Release Date: 21 June 2021
Expiration Date: 20 June 2022
CME / CPD / CNE /PEM point accreditation *(please refer to the test paper for details)*

Prevention of mother-to-child transmission of hepatitis B virus

Introduction

Hepatitis B is a major global health problem. Globally, an estimated 257 million people were chronically infected with hepatitis B virus (HBV) in 2015. About 900 000 deaths were attributed to HBV, mostly as a result of cirrhosis and hepatocellular carcinoma. In Hong Kong, the latest territory-wide epidemiological study conducted in 2015 - 2016 gave an age- and sex-adjusted prevalence of hepatitis B surface antigen (HBsAg) at 7.2%, implying that over 500 000 people were having chronic hepatitis B. The major burden of HBV infections lies in the adult population (aged 30 or above) who did not benefit from the universal childhood hepatitis B immunisation programme, which started in 1988. Surveillance data in 2019 showed that HBsAg seroprevalence among antenatal women was around 4%.

The role of prevention of mother-to-child transmission in HBV elimination

Mother-to-child transmission (MTCT) is an epidemiologically important route of HBV transmission and accounts for the prevalence of HBV infection in Hong Kong. Age is a key factor in determining the risk of chronic HBV infection. Chronicity is common following acute HBV infection in 80 - 90% of neonates and in 30 - 50% of young children under the age of 6 years, while it rarely occurs among healthy adults (<5%) [1]. If left untreated, 15 - 40% of persons with chronic HBV infection will develop cirrhosis, liver failure or liver cancer in their lifetime [2]. Most of the disease burden of chronic HBV infection comes from infection acquired soon after birth or during early childhood, especially in high-prevalence settings [3].

Aiming at eliminating viral hepatitis as a major public health threat by 2030, the World Health Organization (WHO) developed the *Global health sector strategy on viral hepatitis, 2016 - 2021*, which outlines a set of global impact and service coverage targets. WHO has set a clear target of achieving HBsAg prevalence at 0.1% or below among children 5 years of age by 2030, as surrogate of a 90% reduction in incidence of chronic HBV infection [4]. Prevention of MTCT plays a crucial role in hepatitis B elimination.

Interventions to prevent MTCT of HBV

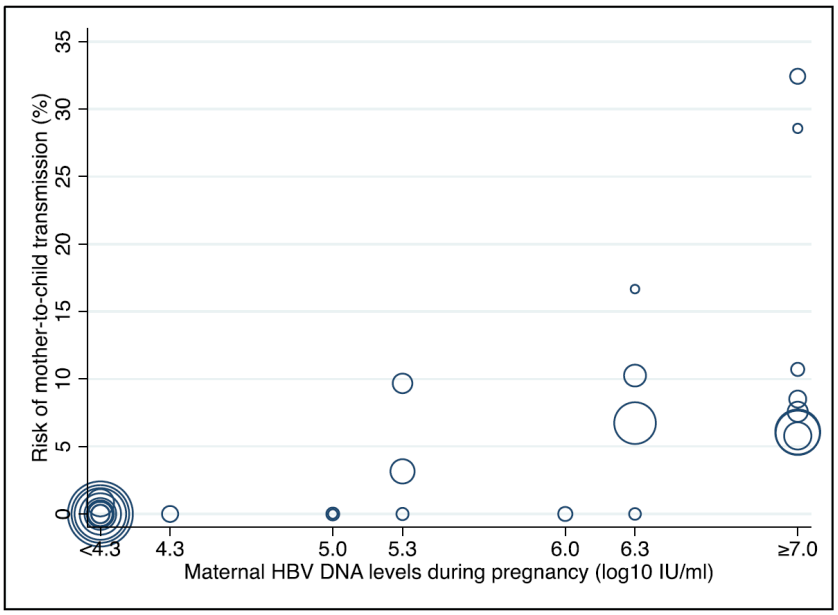
Hepatitis B vaccination is the mainstay of prevention of MTCT. All infants should receive their first dose of hepatitis B vaccine as soon as possible after birth, preferably within 24 hours. The birth dose should be followed by two or three doses to complete the primary series. A primary three-dose hepatitis B vaccination can induce protective antibody concentration in more than 95% of healthy infants, children and young adults [5]. A meta-analysis found that infants who received the first dose at birth, compared to infants receiving placebo or no intervention, were less likely to become infected when born to HBV-infected mothers (relative risk [RR]: 0.28, 95% confidence interval [CI]: 0.20 – 0.40) [6].

