



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

March 2021

Outline

1. Introduction
2. Interventions to prevent mother-to-child transmission of HBV
 - a. Universal childhood hepatitis B vaccination
 - b. Hepatitis B immunoglobulin (HBIG)
 - c. Universal antenatal HBsAg screening
 - d. Use of antiviral prophylaxis during pregnancy
3. Actions in Hong Kong

Introduction

Global burden of hepatitis B virus infection

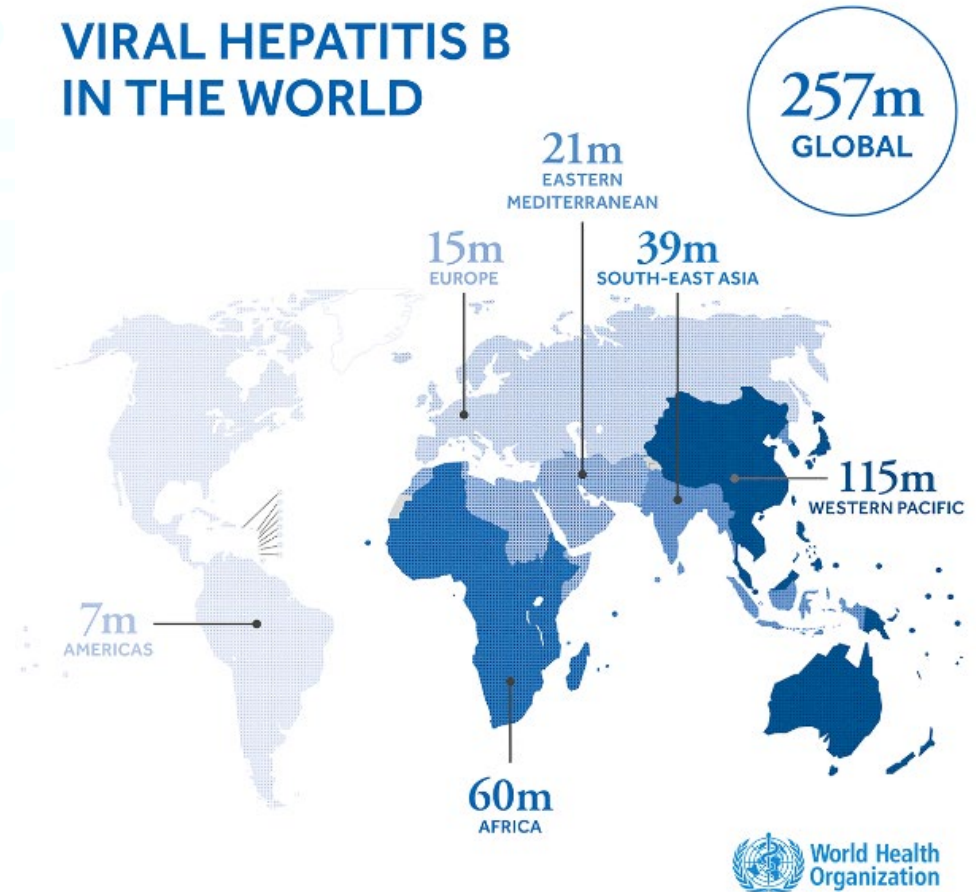
2015

- 257 million people with chronic HBV infection (3.5% world population)
- HBV infection caused around 900000 deaths, mostly due to cirrhosis and hepatocellular carcinoma (HCC)

WHO *Global hepatitis report*, 2017

www.who.int/hepatitis/publications/global-hepatitis-report2017/en/

VIRAL HEPATITIS B IN THE WORLD



Local epidemiology of HBV infection

Prevalence study of hepatitis A to E

- 10 256 HK Chinese aged ≥ 18
- Feb 2015 to July 2016
- Age- and sex-adjusted HBsAg prevalence : **7.2%**

540 000 people with
HBV infection



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A Territorywide Prevalence Study on Blood-Borne and Enteric Viral Hepatitis in Hong Kong

Kevin S H Liu, Wai-Kay Seto, Eric H Y Lau, Danny Ka-Ho Wong, Yuk-Fai Lam, Ka-Shing Cheung, Lung-Yi Mak, Kwan-Lung Ko, Wai-Pan To, Mildred W K Law ... [Show more](#)

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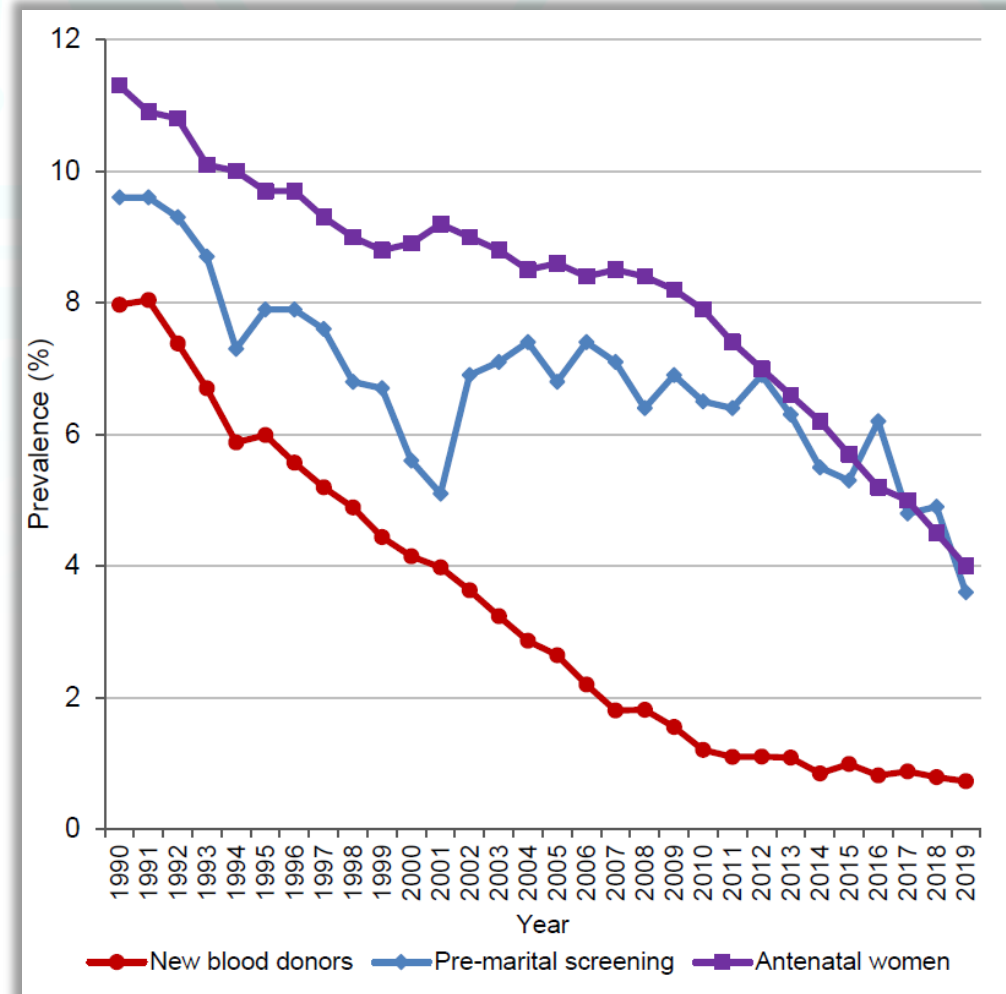
Introduction

