg among children aged 5 years (17). This is because transmission still occurs from infected women with high HBV DNA (viral load) to their infants. Additional interventions, including antenatal HBsAg screening and further evaluation of HBsAg-positive women, with antiviral prophylaxis given to pregnant women with high HBV viral load and hepatitis B immunoglobulin (HBIG) given to newborn infants of HBsAg-positive mothers, further reduce the risk of MTCT of HBV (18).

Infants born to women with chronic HBV infection with HBV DNA $\geq 200\,000$ IU/ml ($5.3 \log_{10}$ IU/ml) at the time of delivery are at increased risk of HBV acquisition, even when they receive timely immunoprophylaxis (16,19). Measurement of HBV DNA in pregnant women with chronic HBV infection identifies those most likely to transmit hepatitis B virus to their infants and allows maternal antiviral prophylaxis against MTCT to be given to reduce the risk of infant infection. HBV DNA testing, however, is not widely available in many countries in the Western Pacific Region. Hepatitis B e antigen (HBeAg) positivity is associated with viral replication, and higher HBV DNA and testing for HBeAg can be used as an alternative to HBV DNA testing (10).

Some countries in the Region are already making progress towards EMTCT of HBV by introducing additional interventions beyond high coverage of timely HepB birth dose and completion of the infant hepatitis B vaccine series and are establishing mechanisms to monitor EMTCT indicators. In 2019, 19 countries and areas in the Region, covering more than 90% of its population, had policies recommending universal antenatal HBsAg screening for hepatitis B. About half of these countries have introduced or are introducing maternal antiviral prophylaxis for preventing MTCT of HBV and offer HBIG to infants of HBsAg-positive mothers. Six countries conduct routine follow-up of HBV-exposed infants including postvaccination serological testing (PVST). Universal antenatal testing for HBsAg also allows hepatitis B vaccine to be offered to women who test negative for HBsAg to protect them from acquiring hepatitis B infection, both during pregnancy and thereafter. However, this is not routine practice in the Region.

EMTCT of HBV is one component of the broader hepatitis B control response presented in the *Global Health Sector Strategy on Viral Hepatitis 2016–2021* (3). Comprehensive antenatal care, which includes antenatal testing for HBsAg, is an important entry point into prevention, care and treatment for pregnant women with chronic HBV infection, their partners and household contacts. It also allows identification of high-risk pregnancies for additional interventions to prevent MTCT of HBV.

This document has been developed at the request of Member States in the Western Pacific following several regional consultations, including:

1. the Informal Consultation on Validation of Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis: Developing the Method for Validating Hepatitis B Virus Elimination, Kuala Lumpur, Malaysia, 27–28 February 2018 (20);
2. the Third Strategic and Technical Advisory Committee (STAC) for viral hepatitis, Manila, Philippines, 17–18 September 2018 (21); and
3. the Meeting on the Implementation of the Regional Action Plan for Viral Hepatitis in the Western Pacific, Manila, Philippines, 13–14 December 2018 (22).

The aim of the document is to compile and summarize information and existing WHO guidance of relevance to countries in the Region on EMTCT of HBV, based on available evidence, experiences and regional consultations.⁸ The target audience is primarily national programme managers and policy-makers in countries and areas in the Region who are planning to integrate EMTCT of HBV into their national hepatitis control programmes and EMTCT strategies.

⁸ Where there are no WHO recommendations available, guidance from other sources is included.

2. COMPREHENSIVE INTERVENTIONS FOR ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS



The *Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific, 2018–2030* (1) proposes a coordinated approach towards achieving triple elimination, with EMTCT interventions included as essential components of high-quality RMNCH services.

EMTCT of HBV requires a comprehensive package of interventions built on a strong infant hepatitis B vaccination programme that achieves high coverage of the timely birth dose and three doses of hepatitis B vaccine.

Provision of additional interventions targeted at HBV-infected women and their infants:

1. reduces maternal morbidity associated with chronic HBV infection through access to treatment for eligible women; and
2. further reduces the risk of MTCT and subsequent development of chronic HBV infection among young children, reducing the overall burden of disease attributable to hepatitis B in the long term.

Some countries have already included EMTCT of HBV in their EMTCT plans by integrating universal antenatal HIV, syphilis and hepatitis B testing, plus prevention and treatment interventions, into their essential package of services. Other countries face challenges of limited capacity and resources that present barriers to the implementation of interventions.

2.1 Summary of key interventions for elimination of mother-to-child transmission of hepatitis B virus

A summary of key interventions related to EMTCT of HBV for pregnant women is presented in Box 1 and for infants in Box 2. Further details are provided in subsequent sections.

WHO recommendations state that all pregnant women should be tested for HIV, syphilis and HBsAg at least once and as early as possible (6). Counselling, education and linkage to care and treatment services should be made available to women with chronic HBV infection (7). All infants (irrespective of the mother's HBV infection status) should be given a timely birth dose of hepatitis B vaccine. This should be followed by at least two additional doses of hepatitis B-containing vaccine, given at intervals of at least four weeks, to complete the vaccine series (4,5,23). Additional interventions to reduce the risk of MTCT of HBV may be offered depending on country context.

Box 1. Elimination of mother-to-child transmission of hepatitis B virus interventions for pregnant women (7)



Antenatal HBsAg testing

- WHO recommends that antenatal HBsAg testing be routinely offered to all pregnant women, in addition to HIV and syphilis testing.

HBsAg testing should be followed by counselling and further interventions determined by the test result:

Counselling for HBsAg-negative pregnant women

- Counsel on prevention of transmission and consider offering hepatitis B vaccination.

Counselling for HBsAg-positive pregnant women

- Counsel and provide education on the implications of hepatitis B infection for the woman's own health and for her baby.
- Explain the importance of facility delivery to ensure the baby can receive the timely HepB birth dose as soon as possible after birth and is linked to follow-up care, in addition to accessing other crucial benefits of having a skilled birth attendant present at delivery.
- Identify partners, other family members and close contacts and offer HBsAg testing. Offer hepatitis B vaccination to people whose HBsAg test is negative. Link anyone who tests HBsAg-positive to care and treatment services.

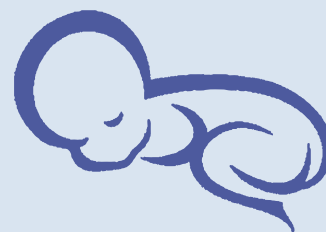
Linkage to care for HBsAg-positive pregnant women

- Link to care and treatment services during pregnancy for assessment of liver disease and evaluation for treatment; continue long-term follow-up after delivery.
- Assess eligibility for maternal antiviral prophylaxis to provide additional protection against MTCT of HBV.

Box 2. Elimination of mother-to-child transmission of hepatitis B virus interventions for infants (4,5,9)

Hepatitis B vaccination for ALL newborn infants

- Hepatitis B vaccine birth dose: WHO recommends that all newborn infants, including those with low birth weight and premature infants, receive a timely birth dose of monovalent hepatitis B vaccine (timely HepB birth dose) as soon as possible after birth and ideally within 24 hours.
- Complete the primary hepatitis B vaccine series by the age of 6 months, giving two or three additional doses of hepatitis B-containing vaccine, each separated by at least four weeks, according to the national infant immunization schedule.



HBIG for infants born to HBsAg-positive mothers

- Consider giving a single dose of HBIG within 12 hours of birth: HBV-exposed infants given HBIG in addition to the timely HepB birth dose are better protected against perinatal HBV infection than those given hepatitis B vaccine alone, particularly if the mother is also HBeAg-positive¹ or has high maternal viral load.

Infant follow-up and PVST

- HBV-exposed infants require follow-up including PVST one to two months after the last dose of hepatitis B vaccine, to identify infected babies who need long-term follow-up and to evaluate programme impact.
- The timing of PVST may be determined by the timing of well-child visits or the routine measles immunization visit.

¹ HBeAg is a protein from HBV that is usually a marker of high viral load (14,18).

2.2 Operational considerations

2.2.1 Infant hepatitis B vaccination

Hepatitis B vaccination of newborn and young infants is the most important intervention for reducing MTCT of HBV. Countries/areas must ensure high coverage of the timely HepB birth dose and completion of the infant hepatitis B vaccine series, both nationally and subnationally. In settings with high numbers of home deliveries this may require exploring or strengthening the use of hepatitis B vaccine out of the cold chain at the point of delivery. Hepatitis B vaccines are heat-stable and may be stored and used out of the cold chain in settings where the cold chain cannot be maintained (24,25).

Hepatitis B vaccine birth dose: WHO recommends that all newborn infants, including those with low birth weight and premature infants, receive a timely birth dose of monovalent hepatitis B vaccine (timely HepB birth dose) as soon as possible after birth and ideally within 24 hours.