Passive immunoprophylaxis by administering hepatitis B immunoglobulin (HBIG) within 24 hours after birth can confer additional protection to infants born to HBsAg-positive mothers, as compared with vaccine alone (RR: 0.54, 95% CI: 0.41 – 0.73) [6].

WHO recommends that, in settings with an intermediate (≥ 2%) or high (≥ 5%) HBsAg seroprevalence in the general population, ***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 also be offered HBV testing services. [7]

Nevertheless, studies showed that 0.7% – 1.1% of infants born to HBV-infected mothers develop infection, despite universal antenatal screening, hepatitis B vaccination, and prophylaxis with HBIG at birth [8-10]. A recent WHO-commissioned meta-analysis of 13 studies assessed the risk of MTCT of HBV according to the maternal HBV viral load during pregnancy. With timely use of birth-dose vaccine and HBIG, there was no breakthrough infection reported when the maternal HBV DNA viral load was below 5.3 $\log_{10}$ IU/mL (200 000 IU/mL). The risk of MTCT increased above this threshold (Figure 1) [11].

Figure 1. Risk of mother-to-child transmission of HBV according to maternal HBV DNA levels during pregnancy



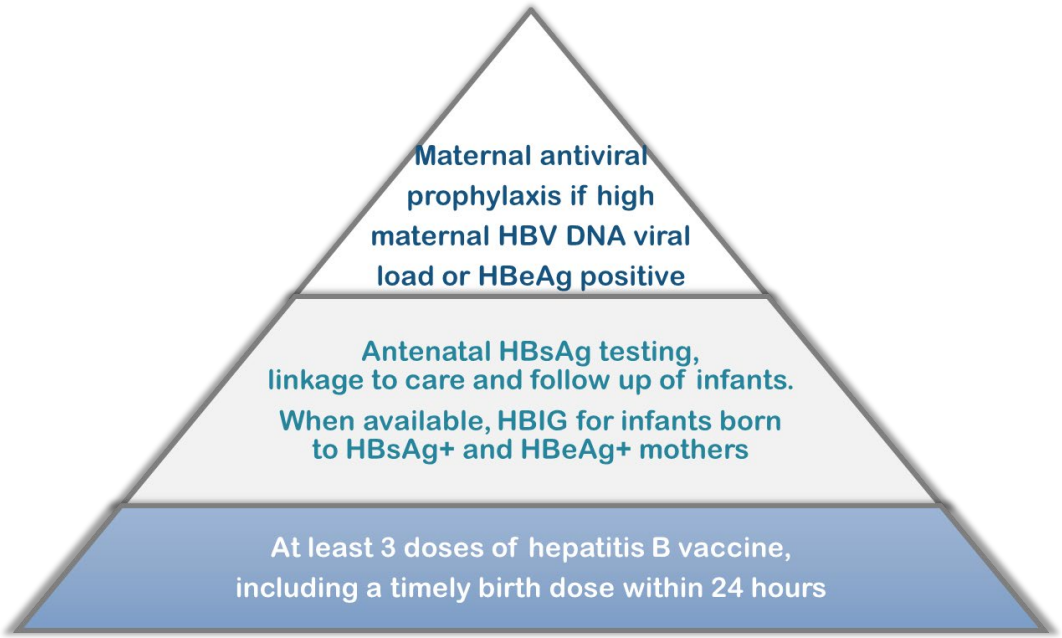
Source: *Prevention of mother-to-child transmission of hepatitis B virus: guidelines on antiviral prophylaxis in pregnancy*. Geneva: World Health Organization; 2020.