Local epidemiology of HBV infection

↓ HBsAg prevalence in populations without specific HBV risk

	1990	2019
New blood donors	8.0 %	0.7 %
Pre-marital screening	9.6 %	3.6 %
Antenatal women	> 10 %	4.0 %

Sources: HK Red Cross Blood Transfusion Services, Family Planning Association, DH Family Health Service



Introduction

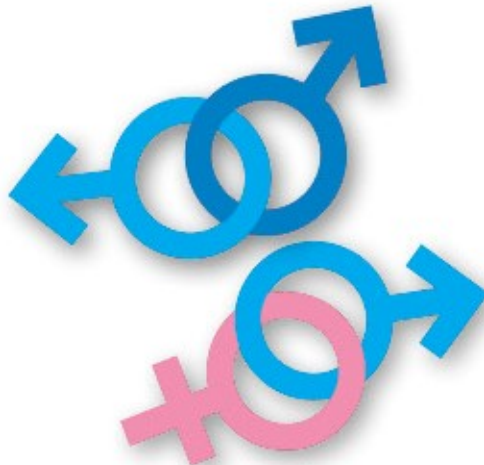
Transmission of HBV

Mother-to-child transmission (MTCT) during birth

- an epidemiologically important route of HBV transmission
- accounts for the prevalence of HBV infection in Hong Kong



Mother-to-child
transmission



Sexual contact



Contact with
contaminated blood or
body fluid

Chronic HBV infection

- Age is a key factor in determining the risk of chronic infection.
- Risk of chronicity following acute infection:

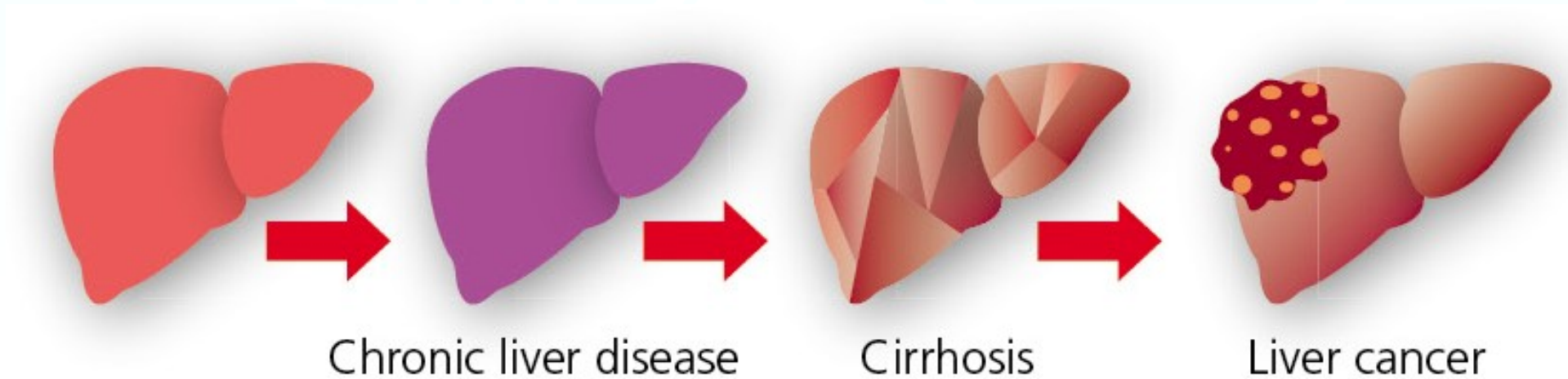
neonates	80 - 90%
children < 6 years	30 - 50%
healthy adults	< 5%

WHO Factsheet on hepatitis B www.who.int/news-room/fact-sheets/detail/hepatitis-b

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

Chronic HBV infection

- **15 - 40%** of untreated persons with chronic HBV infection may develop cirrhosis, liver failure or liver cancer in their lifetime



Lok AS. Chronic hepatitis B. *N Engl J Med* 2002; 346(22):1682-3.

Introduction

- Most of the disease burden of HBV infection comes from infections acquired during infancy through **perinatal** or **early childhood** exposure to HBV.
- From public health perspective, preventing infections acquired at birth and in early childhood is critical.