- The HepB birth dose prevents vertical transmission of infection to infants exposed to HBV during childbirth through post-exposure prophylaxis and initiates active immunization for lifelong

protection against HBV infection. Hepatitis B vaccine administered alone within 24 hours of birth is 70%–95% effective in preventing MTCT of HBV (13).

- Giving a delayed HepB birth dose between 24 hours and up to seven days after birth has some effectiveness in preventing *vertical* transmission, though this effectiveness decreases with time after birth. A delayed HepB birth dose can still prevent *horizontal* transmission.
- WHO recommends that infants who did not receive a HepB birth dose within the first seven days of life receive the late HepB birth dose at the first contact with health-care providers at any time up to the time of the next dose of the primary schedule (see below).

The primary hepatitis B vaccine series should be completed by the age of 6 months by giving two or three additional doses of hepatitis B-containing vaccine, each separated by at least four weeks, according to the national infant immunization schedule.^{9,10,11,12} Completion of the primary hepatitis B vaccine series leads to immunological protection and prevention of infection in > 95% of children (5).

- Once the infant is eligible for the first routine infant immunization (at 4–6 weeks of age), hepatitis B vaccine can be given either as monovalent vaccine or as combination (pentavalent) DTP–Hib–hepatitis B vaccine, according to local and national guidelines, always ensuring at least four weeks between successive doses of hepatitis B-containing vaccines.
- Infants who did not have a HepB birth dose should receive three doses of hepatitis B-containing vaccines as part of routine immunization.
- A booster dose of hepatitis B vaccine is not needed after completion of the primary vaccination series in routine immunization programmes.

2.2.2 Antenatal testing for hepatitis B surface antigen

WHO recommends that all pregnant women be tested for HIV, syphilis and HBsAg at least once and as early as possible (6).

Linkage to counselling and appropriate treatment, as well as intensified management of infants born to HBsAg-positive women, can mitigate the effects of chronic HBV infection, reduce the burden of disease attributable to viral hepatitis and help achieve EMTCT targets.

Antenatal HBsAg testing should be universally offered in every pregnancy¹³ and be integrated with antenatal HIV and syphilis testing as part of triple EMTCT (1). Testing must adhere to WHO's 5C principles (consent, confidentiality, counselling, correct results and connection), which include linkage to prevention, treatment and care services (27).

⁹ There were 15 different national infant hepatitis B vaccine schedules being offered in the Region in 2018. The most commonly followed schedule is 0, 6 weeks, 10 weeks and 14 weeks (12 countries/areas), followed by 0, 1 and 6 months (five countries/areas) and 0, 2, 4 and 6 months (four countries/areas). The other 13 schedules are followed by one or two countries each. One country (Japan) and five areas give the last dose of hepatitis B vaccine between 7 and 18 months of age (26).

¹⁰ Three doses of hepatitis B vaccine are sufficient to induce immunity. However, for programmatic reasons, the monovalent birth dose may be followed by three additional doses in national routine infant immunization schedules:

i) three-dose schedule: three doses of hepatitis B vaccine, the monovalent birth dose followed by two doses (monovalent or as part of a combined vaccine) given at the same time as the first and third doses of DTP-containing vaccine;

ii) four-dose schedule: four doses of hepatitis B vaccine, the monovalent birth dose followed by three doses (monovalent or combined vaccine), usually given with other routine infant vaccines.

¹¹ The HepB3 coverage indicator measures the third dose of hepatitis B vaccine whether or not a fourth dose is given. EMTCT of HBV process targets includes HepB3 coverage of $\geq 95\%$.

¹² Infants with low birth weight and premature infants may have a reduced immunogenic response to the HepB birth dose and should receive a full four-dose series of hepatitis B vaccine (three additional doses after the timely HepB birth dose).

¹³ Antenatal screening programmes should be conducted in private as well as public health-care facilities and cover all pregnant women including non-citizens and those not covered by health insurance.

Approved rapid diagnostic tests (RDTs) with high sensitivity and specificity can be used if available, particularly in settings where there is limited access to laboratory testing and/or in populations where access to rapid testing would facilitate linkage to care and treatment. There are (as of November 2019) three WHO-prequalified RDTs for the detection of HBsAg on the market. WHO guidance does not recommend confirmatory testing in settings with an HBsAg seroprevalence of $\geq 0.4\%$. Taking into account local disease epidemiology, confirmatory testing of positive HBsAg tests may be considered in settings with HBsAg seroprevalence of $< 0.4\%$ (7).

Antenatal HBsAg testing should be linked to additional services of direct benefit to pregnant women, their infants and other family members. These include counselling, enhanced prevention, testing, care and appropriate treatment. Effective systems need to be established to ensure that all antenatal test results are readily available to health-care providers in antenatal clinics at the time of delivery and at postnatal care visits. HBsAg testing should be routinely offered and accessible to partners, other children as well as family and household contacts of HBsAg-positive pregnant women. Pregnant women who are found to be HBsAg-negative during antenatal testing can be offered hepatitis B vaccination if they have not previously been vaccinated (7), particularly if they are at increased risk of acquiring HBV infection.¹⁴ Hepatitis B vaccination is not contraindicated during pregnancy or breastfeeding. Counselling should be provided on protection against bloodborne virus infections including hepatitis B. Counselling should cover correct and consistent condom use, not sharing razors, toothbrushes or other personal care items, plus following standard universal precautions with open cuts or bleeding.

If available, HBV DNA and/or HBeAg testing can be conducted on HBsAg-positive pregnant women to determine eligibility for additional EMTCT interventions (Table 1) and to evaluate the need for antiviral treatment for the woman's own health benefit (see also Box 4). If neither HBeAg nor HBV DNA tests are available, all infants of HBsAg-positive mothers should be considered at high risk of MTCT of HBV and managed accordingly.

Table 1. Antenatal testing for elimination of mother-to-child transmission of hepatitis B virus

	Test	Purpose
All pregnant women	HBsAg	Diagnosis of chronic HBV infection
HBsAg-positive pregnant women	HBeAg and/or HBV DNA	Risk categorization to determine eligibility for further interventions

2.2.3 Antiviral prophylaxis in pregnancy for prevention of mother-to-child transmission of hepatitis B virus

MTCT of HBV may still occur among infants born to women with high HBV DNA viral load, despite timely administration of both HepB birth dose and HBIG to the newborn infant.

WHO recommends that HBsAg-positive pregnant women with an HBV DNA of $\geq 200\,000$ IU/ml ($\geq 5.3 \log_{10}$ IU/ml) receive tenofovir prophylaxis from the 28th week of pregnancy until at least birth to prevent MTCT of HBV. As HBV DNA testing is not universally accessible, WHO also recommends that HBeAg testing can be used as an alternative to HBV DNA testing to determine eligibility for antiviral prophylaxis to prevent MTCT of HBV (Box 3) (10).

¹⁴ Pregnant women who are identified as being at risk for HBV infection during pregnancy (e.g. women who have had more than one sexual partner during the previous six months, have been evaluated or treated for a sexually transmitted disease, have a history of recent or current injecting drug use, or have had an HBsAg-positive sex partner) should be vaccinated (28).

Box 3. WHO recommendations on antiviral prophylaxis to prevent mother-to-child transmission of hepatitis B virus, 2020

Tenofovir prophylaxis to prevent MTCT of HBV

WHO recommends that pregnant women testing positive for HBV infection (HBsAg-positive) with an HBV DNA of $\geq 200\,000$ IU/ml ($5.3 \log_{10}$ IU/ml) receive tenofovir prophylaxis from the 28th week of pregnancy until at least birth to prevent MTCT of HBV. This is in addition to three-dose hepatitis B vaccination, including timely birth dose (*conditional recommendation, moderate quality of evidence*).

Use of HBeAg testing, where HBV DNA testing is not available, to determine treatment eligibility for tenofovir prophylaxis to prevent MTCT of HBV

WHO recommends that in settings in which antenatal HBV DNA testing is not available, HBeAg testing can be used as an alternative to HBV DNA testing to determine eligibility for tenofovir prophylaxis to prevent MTCT of HBV (*conditional recommendation, moderate quality of evidence*).

HBeAg prevalence among HBsAg-positive women of childbearing age in the Asia and Pacific region ranges from 20% to 45% (29). HBeAg positivity is an indication of viral replication and is generally associated with higher HBV DNA. However, some pregnant women have high HBV DNA despite being HBeAg-negative and will not be identified by HBeAg screening. The proportion of HBeAg-negative women with high HBV DNA levels varies by population. Results from studies conducted in Cambodia and China indicate that 8%–11% of HBeAg-negative pregnant women had HBV DNA levels of $\geq 200\,000$ IU/ml ($5.3 \log_{10}$ IU/ml) (30). There is also a small proportion of HBsAg-positive women who are HBeAg-positive but who do not have high HBV DNA levels.