Further evidence has become available on the efficacy and safety of antiviral prophylaxis in pregnant women and their children. A systematic review and meta-analysis commissioned by the WHO indicated a protective effect of using tenofovir disoproxil fumarate (TDF) as peripartum antiviral prophylaxis to reduce the risk of MTCT (Pooled odds ratio [OR]: 0.10, 95% CI: 0.03 – 0.35 for randomised controlled trials; pooled OR: 0.17, 95% CI: 0.10 – 0.29 for non-randomised controlled trials) [12]. The safety of TDF has been documented in the context of preventing MTCT of human immunodeficiency virus (HIV) [13]. As regards the safety in its use for preventing MTCT of HBV, the WHO-commissioned systematic review found that there was no statistically significant differences between treated and control groups in occurrence of maternal or infant adverse events. The meta-analysis findings suggested that cessation of TDF prophylaxis might not increase the risk of postpartum hepatitis B flare as compared with the control group (Risk in treated group: 28/356 [7.9%]; control group: 20/327 [6.1%]; weighted risk difference: -0.020, 95% CI: -0.082 to 0.041) [12].

Based on the latest evidence for overall reassessment of the balance of benefits and harms of antiviral prophylaxis in eligible pregnant women, as well as consideration of patient/health worker values and preferences, resource use, cost–effectiveness, considerations on equity and human rights, and feasibility, WHO formulated the guidelines on the use of antiviral prophylaxis for preventing MTCT of HBV in 2020. WHO recommends that pregnant women testing positive for HBV infection (HBsAg positive) with an HBV DNA ≥ 5.3 $\log_{10}$ IU/mL (≥ 200 000 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 in all infants, including timely birth dose. 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 [14].

The use of maternal antiviral prophylaxis has now become part of an incremental approach to prevent HBV infection at birth and in the first years of life (Figure 2).

Figure 2. Incremental approach to prevention of HBV infection at birth and in the first years of life



Current practices and new initiatives in Hong Kong

In Hong Kong, in addition to routine screening of pregnant women for HBsAg during each pregnancy, universal childhood hepatitis B vaccination and administration of HBIG to babies born to HBsAg-positive mothers have been in place since 1980s. The coverage of hepatitis B vaccination is monitored by the Immunisation Coverage Surveys, which have been conducted among children aged 2 to 5 since 2001. The coverage for birth dose, second dose and third dose of hepatitis B vaccination generally reaches 99% or above [15], much higher than the 2030 WHO target at 90%.

To meet the WHO goal of eliminating viral hepatitis as a major public health threat by 2030, the *Hong Kong Viral Hepatitis Action Plan 2020 – 2024* ("the Action Plan") was launched in October 2020, which formulated the actions under four strategic axes, namely awareness, surveillance, prevention and treatment [16]. The Action Plan emphasises further reduction of MTCT as one of the focuses of prevention and control of hepatitis B. Two new initiatives, namely using antivirals for preventing MTCT of HBV and post-vaccination serologic testing, are introduced.

Using antivirals for preventing MTCT of HBV

The use of antiviral prophylaxis to prevent MTCT of HBV was first piloted in Queen Mary Hospital and Prince of Wales Hospital at the beginning of 2020. The initiative has been rolled out to all birthing hospitals under Hospital Authority (HA) since August 2020. For HBsAg-positive pregnant women under care by HA or Maternal and Child Health Centres of the Department of Health, baseline HBV DNA level is assessed. If their viral load is high at 200 000 IU/mL or more, they are referred to the hepatology clinic for follow-up and consideration of initiating maternal TDF prophylaxis at the third trimester. These mothers will continue to receive long-term management of their liver condition after giving birth. For those with a viral load ≤ 200 000 IU/mL, they would be referred to doctors conversant with HBV treatment for routine assessment and management of the liver condition, in accordance with the prevailing practices for hepatitis B patients.

The implementation of this initiative is supported by widening the indications of the antivirals in HA Drug Formulary, building laboratory capacity and establishing hepatitis nurse clinics to augment the capacity of hepatitis clinics. Initial experience in such enhanced service model found that antenatal testing of HBV DNA level and use of TDF were well accepted by pregnant women [17].