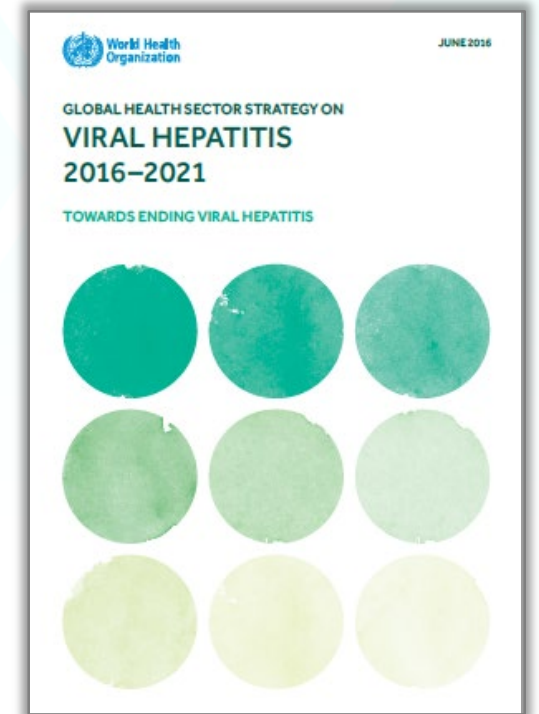
Introduction

WHO Global health sector strategy on viral hepatitis, 2016 - 2021



Goal:

Eliminate viral hepatitis as a major public health threat by 2030



www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/

WHO Global health sector strategy on viral hepatitis, 2016 - 2021

Impact targets in 2030

- ➡ **90% reduction in incidence (new cases)** of chronic HBV and HCV infections (equivalent to 0.1% prevalence of HBsAg among children)
- ➡ **65 % reduction in mortality** from HBV and HCV

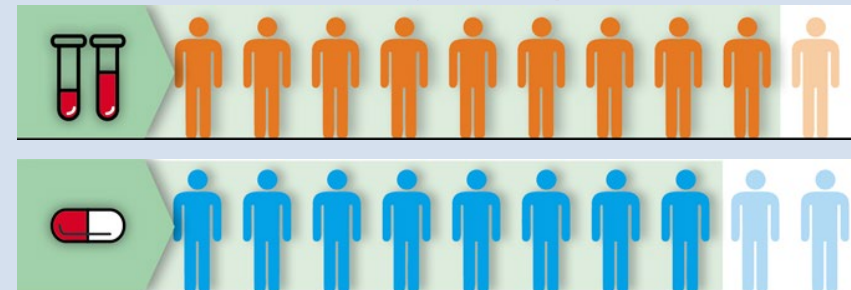
** As compared with the baseline in 2015*

Introduction

WHO Global health sector strategy on viral hepatitis, 2016 - 2021

Service coverage targets in 2030

- ✓ 90% HBV vaccination coverage for the third dose
- ✓ 90% HBV vaccination coverage for birth dose (prevention of MTCT)
- ✓ 100% blood donations screened
- ✓ 90% safe injections (administered with safety-engineered devices)
- ☞ 300 sterile needles and syringes provided per PWID per year (harm reduction)
- ☞ 90% people with HBV / HCV diagnosed
- ☞ 80% eligible HBV / HCV patients treated



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Universal childhood hepatitis B vaccination

WHO position paper – July 2017

- ***All** infants should receive their **first dose** of hepatitis B vaccine as soon as possible after birth, preferably **within 24 hours**;*
- *Delivery of hepatitis B vaccine within 24 hours of birth should be a **performance indicator** for all immunization programmes, and reporting and monitoring systems should be strengthened to improve the quality of data on the birth dose;*
- *The birth dose should be followed by two or three doses to **complete the primary series**.*

Universal childhood hepatitis B vaccination

Hong Kong Childhood Immunisation Programme

- since 1988
- 0, 1m, 6m
- **Immunisation Coverage Survey 2018** (every 2 to 3 years since 2001)
 - > 99% coverage for birth dose, 2nd dose and 3rd dose
- supplementary Primary 6 vaccination programme was introduced in 1998

Hepatitis B immunoglobulin (HBIG)

- for neonates born to HBV-infected mothers **within 24 hours** after birth (regardless of the mother's HBeAg or anti-HBe status)
- as an adjuvant to hepatitis B vaccination
- passive immunoprophylaxis
- high titre of antibody to HBsAg (anti-HBs)

Immunogenicity of HBV vaccine

A primary three-dose hepatitis B vaccination can induce protective antibody (anti-HBs) concentration in **> 95%** of healthy infants, children and young adults

Efficacy of HBV vaccination and HBIG

Meta-analysis of RCT in 2006

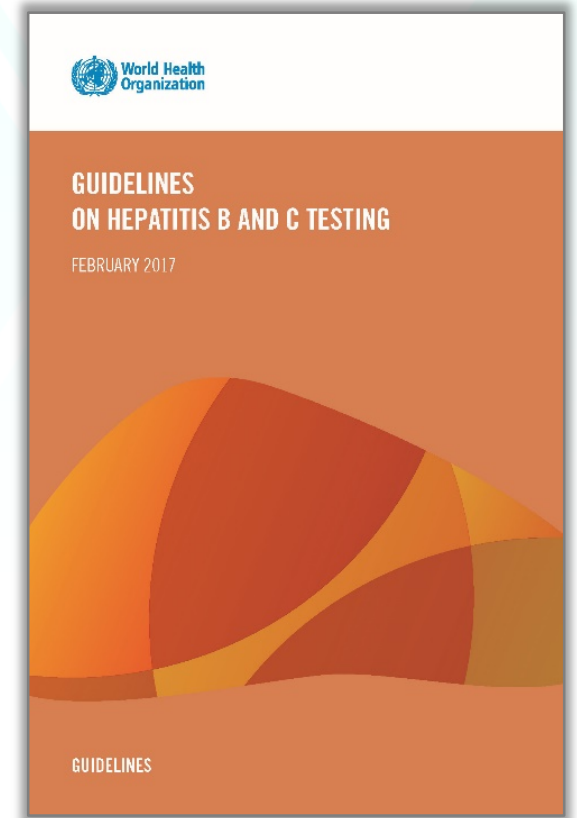


- Infants who were born to HBV-infected mothers and received 1st dose at birth were less likely to become infected
 - **RR 0.28** (95%CI 0.20 - 0.40), compared with placebo/no intervention
- Vaccine plus HBIG could further reduce hepatitis B occurrence
 - RR 0.54 (95%CI 0.41 - 0.73), compared with vaccine alone
 - **RR 0.08** (95%CI 0.03 - 0.17), compared with placebo/no intervention