A number of studies have shown that antivirals (daily TDF, telbivudine or lamivudine) given to pregnant women beginning in the second or third trimester of pregnancy, when combined with infant immunization including timely HepB birth dose and HBIG, reduce maternal HBV viral load and the risk of MTCT of HBV (31–33). In one multicentre double-blind clinical trial conducted in Thailand, there was no significant difference in MTCT of HBV in pregnant women given antivirals compared to women given a placebo (infants in both study arms were given timely HepB birth dose and HBIG). Both HepB birth dose and HBIG were administered within four hours of birth (in 96% of infants), which probably contributed to the low MTCT rate (2%) in the control population. This may also explain why a statistically significant effect of maternal antiviral prophylaxis was not seen (34).

As HBIG is not available, affordable or readily accessible in some countries in the Western Pacific Region, due in part to limited cold chain availability, there is growing interest in the use of antivirals, which are more readily available at lower cost, for maternal prophylaxis against MTCT of HBV. Some of these antivirals are already registered for use in countries by national drug regulatory bodies. However, they may require “prevention of MTCT of HBV” to be added as an additional indication for their use. Studies are ongoing in HBsAg-positive pregnant women with high HBV DNA viral load and pregnant women who are HBeAg-positive to examine the efficacy of maternal antiviral prophylaxis in preventing MTCT of HBV when exposed infants are not given HBIG. Results of these studies are expected in 2020 or 2021 (35,36). Until the results of these studies are reported, it remains standard care in many countries to provide infants born to HBsAg-positive mothers with both timely HepB birth dose and timely HBIG (if available). This is in addition to giving antivirals for prevention of MTCT of HBV during pregnancy to eligible women. All infants should complete the hepatitis B vaccine series irrespective of the mother’s infection status.

TDF is the preferred drug (dose: 300 mg orally once daily) to prevent MTCT of HBV, owing to its antiviral potency, low potential for resistance and favourable safety profile. Telbivudine and lamivudine have been used for EMTCT of HBV in some countries, but have a higher potential for resistance when given as monotherapy than TDF. New WHO guidelines recommend the use of tenofovir (10). Due to the risk of renal toxicity, confirmation of adequate baseline renal function may be considered before starting TDF, in line with global and/or national treatment guidelines (9,37).^{15,16}

HIV–HBV co-infected pregnant women should be on an antiretroviral therapy (ART) regimen that includes both TDF and lamivudine (3TC) or emtricitabine (FTC), as these drugs are active against both HIV and HBV. In the case of an HIV–HBV co-infected person who is failing, ART, TDF and 3TC (or FTC) should be continued as a second line with subsequent ART regimens for the anti-HBV activity and to reduce the risk of hepatitis flare-ups. The preferred second-line regimen would be zidovudine (also known as azidothymidine, or AZT) + TDF + 3TC (or FTC) + a boosted protease inhibitor or an HIV integrase inhibitor (37).

A range of HBV DNA thresholds to determine eligibility for antivirals for prevention of MTCT of HBV have been adopted globally. In the Asia and Pacific region, countries and professional bodies recommend an HBV DNA threshold in the range of 200 000 to 10 million IU/ml (Table 2). A systematic review of available data was conducted during the development of the WHO HBV EMTCT guidelines. This led to the recommendation that an HBV DNA threshold of 200 000 IU/ml ($5.3 \log_{10}$ IU/ml) should be used to determine eligibility for maternal antiviral prophylaxis.

The WHO guidelines on antiviral prophylaxis in pregnancy recommend starting antivirals for EMTCT of HBV from the 28th week of pregnancy to allow sufficient time for HBV DNA suppression by the time of delivery. Factors affecting time to suppression of HBV DNA include the baseline HBV DNA, the duration of prophylaxis,¹⁷ choice of drug and adherence. The guidelines recommend continuing prophylaxis until at least birth because of concerns about the risk of hepatitis flare-ups. Antivirals should not be stopped in women who are taking antivirals for treatment of chronic HBV infection rather than prophylaxis against MTCT of HBV. HBV-infected women need to be linked to care during pregnancy and monitored closely for hepatitis flare-ups during pregnancy and after delivery (section 2.2.4.3, Box 6).

¹⁵ Desirable, if feasible: serum creatinine and estimated glomerular filtration rate (eGFR) for starting TDF, among people with a high risk of adverse events associated with TDF: underlying renal disease, older age group, low body mass index (BMI), diabetes, hypertension and concomitant use of a boosted protease inhibitor (PI) or potential nephrotoxic drugs (37).

¹⁶ Monitoring for TDF toxicity: measurement of baseline renal function and assessment of baseline risk for renal dysfunction should be considered in all persons prior to initiation of antiviral therapy (9).

¹⁷ 12% of women had HBV DNA viral load of > 200 000 IU/ml at delivery, after a median 10.7 weeks of TDF (34). 25% of women had HBV DNA viral load of > 200 000 IU/ml at delivery, after a median 8.6 weeks of TDF (32).

Table 2. Summary of guidance and recommendations for elimination of mother-to-child transmission of hepatitis B virus interventions given in addition to timely HepB birth dose and completion of the hepatitis B vaccine series (Cont.)

	Interventions for pregnant women						Interventions for newborn/young infants	
	Antenatal testing			Antiviral prophylaxis for prevention of MTCT of HBV			Immediately after birth	During the first 12 months after birth
	HBsAg	HBeAg	HBV DNA	Eligibility	Timing	Drug	HBIG for exposed newborn infants	Postvaccination serologic testing
Cook Islands	Yes							
Fiji	Yes	No	No	Roll-out planned in coming weeks to months		TDF	YES, all HBV-exposed infants	Not done
Hong Kong SAR (China)	Yes	No	No (under study)	Under study	Under study	Under study	Yes, all HBV-exposed infants	Under study
Japan	Yes	Yes	Not official policy	NA	NA		Yes	Yes
Kiribati	Yes	Yes (at VIDRL)	Yes (at VIDRL)	-	-	-	No	No, planned
Lao People's Democratic Republic	Yes	No	No	-	-	-	No	No
Macao SAR (China)	Yes	No	No	HBV DNA > 200 000 IU/mL	24–28 weeks until delivery or 3 months postpartum	TDF or TBV	Yes, all HBV-exposed infants	Yes, 9–15 months
Malaysia	Yes	Yes	Yes	HBV DNA > 200 000 IU/mL or HBeAg+	28–32 weeks to 2 or 3 months postpartum	TDF	Yes, all HBV-exposed infants	Yes, 9 months
Mongolia	Yes	Yes	Yes	HBeAg + pregnant women with HBV DNA > 200 000 IU/mL	28 weeks to 12 weeks postpartum	TDF or TBV	Infants of HBeAg+ mothers only < 12 hours	HBsAg, anti-HBs and anti-HBc 2 months after completion of vaccination
New Zealand (42)	Yes	Yes	Yes	HBV DNA > 200 000 IU/mL	30–32 weeks to 6 weeks postpartum	TDF	All HBV-exposed infants < 12 hours, ideally < 4 hours	Anti-HBs and HBsAg 3–12 months after completing primary series
Niue	Yes							
Papua New Guinea	No	No	No	-	-	-	No	No
Philippines	Yes	No	No	-	-	-	-	-

Table 2. Summary of guidance and recommendations for elimination of mother-to-child transmission of hepatitis B virus interventions given in addition to timely HepB birth dose and completion of the hepatitis B vaccine series (Cont.)

	Interventions for pregnant women						Interventions for newborn/young infants	
	Antenatal testing			Antiviral prophylaxis for prevention of MTCT of HBV			Immediately after birth	During the first 12 months after birth
	HBsAg	HBeAg	HBV DNA	Eligibility	Timing	Drug	HBIG for exposed newborn infants	Postvaccination serologic testing
Republic of Korea	Yes			NA	NA		Yes	Yes (free)
	Yes							
Samoa								
Singapore	Yes	Yes	Yes, if necessary	Recommended (HBV DNA > 200 000 IU/mL)	28–32 weeks to 4 weeks postpartum	TDF	Yes, all HBV-exposed infants	Yes, 3 months after completion of vaccination
Solomon Islands	Yes	No	No	-	-	-	No	No
Tonga	Yes							
Thailand	Yes	Yes		HBeAg + pregnant women or HBV DNA > 200 000 IU/mL	26–30 weeks to 4 weeks postpartum	TDF	Yes Out-of-pocket	Yes
Viet Nam	Yes	Yes	Yes	HBV DNA > 200 000 IU/mL	24–28 weeks	TDF	Yes, all HBV-exposed infants	No

Information updated February 2020. NA = (specific recommendation for mother/infant is) not available; AASLD = American Association for the Study of Liver Diseases; APASL = Asian Pacific Association for the Study of the Liver; EASL = European Association for the Study of the Liver; anti-HBs = hepatitis B surface antibody or antibody to hepatitis B surface antigen; TDF = tenofovir disoproxil fumarate; 3TC = lamivudine; TBV = telbivudine. No information available from American Samoa, the Federated States of Micronesia, French Polynesia, Guam, the Marshall Islands, Nauru, New Caledonia, the Commonwealth of the Northern Mariana Islands, Palau, Pitcairn Islands, Tokelau, Tuvalu, Vanuatu, and Wallis and Futuna.