Post-vaccination serologic testing

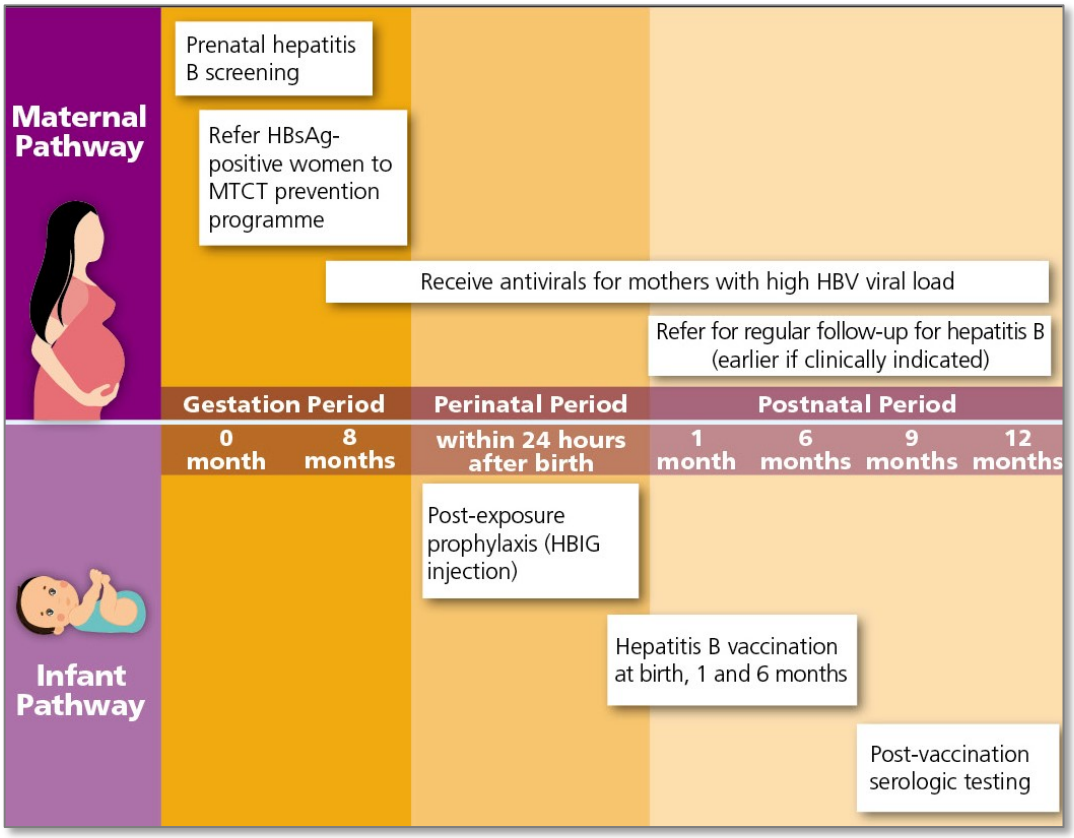
WHO Regional Office of the Western Pacific emphasises that post-vaccination serologic testing (PVST) to babies born to HBsAg-positive mothers is important to determine the effectiveness of prevention of MTCT of HBV when antenatal HBV screening and vaccination programme are in place [18]. PVST includes testing on HBsAg and hepatitis B surface antibody (anti-HBs) of all babies born to HBV-infected women at the age of 9 - 12 months (or 1 - 2 months after the final dose of the vaccine series, if the series is delayed).

The purposes of PVST are threefold. Firstly, babies born to HBV-infected women, who do not have an adequate immune response to an initial hepatitis B vaccine series, will be identified and revaccination will be arranged for them. Secondly, PVST can enable early identification of HBV-infected babies to ensure appropriate medical care for them. Thirdly, PVST would provide useful and systematic information to monitor the effectiveness of the overall MTCT prevention strategy.