Universal antenatal HBsAg screening

WHO Guidelines on Hepatitis B and C Testing, 2017

- *In settings with an intermediate ($\geq 2\%$) or high ($\geq 5\%$) HBsAg seroprevalence in the general population, it is recommended that*
 - *HBsAg serological testing 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*

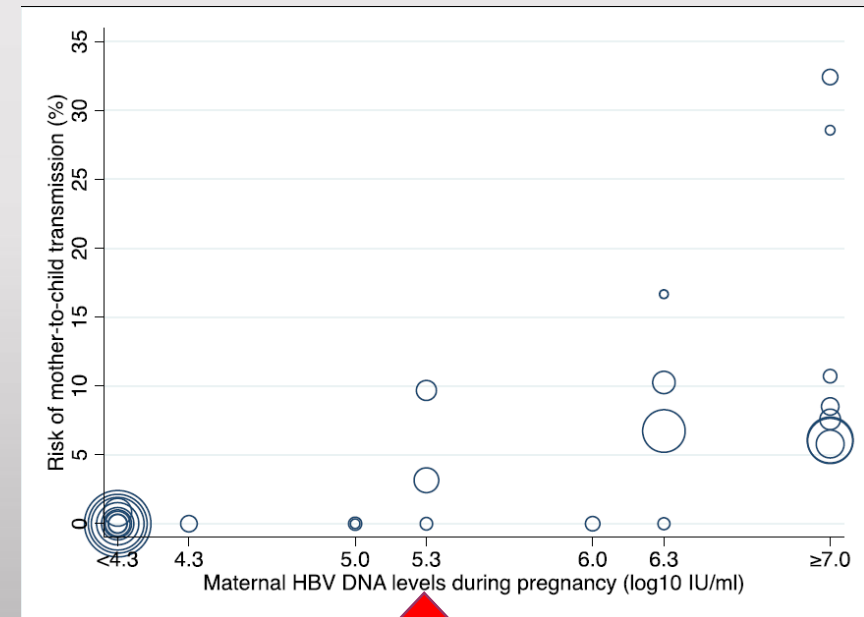


Interventions

Immunoprophylaxis failure

- Despite universal antenatal screening, HBV vaccination and HBIG at birth, **0.7 - 1.1%** infants born to HBV-infected mothers are infected.
- With timely birth dose and HBIG used, there was **no breakthrough** infection reported when the maternal HBV DNA viral load was **below 5.3 log₁₀ IU/mL (200,000 IU/mL)**

Risk of MTCT of HBV according to maternal HBV DNA levels during pregnancy



Kubo A, et al. Prevention of vertical transmission of hepatitis B: an observational study. *Ann Intern Med* 2014;160:828–35.

Schillie S, et al. Outcomes of infants born to women infected with hepatitis B. *Pediatrics* 2015;135:e1141–7.

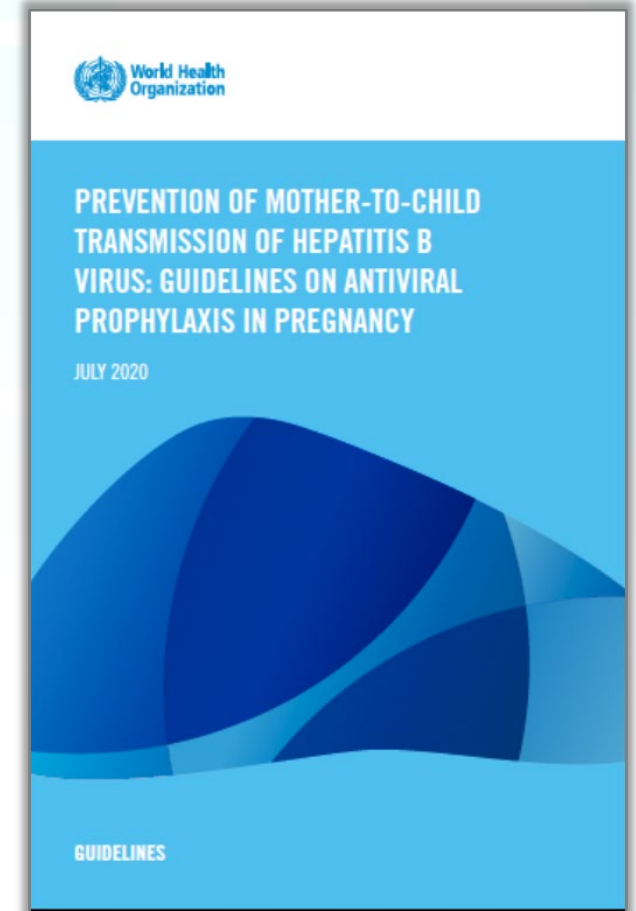
Cheung KW, et al. Immunoprophylaxis failure of infants born to hepatitis B carrier mothers following routine vaccination. *Clin Gastroenterol Hepatol* 2018; 16: 144-5.