2.2.4 Management of pregnant women with chronic hepatitis B virus infection

2.2.4.1 Counselling of pregnant women with chronic hepatitis B virus infection

Women identified as HBsAg-positive should receive counselling on their test result, including clear information on disease course and management. They should be helped to develop birth plans that include delivering in a health facility, postpartum and infant care, infant feeding choices, the need for further tests (including for family members and close contacts), infection control, prevention of transmission, plus lifestyle measures and disclosure (Box 4). Intensified post-test counselling and follow-up by referral to community health workers, peer counsellors or support organizations should be provided as necessary.

Box 4. Key counselling messages for hepatitis B surface antigen-positive pregnant women (9,44,45)

(Note that for most women, their HBV infection does not affect the outcome of pregnancy either for themselves or their baby. Pregnancy does not make liver disease worse.)

- You will be sent for more blood tests and a scan to check your liver *(if services are available)*.
 - If your liver shows signs of damage, you may be started on medicines to treat your infection.
 - If there are no signs of liver damage but the level of virus in your blood is high (HBV DNA $\geq 200\,000$ IU/ml (5.3 log₁₀ IU/ml) and/or a positive HBeAg test), you may be offered medicines to lower the chance of infection passing to your baby. Your doctor will discuss this with you in detail.
- It is very important that you deliver your baby in a health facility. This is safer for both you and your baby and allows your baby to be given the first dose of hepatitis B vaccination as soon as possible after birth. This will protect your baby against infection.
 - *(If HBIG is available in the country)* we can help you to deliver in a health facility where HBIG is available and affordable. HBIG gives your baby extra protection against hepatitis B infection.
- After you go home, your baby will need at least two more doses of hepatitis B vaccine. These may be given together with other routine vaccines. Your child may be offered a blood test to check for hepatitis B infection *(also called PVST)* one to two months after the last dose of hepatitis B vaccine *(e.g. at the time of measles or the first measles, mumps and rubella, or MMR, vaccination)*.
- Your care will be the same as for women without HBV infection, except that you will need regular blood tests to check your liver while you are pregnant and for several months after your baby is born.
 - After delivery, your doctor will advise you on further treatment plans. If you are taking medicines, your doctor will advise you when/if to stop. Do not stop the medicines by yourself.
- Breastfeeding is good for you and your baby, and we encourage you to breastfeed your baby. There is no risk of the hepatitis B infection passing to your baby through breast milk.
- Lifestyle factors
 - Alcohol, smoking, recreational drugs and some medicines can cause health risks to you and your baby. To protect your liver, you are advised to avoid drinking alcohol. Avoid taking medicines or traditional remedies that have not been prescribed by your doctor. If you smoke, you are advised to stop.
 - It is important that you follow a healthy diet, keep to a normal weight and that you exercise regularly, while also allowing plenty of time to rest.
- We suggest that you tell your partner and family about your test result. Your partner, other children and people living in the same house as you have a higher chance of having hepatitis B infection. We suggest they have a blood test to check for hepatitis B infection. If they do have hepatitis B, they will be linked to care and treatment. If they do not have hepatitis B, they may be offered hepatitis B vaccination.
- You may feel uncomfortable about telling other people about your infection if there is stigma related to hepatitis B infection in your community. Tell your health-care worker so he or she can support you.

2.2.4.2 Assessment of liver disease in chronic hepatitis B virus infection

Women who test HBsAg-positive need to be linked as soon as possible to care and treatment services for assessment of their own clinical condition (Box 5) and, if indicated, initiation of treatment for chronic hepatitis B for their own health or consideration of antiviral prophylaxis to reduce the risk of MTCT of HBV. The decision to treat a pregnant woman with chronic HBV infection is based on clinical assessment, age > 30 years, non-invasive assessment of liver disease and evidence of high HBV replication (HBV DNA > 20 000 IU/ml). Women who do not require treatment for their own health benefit but with HBV DNA \geq 200 000 IU/ml ($5.3 \log_{10}$ IU/ml) and/or a positive HBeAg test, should be offered tenofovir antiviral prophylaxis from 28 weeks of pregnancy until at least birth to prevent MTCT of HBV (section 2.2.3, Box 3).

Box 5. Criteria for assessment of liver disease in chronic hepatitis B virus infection and WHO-recommended treatment indications (9)

Clinical criteria for liver disease:

- Decompensated cirrhosis
 - Portal hypertension (ascites, variceal haemorrhage, hepatic encephalopathy)
 - Coagulopathy
 - Jaundice
- Advanced liver disease/cirrhosis
 - Hepatomegaly (may not always be present in advanced liver disease/cirrhosis)
 - Splenomegaly
 - Pruritus
 - Fatigue
 - Arthralgia
 - Palmar erythema
 - Oedema

Non-invasive assessment of liver disease stage:

- Aspartate aminotransferase (AST) to platelet ratio index, or APRI:
- Liver enzymes and platelet count are used to calculate the APRI score to assess for the presence of cirrhosis. $APRI = ((AST \text{ (IU/L)}/\text{upper limit of normal}) \times 100)/\text{platelet count } (10^9/\text{L})$.
- An APRI cut-off of > 2 is used to identify adults with cirrhosis in need of antiviral therapy.
- An online calculator can be found at: <http://www.hepatitisc.uw.edu/page/clinical-calculators/apri>.
- **Transient elastography** (liver stiffness scanning) may be the preferred non-invasive test in settings where it is available and affordable.

WHO criteria to determine which persons with chronic hepatitis B to treat:

- As a priority, all adults, adolescents and children with chronic hepatitis B and clinical evidence of compensated or decompensated cirrhosis (or cirrhosis based on APRI score of > 2 in adults) should be treated, regardless of alanine aminotransferase (ALT) levels, HBeAg status or HBV DNA levels.
- Treatment is recommended for adults with chronic hepatitis B who do not have clinical evidence of cirrhosis (or based on APRI score of \leq 2 in adults), but are aged over 30 years, and have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA > 20 000 IU/mL), regardless of HBeAg status.
- Where HBV DNA testing is not available, treatment may be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status.

2.2.4.3 Caring for pregnant women with chronic hepatitis B virus infection

For most women, pregnancy is not affected by chronic HBV infection and pregnancy does not worsen liver disease. Consequently, management of women with HBV infection *without advanced liver disease* can usually be conducted by providers who are not specialists in liver disease (Box 6). Table 3 summarizes recommendations from a selection of professional guidelines on pregnancy and breastfeeding in women with HBV infection. Women who have *active liver disease* are at higher risk of maternal and fetal complications, and joint management by obstetricians and hepatologists or infectious disease physicians is advisable if available. During pregnancy, immune responses are temporarily reduced, but return to normal after delivery. Some women may experience hepatitis flare-ups, marked by an increase in liver enzymes, during pregnancy or after delivery. These cases are usually asymptomatic and resolve on their own. Peripartum hepatitis flare-ups that progress to liver failure have been reported, but are uncommon.

Box 6. Information for health-care providers caring for hepatitis B surface antigen-positive pregnant women (9)

Assessment of liver disease in pregnant women with chronic HBV infection

- If services are available, link pregnant women whose antenatal HBsAg test is positive to appropriate clinical services for assessment and management of chronic HBV infection.
- Assessment of the stage of liver disease is based on age, clinical criteria and/or non-invasive tests of advanced fibrosis/cirrhosis, inflammation (AST/ALT) and viral replication (HBV DNA). The results determine who to treat and who not to treat (section 2.2.4.1, Box 4). Before starting treatment, baseline renal function tests and assessment of risk factors for renal dysfunction should be considered.
- Pregnant women who do not meet the criteria for antiviral treatment listed above but who have HBV DNA $\geq 200\,000$ IU/ml (HBV DNA $\geq 5.3 \log_{10}$ IU/m) are at increased risk of MTCT of HBV even when their infants receive timely HBIG and timely HepB birth dose.
 - Maternal antiviral prophylaxis with TDF gives additional protection to the infant and is recommended from 28 weeks' gestation at least until birth.
 - Women who present late in pregnancy who meet eligibility criteria for antiviral prophylaxis should be started on TDF without delay. Their infants need to be prioritized for timely HepB birth dose and timely HBIG (if available) as there will be limited time for antiviral drugs to reduce maternal HBV DNA levels in this situation.