Following the introduction of programmes for the use of antiviral prophylaxis and PVST, preventing MTCT of HBV would be further enhanced in Hong Kong (Figure 3), with a view to realising an “HBV-free generation” and progressing towards the elimination of the public health threat posed by viral hepatitis.

Figure 3.

Hepatitis B MTCT prevention pathways with the use of antivirals and PVST



Reference

1. Hyams KC. Risks of chronicity following acute hepatitis B virus infection: a review. Clin InfectDis 1995; 20(4):992-1000.

2. Sarin SK, Kumar M, Lau GK, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. Hepatol Int 2016; 10(1):1-98.

3. Indolfi G, Easterbrook P, Dusheiko G, et al. Hepatitis B virus infection in children and adolescents. Lancet Gastroenterol Hepatol 2019; 4(6):466-476.

4. Global health sector strategy on viral hepatitis 2016-2021. Geneva: World Health Organization; 2016 (https://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/ , accessed April 2021).

5. Hepatitis B vaccines: WHO position paper – July 2017. Wkly Epidemiol Rec 2017; 92(27):369-92.

6. Lee C, Gong Y, Brok J, et al. Hepatitis B immunisation for newborn infants of hepatitis B surface antigen-positive mothers. Cochrane Database Syst Rev 2006; (2):CD004790.

7. Guidelines on hepatitis B and C testing. Geneva: World Health Organization; 2017 (https://www.who.int/hepatitis/publications/guidelines-hepatitis-c-b-testing/en/, accessed April 2021).

8. Kubo A, Shlager L, Marks AR, et al. Prevention of vertical transmission of hepatitis B: an observational study. Ann Intern Med 2014; 160(12):828-35.

9. Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. Pediatrics 2015; 135(5):e1141-7.

10. Cheung KW, Seto MT, Kan AS, et al. Immunoprophylaxis failure of infants born to hepatitis B carrier mothers following routine vaccination. Clin Gastroenterol Hepatol 2018; 16(1):144-5.

11. Boucheron P, Lu Y, Yoshida K, et al. Accuracy of HBeAg to identify pregnant women at risk of transmitting hepatitis B virus to their neonates: a systematic review and meta-analysis. Lancet Infect Dis 2021; 21(1):85-96.

12. Funk AL, Lu Y, Yoshida K, et al. Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis. Lancet Infect Dis 2021; 21(1):70-84.

13. Nachega JB, Uthman OA, Mofenson LM, et al. Safety of tenofovir disoproxil fumarate-based antiretroviral therapy regimens in pregnancy for HIV-infected women and their infants: a systematic review and meta-analysis. J Acquir Immune Defic Syndr 2017; 76(1):1-12.

14. Prevention of mother-to-child transmission of hepatitis B virus: guidelines on antiviral prophylaxis in pregnancy. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/978-92-4-000270-8, accessed April 2021).

15. Surveillance of Viral Hepatitis in Hong Kong – 2019 Report. Hong Kong: Department of Health; 2020 (https://www.hepatitis.gov.hk/tc_chi/document_cabinet/files/hepsurv19.pdf, accessed April 2021).

16. Hong Kong Viral Hepatitis Action Plan 2020 – 2024. Hong Kong: The Government of the Hong Kong Special Administrative Region; 2020 (https://www.hepatitis.gov.hk/doc/action_plan/Action Plan_Full Version_PDF_en.pdf, accessed April 2021).

17. Hui PW, Ng C, Cheung KW, et al. Acceptance of antiviral treatment and enhanced service model for pregnant patients carrying hepatitis B. Hong Kong Med J 2020; 26(4):318-22.

18. Hepatitis B control through immunization: a reference guide. Manila: WHO Regional Office for the Western Pacific. (https://iris.wpro.who.int/handle/10665.1/10820 , accessed April 2021).