WHO Prevention of MTCT of HBV: guidelines on antiviral prophylaxis in pregnancy. July 2020

Use of antiviral prophylaxis during pregnancy

WHO Prevention of MTCT of HBV: guidelines on antiviral prophylaxis in pregnancy, July 2020

- *WHO recommends that pregnant women testing positive for HBV infection (HBsAg positive) with an **HBV DNA $\geq 5.3 \log_{10}$ IU/mL ($\geq 200,000$ 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 in all infants, including timely birth dose.*



Tenofovir disoproxil fumarate (TDF) 替諾福韋

- High barrier to drug resistance (Vs lamivudine and telbivudine)
- Meta-analysis demonstrated protective effect to reduce risk of MTCT

	Pooled odds ratio	95% CI
RCT (n=5)	0.10	0.03 - 0.35
Non-randomised studies (n=14)	0.17	0.10 - 0.29

- No statistically significant difference in occurrence of adverse events (including HBV flare after discontinuation) between TDF group and control group

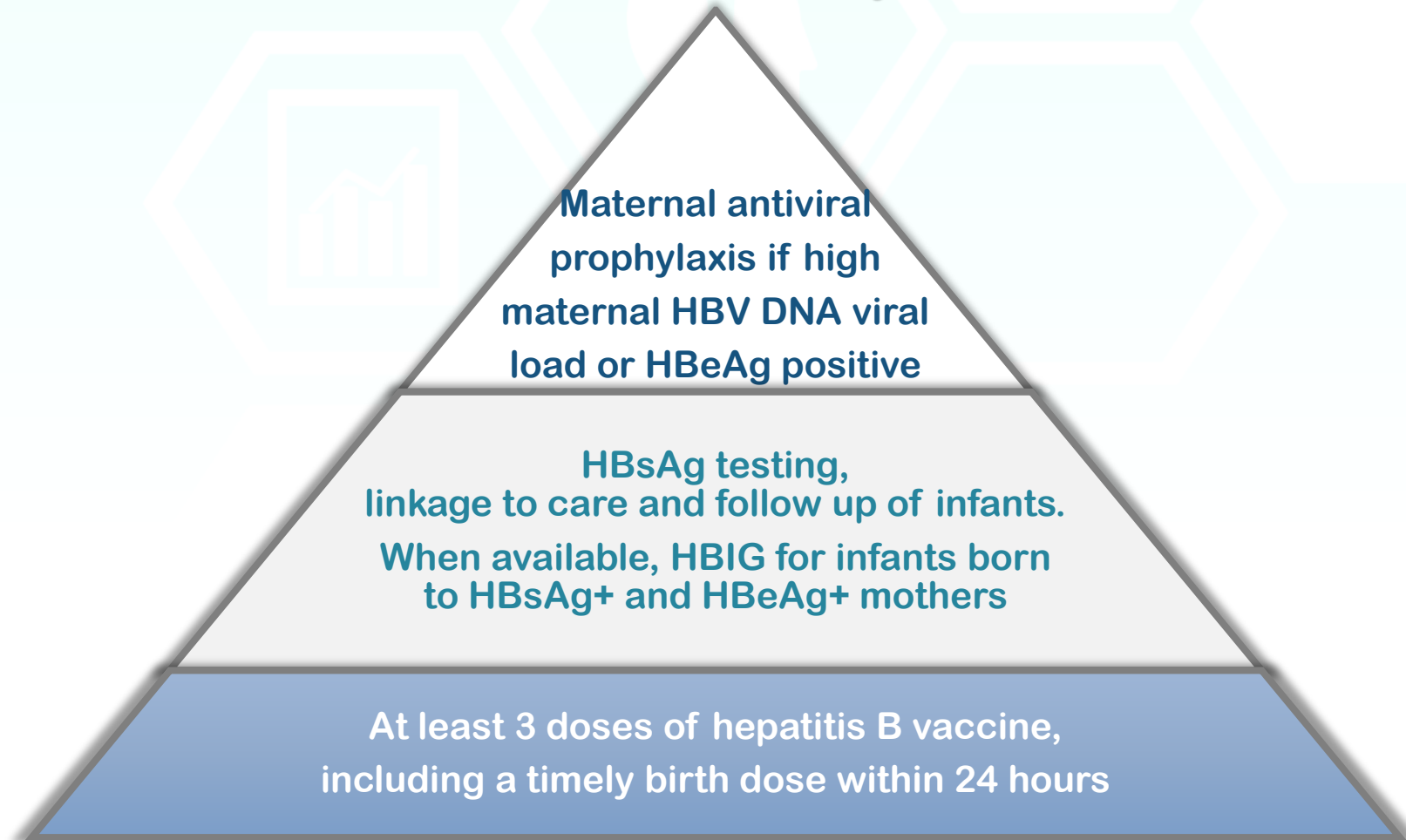
Funk AL, et al. Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis. *Lancet Infect Dis* 2021; 21(1):70-84.

WHO Prevention of MTCT of HBV: guidelines on antiviral prophylaxis in pregnancy. July 2020

Salvadori N, et al. Maternal and infant bone mineral density 1 year after delivery in a randomized, controlled trial of maternal tenofovir disoproxil fumarate to prevent mother-to-child transmission of hepatitis B virus. *Clin Infect Dis* 2019; 69(1):144-6.