Management of pregnancy

- Antenatal management of pregnant women with chronic HBV infection is generally the same as for uninfected women: monitor ALT (and HBV DNA levels if available) for hepatitis flare-ups during pregnancy.

Management of labour and delivery

- Reassure women that their delivery will be managed in a similar way to that for women without HBV infection.
- Practise careful infection control measures and universal precautions during delivery, as for any pregnancy.
- Conduct caesarean section only if there are obstetric indications.

Infant immunization

- Ensure that infants of HBsAg-positive mothers receive the timely HepB birth dose (and HBIG if available) as soon as possible after delivery (and within 24 hours).

Box 6. Information for health-care providers caring for hepatitis B surface antigen-positive pregnant women (9) (Cont.)

Breastfeeding

- HBV-infected mothers are encouraged to breastfeed their infants as there is no evidence of HBV transmission through breastfeeding.
- There is limited information available on breastfeeding in women taking TDF for treatment of chronic hepatitis B, but breastfeeding can be considered in this situation (note that **HIV-infected** women taking TDF as part of their antiretroviral therapy (ART) regimen are advised to continue breastfeeding and there are data from the HIV literature to support the safety of TDF during breastfeeding) (46,47).

Monitoring women after pregnancy

- Monitor ALT (and HBV DNA levels if available) monthly for the first three months after delivery and then every three months during the first year for hepatitis flare-ups, especially if ART has been stopped after delivery.
- Review the woman's clinical condition at least every 12 months and conduct available tests (ALT, HBV DNA, HBeAg and APRI score or liver stiffness scanning). Start antiviral treatment if indicated.
- Monitor renal function every 12 months if taking TDF.

Mothers of infants with chronic HBV infection

- If the infant's HBsAg test is positive (1–2 months after completing the hepatitis B vaccine series), provide education on prevention of transmission to caregivers and ensure that all family members and close household contacts have been identified and offered HBsAg testing and hepatitis B vaccination if unprotected.
- Ensure the infant is linked to regular follow-up to monitor liver enzymes (AST/ALT), HBV serology and viral replication (HBV DNA viral load).

Table 3. Pregnancy and breastfeeding recommendations for women with chronic hepatitis B virus infection in selected guidelines

Intervention	Royal Australian and New Zealand College of Obstetricians and Gynaecologists: 2016 (42)	American Association for the Study of Liver Diseases (AASLD): 2016, 2018 (38,39)	European Association for the Study of the Liver (EASL): 2017 (41)	Asian-Pacific clinical practice guidelines: 2015 (40)
Prenatal counselling	<ul style="list-style-type: none"> • Counsel on potential risk of transmission with invasive procedures. • Non-invasive testing may be an option (cell-free DNA-based testing). • Amniocentesis carries a lower risk than chorionic villus sampling. • Avoid transplacental amniocentesis. 	<ul style="list-style-type: none"> • Discuss the potential risk of MTCT of HBV with amniocentesis with HBsAg-positive mothers who have a high HBV DNA level. 	Not mentioned	Not mentioned
Clinical management	<ul style="list-style-type: none"> • Link to care and treatment services for long-term follow-up. 	<ul style="list-style-type: none"> • Treat women who meet standard indications for treatment of HBV infection. • Manage women with cirrhosis as high-risk obstetric cases and treat with TDF to prevent decompensation. 	<ul style="list-style-type: none"> • Treat pregnant women with advanced fibrosis or cirrhosis, with TDF. • Continue TDF in women already on therapy. 	<ul style="list-style-type: none"> • Treat pregnant women who need antiviral therapy with TDF.
Mode of delivery	<ul style="list-style-type: none"> • Conduct caesarean section for obstetric indications only 	<ul style="list-style-type: none"> • Caesarean section is not indicated. 	Not mentioned	Not mentioned
Invasive procedures during labour	Avoid: <ul style="list-style-type: none"> • fetal scalp electrodes • fetal scalp blood sampling 	Not mentioned	Not mentioned	Not mentioned
Breastfeeding in women with chronic HBV infection	<ul style="list-style-type: none"> • Breastfeeding not shown to increase rates of perinatal transmission, provided appropriate immuno-prophylaxis has been given to the infant at birth. 	<ul style="list-style-type: none"> • Breastfeeding is not prohibited. 	<ul style="list-style-type: none"> • Breastfeeding is not contraindicated. 	<ul style="list-style-type: none"> • Breastfeeding is not discouraged if the newborn infant receives immuno-prophylaxis.

Table 3. Pregnancy and breastfeeding recommendations for women with chronic hepatitis B virus infection in selected guidelines (Cont.)

Intervention	Royal Australian and New Zealand College of Obstetricians and Gynaecologists: 2016 (42)	American Association for the Study of Liver Diseases (AASLD): 2016, 2018 (38,39)	European Association for the Study of the Liver (EASL): 2017 (41)	Asian-Pacific clinical practice guidelines: 2015 (40)
Breastfeeding in women taking TDF for treatment or prevention of MTCT of HBV	<ul style="list-style-type: none"> Breastfeeding is not contraindicated in women receiving TDF. 	<ul style="list-style-type: none"> Breastfeeding is not contraindicated. Drug labels do not recommend breastfeeding when taking TDF, but data from HIV literature support its safety. TDF is minimally excreted in breast milk. 	<ul style="list-style-type: none"> Breastfeeding is not contraindicated in women on TDF-based treatment or prophylaxis. 	<ul style="list-style-type: none"> Breastfeeding is discouraged during treatment. TDF given for prevention of MTCT of HBV can be stopped at birth so that the mother can breastfeed.
Follow-up of mothers	<ul style="list-style-type: none"> Monitor closely for hepatitis flare-up for several months postpartum. Follow up lifelong to monitor complications such as liver disease and liver cancer. 	<ul style="list-style-type: none"> Monitor closely for up to six months after delivery for hepatitis flare-ups. Follow up long term to assess future need for therapy. 	Not mentioned	Not mentioned

2.2.4.4 Breastfeeding and chronic hepatitis B virus infection

HBV is not transmitted through breastfeeding and women with chronic HBV infection can be encouraged to breastfeed their newborn infants.

WHO guidance states that eligible pregnant and breastfeeding women living with HBV infection can safely use tenofovir (10). TDF levels in breast milk are low and its oral bioavailability is limited. Exposure to TDF is lower from breastfeeding than from in utero exposure. Existing data from the HIV literature suggest that TDF can safely be continued during breastfeeding, although drug labels generally recommend avoidance of breastfeeding, citing lack of evidence of safety (46).

2.2.5 Hepatitis B immunoglobulin for infants born to women with chronic hepatitis B virus infection

There is a longstanding body of evidence demonstrating improved protection against MTCT of HBV when timely HBIG is given in addition to the timely HepB birth dose to infants of HBsAg-positive mothers, particularly when the mother is also HBeAg-positive (5,9,13). Timely HBIG given in addition to HepB birth dose prevents 94% of perinatal infections (48–51). Full-term babies born to mothers who are HBsAg-positive but HBeAg-negative are at lower risk of MTCT of HBV than those whose mothers are also HBeAg-positive. Protection against perinatally acquired HBV infection may not be significantly improved by the addition of HBIG to the timely HepB birth dose for these infants.

There is no formal WHO recommendation on the use of HBIG for infants born to women with chronic HBV infection. However, WHO recognizes that HBIG prophylaxis given together with hepatitis B vaccination may

be of additional benefit to newborn infants whose mothers are HBsAg-positive, particularly if they are also HBeAg-positive (16). Use of HBIG is standard care in many countries. Where HBIG is available, infants born to all HBsAg-positive mothers are given a single dose of HBIG within 12 to 24 hours of birth in addition to the timely HepB birth dose. Injections should be given in different sites.

HBsAg-positive pregnant women should be encouraged and supported to deliver at a health facility where HBIG is available to ensure that it can be given within 24 hours of birth or sooner. Strategies for ensuring timely administration of HepB birth dose and HBIG in areas where substantial numbers of deliveries take place outside health facilities may need to be developed and strengthened.

2.2.6 Follow-up of infants born to women with chronic hepatitis B virus infection

Follow-up of HBV-exposed infants, including postvaccination serological testing (PVST), conducted 1–2 months after completion of the hepatitis B vaccine series, is important for clinical and programmatic reasons (Table 4).

Follow-up guides clinical management of the infant/young child born to an HBV-infected mother. Several scenarios are possible. The infant may be:

1. infected with HBV;
2. uninfected and have responded adequately to the hepatitis B vaccine series; or
3. uninfected but may not have responded to the hepatitis B vaccine and needs to be revaccinated.