Useful resources

Description of Materials	Hyperlink	QR code	Cover
Pamphlet – Prevention of Perinatal Hepatitis B	https://www.hepatitis.gov.hk/tc_chi/resources/files/leaflet2020_3.pdf		
Pamphlet – Stop Maternal Transmission of Hepatitis B	https://www.hepatitis.gov.hk/tc_chi/resources/files/stop-transmiss-leaflet-w3c.pdf		
Pamphlet – Oral Antiviral Treatment for Hepatitis B	https://www.hepatitis.gov.hk/tc_chi/resources/files/pamphlet-Oral-w3c.pdf		
Poster – Prevention of Perinatal Hepatitis B	https://www.hepatitis.gov.hk/tc_chi/resources/files/poster2020_3.pdf		
Poster – Stop Maternal Transmission of Hepatitis B	https://www.hepatitis.gov.hk/tc_chi/resources/files/poster2020_4.pdf		
Presentation slides – Prevention of mother-to-child transmission of hepatitis B	https://www.hepatitis.gov.hk/english/health_professionals/files/Prevention_of_MTCT_of_HBV_web.pdf		

Test paper

Please submit the completed answer sheet within the validity period by email to hepatitis@dh.gov.hk.

CME/CPD/CNE/PEM point: 1

Validity Period: 21 June 2021 to 20 June 2022

College/ Programme	CME/ CPD Point	CME/CPD Category
Anaesthesiologists	1	Non ANA Passive
Community Medicine	1	AP-SS
Dental Surgeons	1	Self-Study
Emergency Medicine	1	PP
Family Physicians	1	Cat 5.2
Obstetricians and Gynaecologists	1	Self-Study
Ophthalmologists	1	Passive
Orthopaedic Surgeons	1	Cat B
Otorhinolaryngologists	1	Cat 1.2
Paediatricians	1	Cat E
Pathologists	1	PP
Physicians	1	-
Psychiatrists	1	SSOL
Radiologists	1	Cat B
Surgeons	1	Passive
MCHK CME Programme for Practising Doctors who are not taking CME Programme for Specialists	1	Passive (Accredited by DH)

Please contact respective authorities directly for CME/CPD accreditation if it is not listed above.

Prevention of mother-to-child transmission of hepatitis B virus

1. Which of the following is **NOT** a correct description about mother-to-child transmission (MTCT) of hepatitis B virus (HBV)?
   A. Chronicity is more common following acute HBV infection in neonates.
   B. In Hong Kong, the hepatitis B surface antigen (HBsAg) seroprevalence in antenatal mothers was around 4% in 2019.
   C. MTCT is an epidemiologically important route of HBV transmission.
   D. Most of the disease burden of chronic HBV infection comes from infection acquired soon after birth or during early childhood, especially in high-prevalence settings.
   E. Hepatitis B vaccination is the only intervention to prevent MTCT of HBV.

2. As outlined in *Global health sector strategy on viral hepatitis, 2016 - 2021*, what is the surrogate for the target of a 90% reduction in incidence of chronic HBV infection by 2030?
   A. HBsAg prevalence at 0.1% or below among children 5 years of age
   B. HBsAg prevalence at 1% or below among children 5 years of age
   C. HBsAg prevalence at 5% or below among children 5 years of age
   D. HBsAg prevalence at 1% or below among adult population
   E. HBsAg prevalence at 3% or below among adult population

3. Which of the following is recommended by World Health Organization (WHO) as regards antenatal HBV screening?
   A. Hepatitis B surface antibody (anti-HBs) is the test recommended for screening chronic HBV infection among pregnant women.
   B. HBsAg serological testing should only be offered to those pregnant women with family history of chronic HBV infection.
   C. HBsAg serological testing should only be offered to those pregnant women with personal history of chronic HBV infection.
   D. HBsAg serological testing should be routinely offered to all pregnant women in antenatal clinics only when the HBsAg seroprevalence in the general population is >10%.
   E. HBsAg serological testing should be routinely offered to all pregnant women in settings with an intermediate (≥ 2%) or high (≥ 5%) HBsAg seroprevalence in the general population