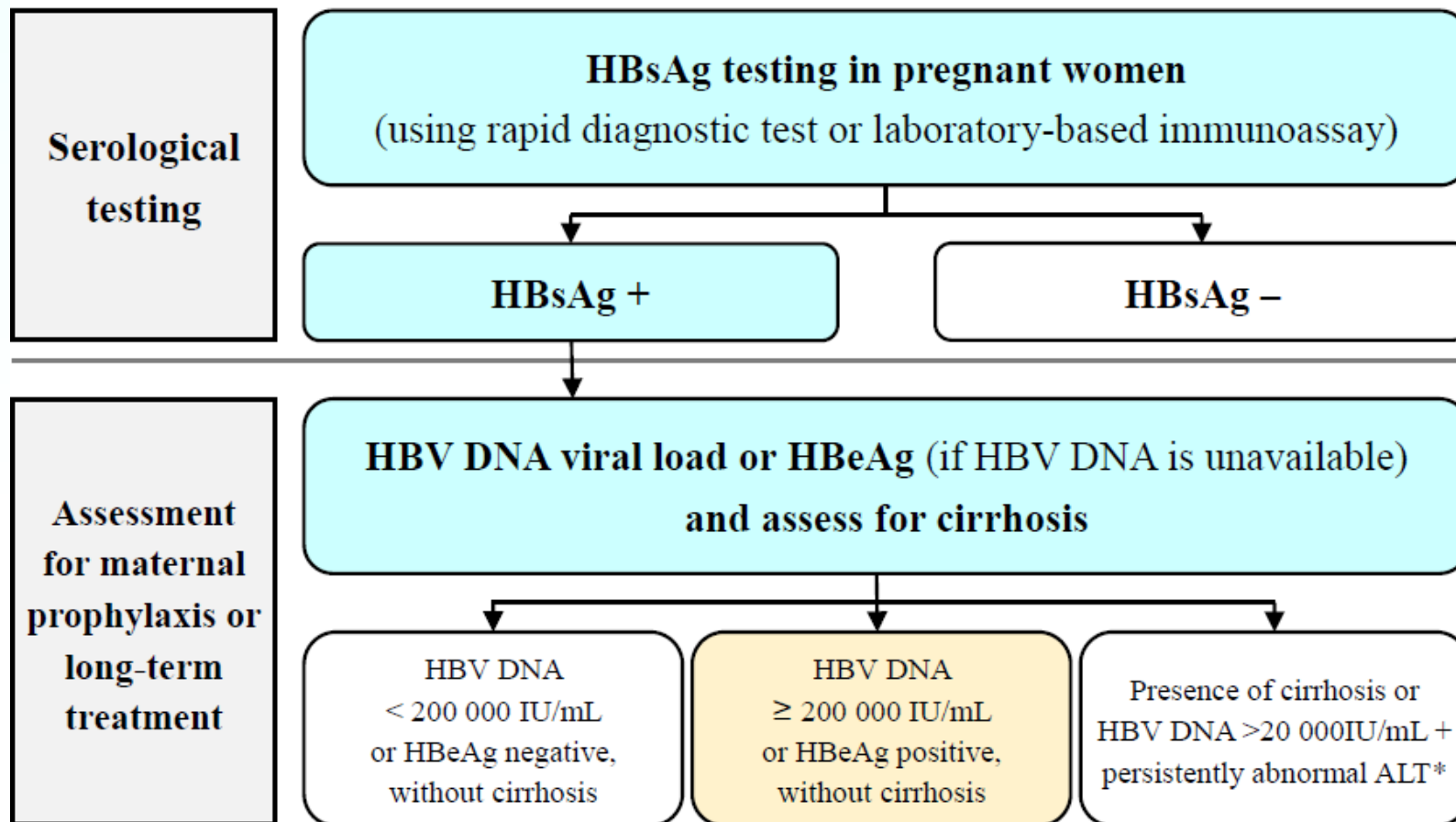
Interventions

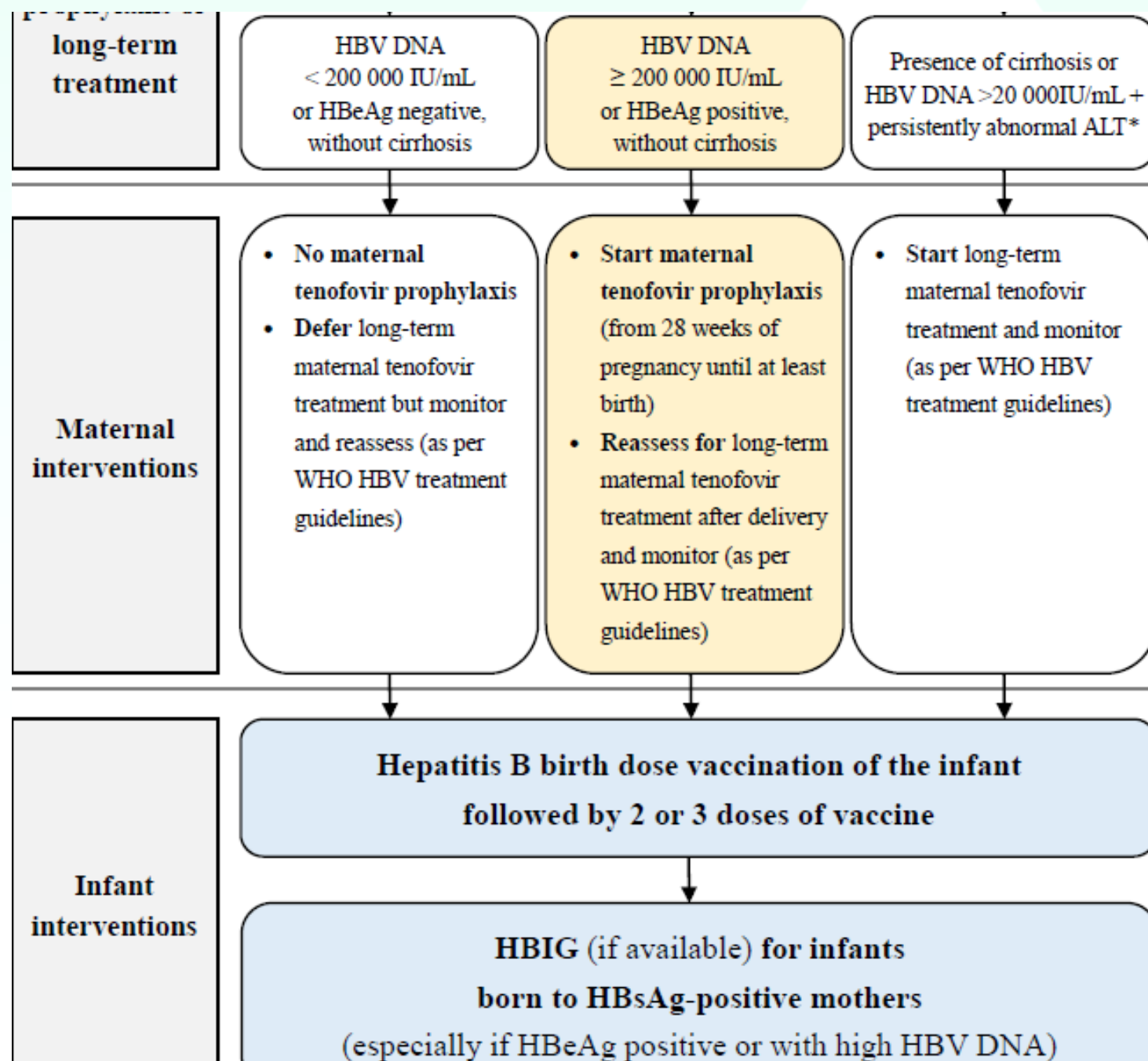
Incremental approach to prevention of HBV infection at birth and in the first years of life