PVST is also essential to monitor the outcomes and impact of services and interventions for the prevention of MTCT of HBV. The MTCT rate is calculated as the proportion of infants with chronic HBV infection among women who had a positive HBsAg test during antenatal screening.

HBsAg testing: The primary purpose of PVST is to detect or exclude chronic HBV infection in the infant through HBsAg testing. If a rapid, point-of-care test is used and the result is positive, confirmatory testing may be considered, if available. Infants found to have hepatitis B infection (i.e. those who are HBsAg-positive) must be linked to appropriate clinical care and follow-up and their caregivers counselled on measures to prevent transmission of infection. Family and household members should be offered HBsAg testing followed by hepatitis B vaccination if uninfected and unvaccinated, or linkage to care and treatment if indicated.

Anti-HBs testing: Countries may choose to offer hepatitis B surface antibody (anti-HBs) testing (testing for antibody to HBsAg, a marker of immunity to HBV) (9) in addition to HBsAg testing, using a method that allows quantitative determination of anti-HBs levels. The detection limit of the test should be < 10 mIU/ml (5). An anti-HBs level of ≥ 10 mIU/ml indicates immunity (Table 5). HBV-exposed infants who completed the primary series but remain both anti-HBs and HBsAg-negative may be considered for a revaccination schedule¹⁸ followed by repeat PVST 1–2 months after the last dose of hepatitis B vaccine (48).

The WHO position paper on hepatitis B vaccines states that PVST should be carried out 1–2 months after administration of the last dose of the hepatitis B vaccine series when the antibody response is greatest (5).

From a programmatic perspective, infant follow-up and PVST are best integrated into well-child services. The timing can be guided by existing routine health-care interventions for the child (such as the time of the first measles vaccination at 9 months of age).

¹⁸ United States Advisory Committee on Immunization Practices (ACIP) 2018: HBsAg-negative infants with anti-HBs < 10 mIU/mL should be revaccinated with a single dose of hepatitis B vaccine and receive postvaccination serologic testing 1–2 months later (new recommendation in 2018). Infants whose anti-HBs remains < 10 mIU/mL following single-dose revaccination should receive two additional doses of hepatitis B vaccine to complete the second series, followed by postvaccination serologic testing 1–2 months after the final dose.

Table 4. Purpose of tests conducted during postvaccination serological testing

PVST conducted on infants born to HBsAg-positive mothers	Test	Purpose
	HBsAg	Diagnosis of chronic HBV infection in HBV-exposed infants Monitoring of the EMTCT programme
	Anti-HBs	Evaluation of the HBV-exposed infant's response to vaccination

Table 5. Interpretation of postvaccination serological testing results and actions to be taken

PVST results	Interpretation	Action
HBsAg-positive	Infant with confirmed hepatitis B infection	Refer to clinical services for follow-up and care Offer HBsAg testing to household contacts
HBsAg-negative Anti-HBs \geq 10 mIU/ml	Infant immune to hepatitis B infection	Infant is protected and needs no further management
HBsAg-negative Anti-HBs < 10 mIU/ml	Uninfected, susceptible (non-immune) infant	Consider revaccination with three doses of hepatitis B vaccine

2.3 Programmatic considerations

2.3.1 Governance

Strong government leadership, commitment and multisectoral collaboration with a wide range of stakeholders are needed at all levels, backed by sufficient and sustainable financing. Collaboration with and between RMNCH, Expanded Programme on Immunization (EPI) and HIV/STI programmes is critical for the success of the EMTCT programme. Also, EMTCT of HBV activities must be situated within the broader national/regional response to hepatitis B/viral hepatitis. Normative guidance, including policies, plans, guidelines and implementation protocols, is needed to ensure standardized implementation of services. Legal barriers to the successful implementation of triple EMTCT interventions within a human rights framework may need to be examined and addressed, if present. Civil society involvement in the planning and development of the EMTCT programme and continuing all the way through to implementation can significantly strengthen EMTCT and other programmes and should be encouraged.

2.3.2 Financing of programmes and services

Provision of EMTCT of HBV interventions for pregnant women should be guided by the principles of universal health coverage (UHC) so that a pregnant woman's ability to pay does not determine her access to available services. Including HBV EMTCT interventions in essential service packages for antenatal, delivery and postpartum care and in national health insurance schemes, where available, can minimize out-of-pocket expenses. This will ensure that cost is not a barrier to sustainable access to triple EMTCT services for all pregnant women and their families.

Integration of EMTCT of HIV, hepatitis B and syphilis (triple EMTCT) into RMNCH services to improve efficiencies in the use of health system resources enables greater coverage and reduces missed opportunities. Benefits of

introducing universal antenatal HBsAg testing go beyond prevention of MTCT of HIV, hepatitis B and syphilis. They include linkage to prevention interventions for pregnant women whose tests are negative as well as to care and treatment for pregnant women who test positive. Identification of HBsAg-positive pregnant women and treatment of eligible women with chronic HBV infection enables prevention of cirrhosis and cancer and expansion of testing and care for other affected family members.

Cost-effectiveness analyses of antenatal testing and other interventions can be used to support high-level advocacy for allocation of resources. A modelling study in Cambodia showed that implementing integrated triple EMTCT services was highly cost-effective and would reduce MTCT of HBV by an estimated 76%, from 14.1% to 3.4%; MTCT of syphilis by 51%, from 9.4% to 4.6%; and MTCT of HIV by 8%, from 6.6% to 6.1%. Annually, 3200 infant hepatitis B infections would be prevented, at a cost of US\$ 114 per disability-adjusted life year prevented (52).

WHO recommends serological testing for HCV antibody for adults and adolescents who are either part of a population with high HCV seroprevalence or who have a history of exposure and/or high-risk behaviours for HCV infection. Depending on country considerations and epidemiological context, HCV testing should also be offered in settings with a $\geq 2\%$ or $\geq 5\%$ HCV antibody seroprevalence in the general population, with linkage to prevention, care and treatment services. Mongolia offers antenatal HCV testing to all pregnant women as part of EMTCT+;¹⁹ in the Region of the Americas, pregnant women are offered testing for Chagas disease under EMTCT Plus (53).

2.3.3 Stigma and discrimination

Stigma and discrimination may be experienced by families affected by hepatitis B, and antenatal HBsAg testing has the potential to generate stigma and discrimination against people diagnosed with chronic HBV infection. Confidentiality of test results must always be ensured. Steps should be taken to prevent stigma and discrimination against pregnant women and other family members living with hepatitis B, in health-care settings and in the community.

Lessons learnt in the programmatic response to stigma and discrimination in the context of HIV can be applied to hepatitis B. Health workers need to receive appropriate training and be knowledgeable about viral hepatitis and EMTCT of HBV to reduce stigma and discrimination in health-care facilities. Integration of services for viral hepatitis at the primary care level where RMNCH services are also provided can reduce stigma and discrimination by normalizing services. Community-based services and engagement of affected populations can help to raise awareness and improve acceptability and utilization of services.

Educating pregnant women and their families about hepatitis B transmission and the benefits of vaccination can reduce stigma in the community and improve vaccination coverage. Infected pregnant women should receive information about the benefits of timely HepB birth dose, HBIG (where available) and antiviral prophylaxis for pregnant women with high HBV DNA to prevent MTCT of HBV. PVST of infants born to mothers with chronic hepatitis B identifies infants with an inadequate immune response to the initial hepatitis B vaccine series who might require additional vaccination and infants who developed chronic HBV infection and need further follow-up.

2.3.4 Introducing additional interventions beyond immunization

High coverage of hepatitis B vaccination of newborn and young infants remains the most effective and cost-effective means of providing hepatitis B prevention in all countries (Table 6). Hepatitis B vaccination programmes should be strengthened nationally and subnationally, with the aim of achieving $\geq 95\%$ coverage

¹⁹ Order of the Health Minister of Mongolia Number 288 (2018).

of the timely HepB birth dose and HepB3 for all infants nationwide, regardless of the HBsAg status of their mothers. Areas where deliveries away from health facilities are still common should develop strategies to guarantee the timely administration of HepB birth dose (and HBIG).

Universal antenatal HBsAg testing should be introduced as a programmatic addition to optimal delivery of the timely HepB birth dose and completion of the hepatitis B vaccine series for all infants. Introduction of universal antenatal HBsAg testing provides an opportunity to offer preventive interventions for women who test HBsAg-negative and improve the management of HBV-infected pregnant women as part of the broader viral hepatitis response as well as to reduce MTCT of HBV further towards global elimination targets. A positive antenatal HBsAg test indicates the need for further interventions to protect the health of mothers and their infants.