4. Which of the following is **NOT** included in the incremental approach to prevention of HBV infection at birth and in the first years of life?
   A. 3 doses of hepatitis B vaccine, including a timely birth dose within 24 hours
   B. Administration of hepatitis B immunoglobulin to infants born to HBsAg-positive mothers
   C. Administration of hepatitis B immunoglobulin to pregnant women
   D. Maternal use of antiviral prophylaxis if maternal HBV DNA viral load is high
   E. Antenatal HBsAg testing, linkage to care and follow up of infants

5. Which of the following is **NOT** a correct description about the safety and efficacy of antiviral prophylaxis in pregnant women?
   A. The safety and efficacy of antiviral prophylaxis in pregnant women and their children have been evaluated in systematic reviews and meta-analyses.
   B. Using tenofovir disoproxil fumarate (TDF) prophylaxis in pregnancy has been shown to be effective in reducing the risk of MTCT of HBV.
   C. The safety of TDF has been documented in the context of preventing MTCT of human immunodeficiency virus (HIV).
   D. TDF was proven to be significantly associated with higher occurrence of maternal or infant adverse events.
   E. The latest systematic review commissioned by WHO did not find an increased risk of postpartum hepatitis B flare after cessation of TDF prophylaxis as compared with the control group.

6. According to WHO latest guidelines in 2020, what is the recommended threshold of maternal HBV viral load for using antiviral prophylaxis in pregnancy to prevent MTCT of HBV?
   A. $\geq 4.3 \log_{10}$ IU/mL ($\geq$ 20 000 IU/mL)
   B. $\geq 5.3 \log_{10}$ IU/mL ($\geq$ 200 000 IU/mL)
   C. $\geq 6.3 \log_{10}$ IU/mL ($\geq$ 2 000 000 IU/mL)
   D. $\geq 7.3 \log_{10}$ IU/mL ($\geq$ 20 000 000 IU/mL)
   E. $\geq 8.3 \log_{10}$ IU/mL ($\geq$ 200 000 000 IU/mL)

7. To prevent MTCT of HBV, when should the antiviral prophylaxis start for eligible pregnant women having high HBV viral load?
   A. Immediately after knowing the test results of viral load in the first trimester
   B. By the end of the first trimester
   C. In the third trimester
   D. During delivery
   E. After delivery

8. Which of the following measures is a new initiative for preventing MTCT of HBV in Hong Kong, as outlined in *Hong Kong Viral Hepatitis Action Plan 2020 – 2024*?
   A. Routine screening of pregnant women for HBsAg during each pregnancy
   B. Universal childhood hepatitis B vaccination
   C. Administration of HBIG to babies born to HBsAg-positive mothers
   D. Provision of the treatment option to use antiviral prophylaxis for pregnant women having high HBV viral load
   E. Post-vaccination serologic testing for all new-borns in Hong Kong

9. Which of the following is **NOT** a correct description as regards the use of antiviral prophylaxis to prevent MTCT of HBV in Hong Kong?
   A. Use of antiviral prophylaxis for pregnant women with high viral load has been rolled out to all birthing hospitals under Hospital Authority (HA) since August 2020.
   B. Baseline HBV DNA level would be assessed for HBsAg-positive pregnant women under care by HA or Maternal and Child Health Centres of the Department of Health.
   C. Pregnant women having high viral load (≥ 200 000 IU/mL) would be referred to the hepatology clinic for follow-up and consideration of initiating maternal TDF prophylaxis.
   D. Pregnant women having viral load less than 200 000 IU/mL would be referred to doctors conversant with HBV treatment for routine assessment and management of the liver condition in accordance with the prevailing practices for hepatitis B patients.
   E. The use of antiviral prophylaxis is offered to all pregnant women tested positive for HBsAg.

10. Which of the following is **NOT** the purpose of post-vaccination serologic testing programme for babies born to HBsAg-positive mothers?
    A. To identify babies who do not have an adequate immune response to an initial hepatitis B vaccine series
    B. To arrange hepatitis B re-vaccination if needed
    C. To examine the liver function of all babies born to HBsAg-positive mothers
    D. To enable identification of HBV-infected babies for appropriate medical care
    E. To provide useful and systematic information to monitor the effectiveness of the overall MTCT prevention strategy