Interventions

Algorithm on maternal and infant interventions for prevention of MTCT and assessment of eligibility of mother for antiviral treatment





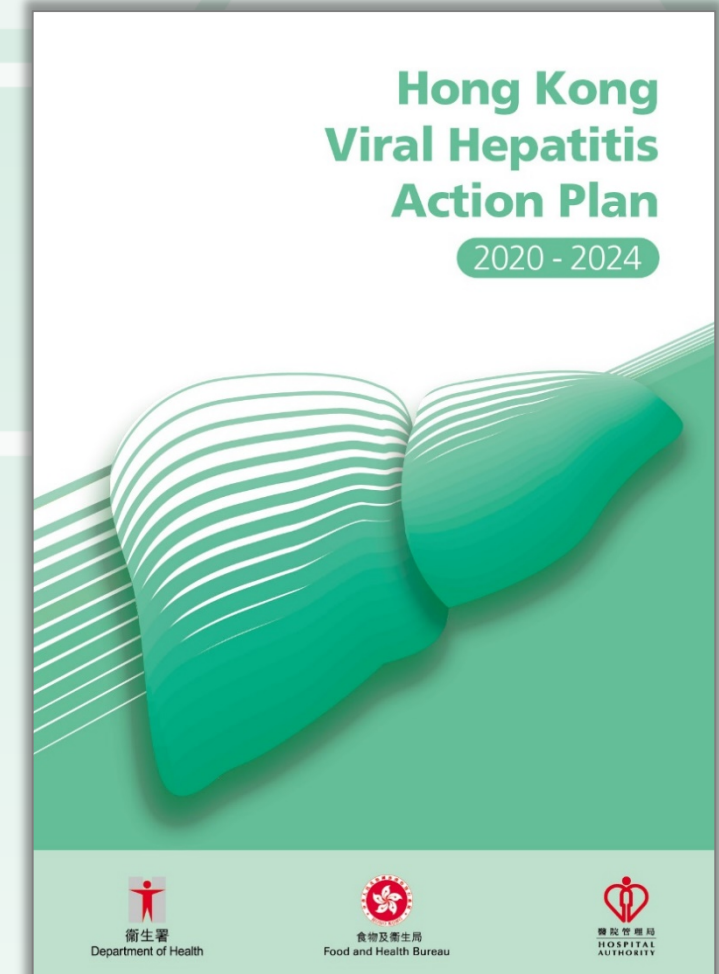
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3. **Actions in Hong Kong**

Actions in HK

Hong Kong Viral Hepatitis Action Plan, 2020 - 2024

- Launched in October 2020
- Actions under 4 strategic axes
- DH, HA and other community stakeholders



Vision

Hong Kong will be a place where new viral hepatitis infections have ceased, and where everyone with chronic viral hepatitis has access to effective and affordable care and treatment.

Goals

- Reduce transmission of viral hepatitis
- Reduce morbidity and mortality due to viral hepatitis



Strategy 3: Promoting Prevention

- 🦋 Universal screening for pregnant women and neonatal vaccination for hepatitis B
- 🦋 Use antivirals for preventing MTCT of HBV
- 🦋 Post-vaccination serologic testing
- 🦋 Prevent healthcare-related transmission of HBV and HCV
- 🦋 Reduce the risk and disease burden in vulnerable populations

Antiviral prophylaxis to prevent MTCT

- Pilot started in early 2020 in QMH and PWH
- The initiative was rolled out to all birthing hospitals in **August 2020**
- For HBV-infected pregnant women under care by HA or MCHC
 - Baseline HBV DNA done
 - If **$\geq 200\ 000\ \text{IU/mL}$** → early referral to Hepatology Clinic
 - Offer **tenofovir 300mg daily** starting from **28th week** of gestation
- **Hepatitis nurse clinics** are set up to augment the capacity of hepatology clinic

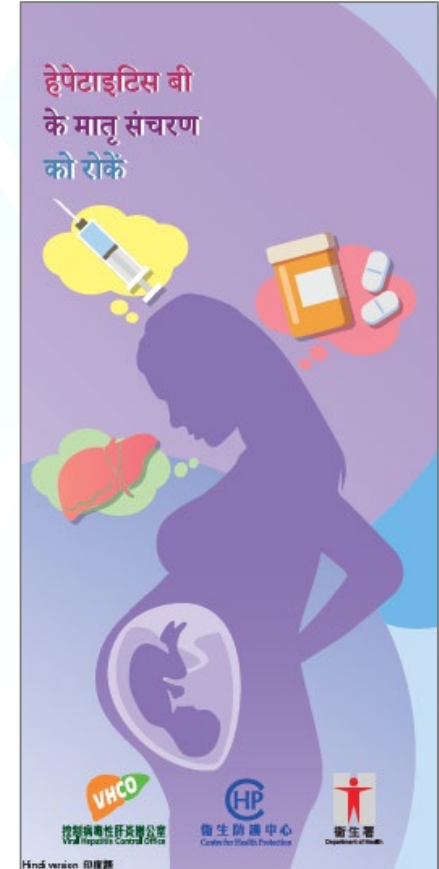
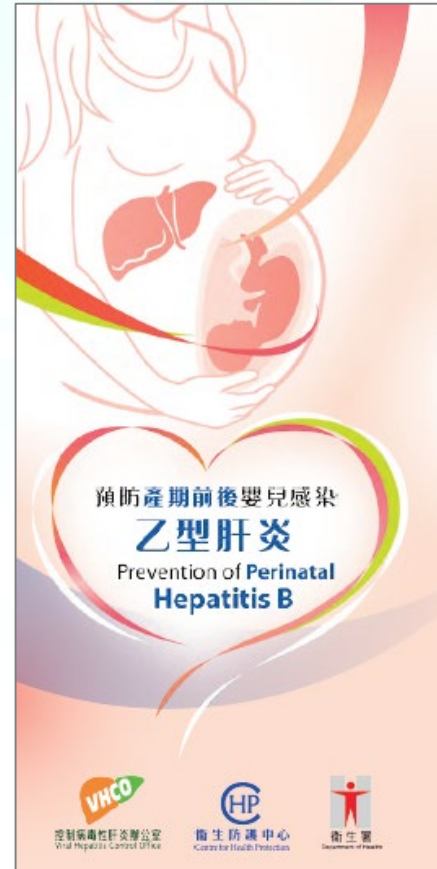
Actions in HK