As a minimum, HBsAg-positive pregnant women should receive counselling and information on hepatitis B infection. This should include how to avoid transmission of infection to family and household members and the importance of facility-based delivery to ensure that their infant receives a timely HepB birth dose (as well as the additional benefits of facility delivery). Other interventions needed to achieve EMTCT of HBV include timely HBIG given to exposed infants and linkage of pregnant women with chronic HBV to clinical services for further assessment.

Table 6. Protective efficacy of interventions to prevent mother-to-child transmission of hepatitis B virus

		MTCT of HBV
No intervention (13)	Mother HBsAg-positive and HBeAg-positive	70%–90% of infants become infected 90% of infected infants develop chronic infection
	Mother HBsAg-positive only	10% of infants become infected 90% of infected infants develop chronic infection
Interventions		Protective efficacy in preventing MTCT of HBV
Timely HepB birth dose alone		70%–95% (13)
Timely HepB birth dose + HBIG		94% (48–51)
Timely HepB birth dose + completion of hepatitis B vaccine series		> 95% (5)
Timely HepB birth dose + completion of hepatitis B vaccine series + HBIG + maternal antiviral prophylaxis		> 98% (31–34)
Timely HepB birth dose + completion of hepatitis B vaccine series without HBIG but with maternal antiviral prophylaxis		Awaiting results of trials

When planning for the introduction of interventions beyond high hepatitis B vaccination coverage of infants (timely HepB birth dose plus HepB3), countries need to consider whether to target all HBsAg-positive pregnant women and their infants for additional interventions for preventing MTCT of HBV. Alternatively, they could prioritize those at highest risk (i.e. pregnant women who are HBeAg-positive and/or have high HBV DNA).

Countries conducting antenatal HBsAg testing and planning to introduce or scale up HBIG access may decide whether HBIG is given to infants of all HBsAg-positive women or, if HBeAg testing is available, selectively to infants of HBeAg-positive mothers. Evidence of clinical benefit is greatest for infants of HBeAg-positive

mothers. Selective provision of HBIG to infants born to HBsAg-positive mothers who are also HBeAg-positive may have advantages in terms of cost, procurement and distribution of HBIG, as fewer doses will be required. From a programmatic perspective, however, it may be simpler and more effective to give HBIG to infants of all HBsAg-positive mothers, regardless of maternal HBeAg status. This would help to ensure that babies at high risk are not missed due to gaps in HBeAg testing coverage²⁰ or problems with returning and acting on results in a timely manner. Adopting this latter approach does have other programmatic implications related to supply, quality assurance (including maintenance of the cold chain) as well as cost of procurement and administration of HBIG, which need to be taken into consideration.

HBV DNA testing is the gold standard for assessing eligibility of HBsAg-positive pregnant women for maternal antiviral prophylaxis, but it is costly and may not be widely available in resource-limited settings. HBeAg testing may be used as an alternative to HBV DNA or as a screening test to identify high-risk women for HBV DNA testing in resource-limited settings. However, currently (December 2020) there is no WHO-prequalified point-of-care HBeAg test available.

Integrating antenatal HBV testing with routine antenatal HIV and syphilis testing conducted at the first antenatal visit can bring programmatic and individual benefits, increasing the efficiency and quality of RMNCH services. For example, staff at antenatal clinics can provide pretest information and conduct testing for all three infections together. Also, pregnant women can be offered more comprehensive antenatal care during the same visit at the same facility. Women benefit through fewer clinic visits, saving time and travel expenses while ensuring rapid diagnosis and facilitating linkage to care. Programmatic benefits include increasing efficiencies during antenatal care, reducing missed opportunities for diagnosis, improving linkage to care and reducing loss to follow-up.

The use of rapid tests (including dual tests for HIV and syphilis and in the future multiplex tests incorporating hepatitis B and other tests) facilitates integrated antenatal testing. This enables decentralized point-of-care testing with rapid access to results, reduced delays in linkage to care and treatment and less loss to follow-up. Collaboration between disease-specific, immunization and RMNCH programmes allows programmatic activities and training to be harmonized. This has a synergistic effect on decreasing MTCT of multiple diseases (52).

2.3.5 Health workforce development and training

Health workforce development may be needed to ensure that all staff involved in providing EMTCT interventions are trained appropriately. Staff at antenatal clinics must be trained to include information on EMTCT of HIV, hepatitis B and syphilis in antenatal education, to conduct universal antenatal testing for HIV, hepatitis B and syphilis and link HBsAg-positive pregnant women identified through antenatal testing to care and treatment.

Capacity-building strategies related to EMTCT of HBV may include the development and introduction of testing and clinical management algorithms for antenatal testing of all pregnant women and timely administration of the HepB birth dose to all infants. Health-care providers involved in the management of pregnant women with chronic hepatitis B may require additional training on the use of antiviral drugs for treatment or prophylaxis, the importance of health facility deliveries and timely infant HepB birth dose and the use of HBIG (if available). They may also require training on follow-up of exposed infants, including routine PVST and management and follow-up of women with HBV infection during pregnancy and after delivery.

²⁰ In settings with high levels of HBV–HDV co-infection, it may be preferable to give HBIG to infants of all HBsAg-positive mothers, pending further evidence on transmission risk in HBV–HDV co-infected women.

2.3.6 Diagnostic tests and commodities

It is critical that diagnostic tests used for antenatal testing of pregnant women and PVST of HBV-exposed infants are of high quality and produce consistent results. WHO-prequalified tests or tests that have been quality-assured by stringent regulatory authorities provide the benchmark for diagnostics. In situations without access to WHO-prequalified commodities and no stringent regulatory authority, diagnostic tests used for clinical or public health purposes must be evaluated for high sensitivity and specificity by national regulatory authorities. A uniform national approach to testing and standardization of test kits used throughout the country may enable bulk procurement at better prices and simplify quality assurance procedures.

Relevant policies and standard operating procedures, disseminated to both government and private health facilities, need to be in place to ensure that monovalent hepatitis B vaccine is always available in delivery rooms and postnatal wards. This will ensure that the timely HepB birth dose can be given to all newborn infants, including those delivered via caesarean section and those with low birth weight. The quality and safety of HBiG must be ensured through national regulatory, procurement and supply systems. Licensing/registration of TDF and other antivirals for use in treatment of chronic hepatitis B and prevention of MTCT of HBV and inclusion in the essential medicines list may be required.

2.3.7 Data

High-quality data systems are needed to track triple EMTCT interventions and outcomes across the clinical continuum from pre-conception through pregnancy and delivery to postpartum care of the woman and follow-up of the infant. Data are needed to monitor and evaluate the EMTCT programme to improve management of pregnant women and their infants and to generate information on programme outcomes and achievement of targets. Programmatic data parameters are entered into mathematical models used to calculate MTCT rates and other information needed for validation of EMTCT.

There are often challenges with collecting and reporting triple EMTCT-related data because they are traditionally collected by different programmes (RMNCH and EPI as well as disease-specific programmes). Data systems need to be modified and additional indicators introduced to capture the full range of HBV EMTCT-related interventions including infant follow-up and results of PVST. HBV EMTCT data are also important as a component of the broader hepatitis response, and consideration needs to be given to how to link all the data.

Data on women who are diagnosed with hepatitis B during pregnancy, labour, delivery or postnatally need to be captured by national health information or surveillance systems. The mother's HBsAg test result should be entered in the maternal health record and included together with the infant's vaccination status in the child health record or vaccination card. This will enable linking of mother–infant pairs for monitoring purposes. Hepatitis B immunization data should be maintained, reported, monitored and linked to EMTCT data.

3. VALIDATION OF ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS



3.1 Global and regional targets for viral hepatitis and elimination of mother-to-child transmission of HIV, hepatitis B and syphilis

Global and regional targets for viral hepatitis and EMTCT of HIV, hepatitis B and syphilis are set out and aligned in the *Global Health Sector Strategies on HIV, Viral Hepatitis and Sexually Transmitted Infections (STIs), 2016–2021* (3,54,55), the *Global Guidance on Criteria and Processes for Validation: Elimination of Mother-to-Child Transmission of HIV and Syphilis* (54), the *Regional Action Plan for Viral Hepatitis in the Western Pacific 2016–2020* (57) and the *Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific, 2018–2030* (1).

The WHO *Global Health Sector Strategy on Viral Hepatitis 2016–2021* defines targets for elimination of viral hepatitis as a major global public health threat by 2030, with interim targets set for 2020 (3). The *Regional Action Plan for Viral Hepatitis in the Western Pacific 2016–2020* aligns with the Global Health Sector Strategy, setting regional 2017 milestones and 2020 targets (Table 7) for hepatitis control. Other WHO regions use different HBsAg prevalence levels and age group definitions²¹ to define intermediate control targets for 2020. All regions are working towards the 2030 global hepatitis B elimination target of a 90% reduction in new cases of chronic hepatitis B infection (equivalent to < 0.1% HBsAg prevalence among children aged 5 years).

In September 2018, the Western Pacific Region Expert Resource Panel (ERP) on Hepatitis B proposed an interim target of < 0.3% HBsAg prevalence among children aged 5 to be achieved by 2025 by countries that had already reached the < 1% target among 5-year-old children. The Panel stated that all countries in the Region should reach the < 1% target by 2025 (21). This target remains under discussion.

Table 7. Global and regional targets for hepatitis B

	Year	Target
Global ^a	2030	<ul style="list-style-type: none"> • 90% reduction in new cases of chronic viral hepatitis B infections (equivalent to 0.1% HBsAg prevalence among children) • 90% coverage of timely HepB birth dose vaccination and other interventions to prevent MTCT of HBV (hepatitis core indicator C3a)^d • 90% coverage of HepB3 (hepatitis core indicator C3b)
	2020	<ul style="list-style-type: none"> • 30% reduction in new cases of chronic viral hepatitis B infections (equivalent to 1% HBsAg prevalence among children) • 50% coverage of timely HepB birth dose vaccination and other interventions to prevent MTCT of HBV (hepatitis core indicator C3a) • 90% coverage of HepB3 (hepatitis core indicator C3b)
Western Pacific Region ^b	2025 targets (proposed) ^c	<ul style="list-style-type: none"> • Reduce HBsAg prevalence to < 1% in 5-year-old children in all countries/areas • In countries/areas with < 1% HBsAg prevalence in 5-year-olds by 2017, further reduce HBsAg prevalence to < 0.3%
	2020 targets	<ul style="list-style-type: none"> • MTCT rate of HBV < 2% in countries that have achieved < 1% HBsAg seroprevalence in children aged 5 years • In countries that have achieved < 1% HBsAg seroprevalence in children aged 5 years, further reduce MTCT of HBV
	2017 milestones	<ul style="list-style-type: none"> • HepB birth dose coverage ≥ 95% and HepB3 coverage ≥ 95% • < 1% HBsAg seroprevalence in children aged 5 years^e

^a Global health sector strategy on viral hepatitis 2016–2021 (3).

^b Regional action plan for viral hepatitis in the Western Pacific 2016–2020 (57).

^c Third Strategic and Technical Advisory Committee (STAC) for viral hepatitis, Manila, Philippines, 17–18 September 2018 (21).

^d Monitoring and evaluation for viral hepatitis B and C: recommended indicators and framework (58).

^e WHO Regional Committee for the Western Pacific resolution WPR/RC64.R5 (59).

²¹ WHO's African Region < 2% in < 5-year-olds; Eastern Mediterranean Region < 1% in < 5-year-olds; Western Pacific Region < 1% in ≥ 5-year-olds; South-East Asia Region ≤ 1% in 5-year-olds; European Region ≤ 0.5% in 5 to 10-year-olds; and Region of the Americas ≤ 0.1% in 5-year-olds.

The impact indicator and target for elimination of hepatitis B set in the *Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific, 2018–2030* are shown in Table 8, together with the impact indicators and targets for EMTCT of HIV and syphilis. The indicator for HBsAg prevalence among children aligns with the *Global Health Sector Strategy on Viral Hepatitis 2016–2021* incidence indicator, while the MTCT rate of HBV indicator was proposed in the *Regional Action Plan for Viral Hepatitis in the Western Pacific 2016–2020*.

Table 8. Triple elimination of mother-to-child transmission impact indicators and targets

	Impact indicator	Target
Hepatitis B	HBsAg prevalence among children	≤ 0.1%
	MTCT rate of HBV	< 2%
HIV	Case rate of new paediatric HIV infections due to MTCT of HIV AND	≤ 50 per 100 000 live births
	MTCT rate of HIV	< 5% in breastfeeding populations OR < 2% in non-breastfeeding populations
Syphilis	Case rate of congenital syphilis infections	≤ 50 per 100 000 live births ^a

^a The WHO global surveillance case definition for congenital syphilis is:

- 1) a live birth or fetal death at > 20 weeks of gestation or birth weight > 500 g (including stillbirth) born to a woman with positive syphilis serology and without adequate syphilis treatment; or
- 2) a live birth, stillbirth or child aged < 2 years born to a woman with positive syphilis serology or with unknown serostatus and with laboratory and/or radiographic and/or clinical evidence of syphilis infection (regardless of timing or adequacy of maternal treatment) (56).

The Regional EMTCT Framework also defines EMTCT process indicators and targets for hepatitis B, HIV and syphilis as well as for RMNCH indicators (Table 9). A comparison of infant hepatitis B vaccination coverage targets for the Global Health Sector Strategy, the Regional Action Plan and the Regional EMTCT Framework is shown in Table 10.

Table 9. Triple elimination of mother-to-child transmission process indicators and targets

	Process indicator	Target
RMNCH	Percentage of pregnant women attending antenatal care at least once (ANC1)	≥ 95%
	Percentage of pregnant women attending antenatal care at least four times (ANC4) ^b	≥ 95%
	Proportion of births attended by skilled health personnel	≥ 95%
Hepatitis B^a	Percentage of ANC attendees tested for HBsAg	≥ 95%
	Percentage of infants receiving a birth dose of hepatitis B vaccine	≥ 95%
	Coverage of hepatitis B vaccine third dose (HepB3) among infants	≥ 95%
HIV	Percentage of pregnant women with known HIV status (includes both newly tested and those with known status)	≥ 95%
	Percentage of pregnant women living with HIV who received antiretroviral therapy (ART)	≥ 95%
Syphilis	Percentage of women accessing ANC who were tested for syphilis	≥ 95%
	Percentage of pregnant women with positive syphilis serology who were treated adequately	≥ 95%
	Stillbirth rate (per 1000 total births) ^c	< 12

^a Additional indicators and targets may be added based on evolving WHO guidance and recommendations on additional interventions required for EMTCT of HBV (e.g. antiviral treatment coverage of HBV-infected pregnant women).

^b Additional indicator for validation of EMTCT.

^c Countries are encouraged to evaluate the percentage of stillbirths attributable to maternal syphilis.

Table 10. Comparison of infant hepatitis B vaccination coverage targets

	Year	HepB birth dose	HepB3
Global health sector strategy on viral hepatitis 2016–2021	2020	50%	90%
	2030	90%	90%
Regional action plan for viral hepatitis in the Western Pacific 2016–2020	2017	≥ 95%	≥ 95%
Regional framework for the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018–2030	Process target for elimination	≥ 95%	≥ 95%

3.2 Existing validation mechanisms

3.2.1 Hepatitis B verification

The verification process for documenting achievement of < 1% HBsAg seroprevalence among 5-year-old children in the Western Pacific Region was established in 2007 and revised in 2011 (4,60,61). Verification is conducted by the ERP, an independent international group of experts appointed by the WHO Regional Director for the Western Pacific. Verification is based on HBsAg seroprevalence data obtained through a nationally representative serological survey among children aged 5 years or older, using quality-assured testing assays and laboratory procedures. In addition, programmatic data indicating achievement of key vaccination targets for hepatitis B vaccine coverage nationally and subnationally for five years preceding the verification are examined by the verification panel.

3.2.2 Elimination of mother-to-child transmission of HIV and syphilis

The *Global Guidance on Criteria and Processes for Validation: Elimination of Mother-to-Child Transmission of HIV and Syphilis* was issued by WHO in 2014 and updated in 2017 (56). It has been adapted for use in the Asia and Pacific region (62). EMTCT of HBV is not included in this Global Guidance but is planned for the next revision in 2021, as there is recognition of the benefits of an integrated approach to triple EMTCT. Also, several regions are moving towards triple EMTCT or triple EMTCT+ (which includes EMTCT of HCV in Mongolia and EMTCT of Chagas disease in the Region of the Americas). Validation assessments of EMTCT of HIV and syphilis are conducted (jointly or separately) by a Regional Validation Team, drawn from a pool of independent experts. This Team submits a report to the Global Validation Advisory Committee via the Regional Validation Secretariat, for further review. Official notification of validation is provided by the Global Validation Secretariat. Validation assessments are based on evidence submitted by the National Validation Committee, covering details of EMTCT-related data (both programme and modelled data) and programme and laboratory services. Interventions must be implemented in a manner consistent with national, regional and global standards of human rights, considering principles of gender equality and including meaningful community engagement.

3.2.3 Definition, methods and metrics for elimination of mother-to-child transmission of hepatitis B virus

The methods and metrics for validating EMTCT of HBV are a work in progress. For details of ongoing discussions, see *Prevention of Mother-to-Child Transmission of Hepatitis B Virus (HBV): Guidelines on Antiviral Prophylaxis in Pregnancy* (10).

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