Other promotional actions

Focused education materials for pregnant women

- [Hindi](#) (हिन्दी)
- [Bahasa Indonesia](#)
- [Nepali](#) (नेपाली)
- [Tagalog](#)
- [Thai](#) (ไทย)
- [Urdu](#) ((اردو))

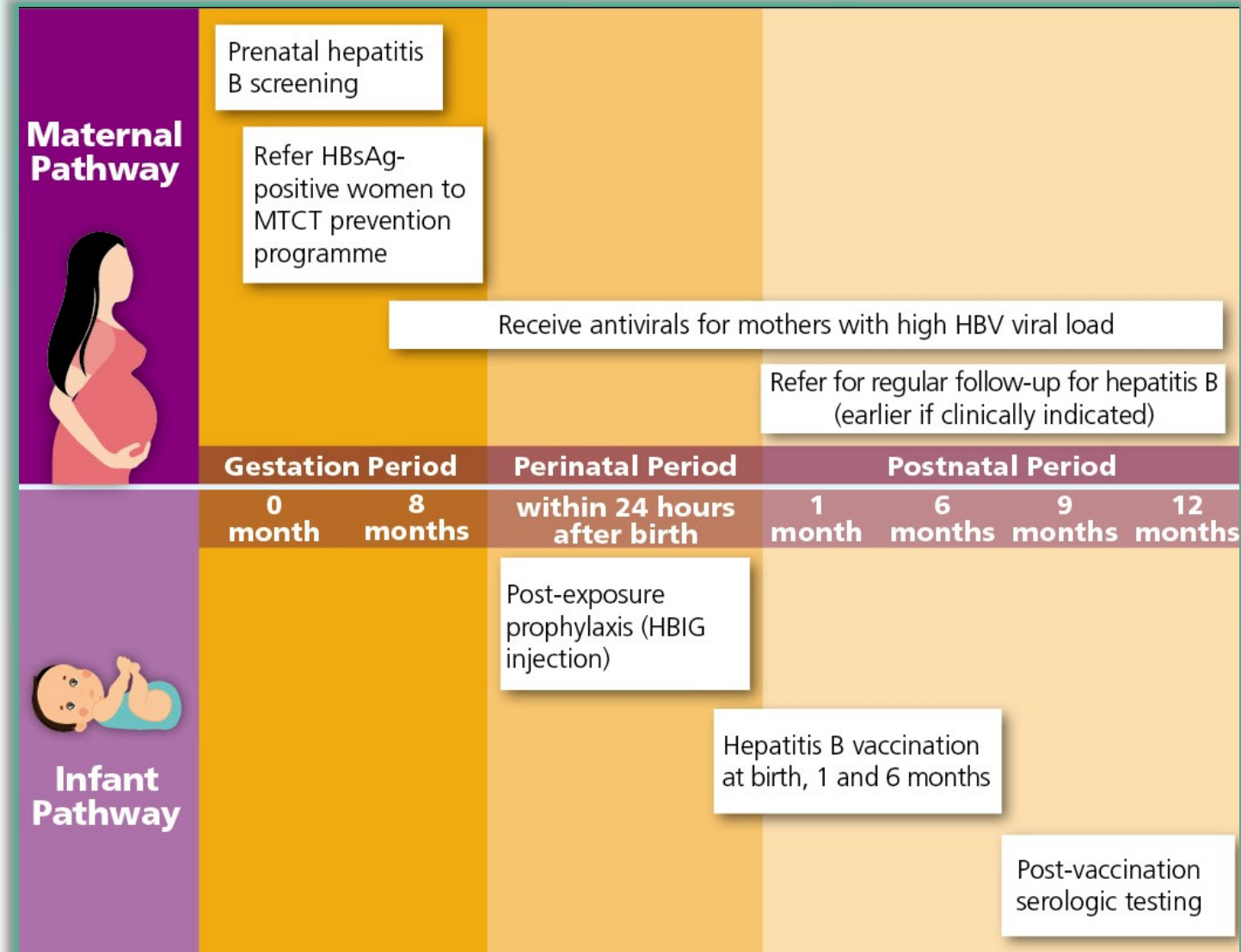
Professional training



Post-vaccination serologic test (PVST)

- HBsAg and anti-HBs testing for all infants born to HBV-infected women at age 9 -12 months
 - **Revaccination** and re-testing for infants who fail to develop immunity after completing the primary series
 - **Referral for management** for infants who are infected with hepatitis B
- To be implemented in 2022 tentatively

HBV prevention pathways with use of antiviral and PVST



斷絕乙肝母嬰傳播 實現無乙肝新一代

**Stop mother-to-child transmission to
realise an *HBV-free generation***



控制病毒性肝炎辦公室
Viral Hepatitis Control Office



衛生防護中心
Centre for Health Protection



衛生署
Department of Health

Hong Kong Viral Hepatitis Action Plan 2020–2024

www.hepatitis.gov.hk



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Department of Health



食物及衛生局
Food and Health Bureau



醫院管理局
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