Serologic testing after hepatitis B vaccination for babies born to mothers infected with hepatitis B virus

December 2021

控制病毒性肝炎辦公室 Viral Hepatitis Control Office
衞生防護中心 Centre for Health Protection
衞生署 Department of Health

Outline

1. Introduction
   - Transmission of HBV and chronic HBV infection
   - Hepatitis B vaccination
   - WHO targets to eliminate viral hepatitis as a public health threat by 2030
   - Situation in Hong Kong

2. Post-vaccination serologic testing (PVST)
   - International recommendations
   - PVST initiative in Hong Kong
   - Experience of PVST programme in other places
   - Useful resources

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Transmission of HBV

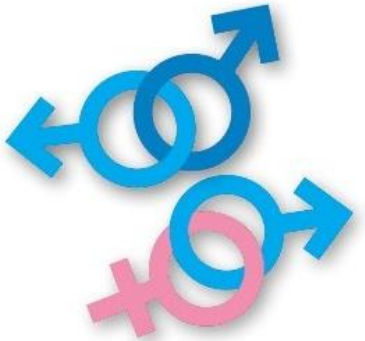
Mother-to-child transmission (MTCT) at birth

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

Mother-to-child transmission

Sexual transmission

- more prevalent in unvaccinated persons with multiple sexual partners



Sexual contact

Contact with contaminated blood or body fluid

- horizontal transmission esp during first 5 years of life
- needlestick injury, tattooing, piercing
- reuse of contaminated needles and syringes (e.g. among persons who inject drugs)

Contact with contaminated blood or body fluid

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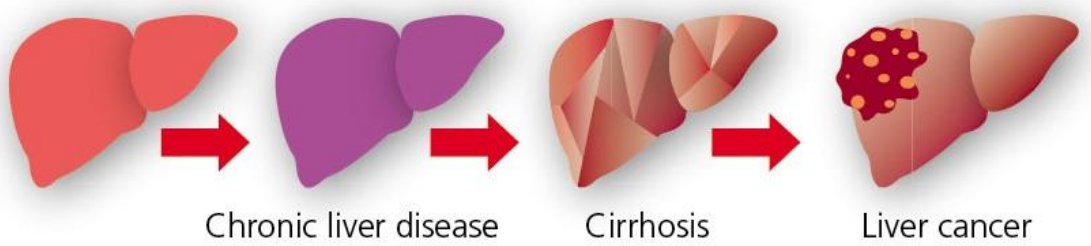
Chronic HBV infection

- The development of chronic HBV infection is common in infants infected from their mothers or before the age of 5 years
- 15 - 40% of untreated persons with chronic HBV infection may develop cirrhosis, liver failure or liver cancer in their lifetime

Risk of chronicity following acute infection	
neonates	80 ~ 90%
children < 6 yrs	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
Lok AS. Chronic hepatitis B. *N Engl J Med* 2002; 346(22):1682-3.

Chronic HBV infection

- 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
- This is the basis for strengthening and prioritizing infant and childhood vaccination

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

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

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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; followed by two or three doses at least 4 weeks apart to complete the primary series.
- A primary three-dose hepatitis B vaccination can induce protective antibody concentration in > 95% of healthy infants, children and young adults.
- Hepatitis B surface antibody (anti-HBs) concentration of ≥10 mIU/mL measured 1–2 months after administration of the last dose of the primary vaccination series is considered a reliable serological marker of long-term protection against HBV infection.

www.who.int/immunization/policy/position_papers/hepatitis_b/en/

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Hepatitis B vaccination

- The final median seroprotection proportions
  - did not vary appreciably by maternal hepatitis B surface antigen (HBsAg) status or hepatitis B immunoglobulin (HBIG) administration
  - lower among infants with birth weights < 2000 grams (93%) [98% for BW ≥ 2000gm]

Schillie SF, Murphy TV. Seroprotection after recombinant hepatitis B vaccination among newborn infants: a review. Vaccine 2013; 31(21):2506-16.

WHO SAGE Meeting – October 2016, Background documents(www.who.int/immunization/sage/meetings/2016/october/5_Update_seroprotection_after_hep_b_in_newborns.pdf?ua=1).

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Hepatitis B vaccination

Long term protection in adequately vaccinated and immunocompetent individuals

Meta-analysis of 22 studies (11 090 subjects)

- the overall cumulative incidence of subclinical HBV breakthrough infection* 5 – 20 years after primary vaccination was 0.7% (95% CI: 0.5% – 1.0%)
- none developed chronic HBV infection

(at least 2 consecutive serum specimens positive for hepatitis B core antibodies (anti-HBc))*

Local 30-year cohort study of 1112 neonates born to hepatitis B mothers recruited in 1983

- 92.6 % developed anti-HBs positivity (≥ 10 mIU/mL) upon completion of the 3-dose hepatitis B vaccination
- 3.5% were tested positive for HBsAg before the age of two
- anti-HBs antibody levels of about two thirds of vaccinees dropped below 10 mIU/mL after 30 years
- no new infection was found after the second year of follow-up

Poorolajal J, Mahmoodi M, Majdzadeh R, et al. Long-term protection provided by hepatitis B vaccine and need for booster dose: a meta-analysis. Vaccine 2010; 28(3):623-31.
Lin AW, Wong KH. Long-term protection of neonatal hepatitis B vaccination in a 30-year cohort in Hong Kong. J Hepatol 2013; 59(6):1363-4.

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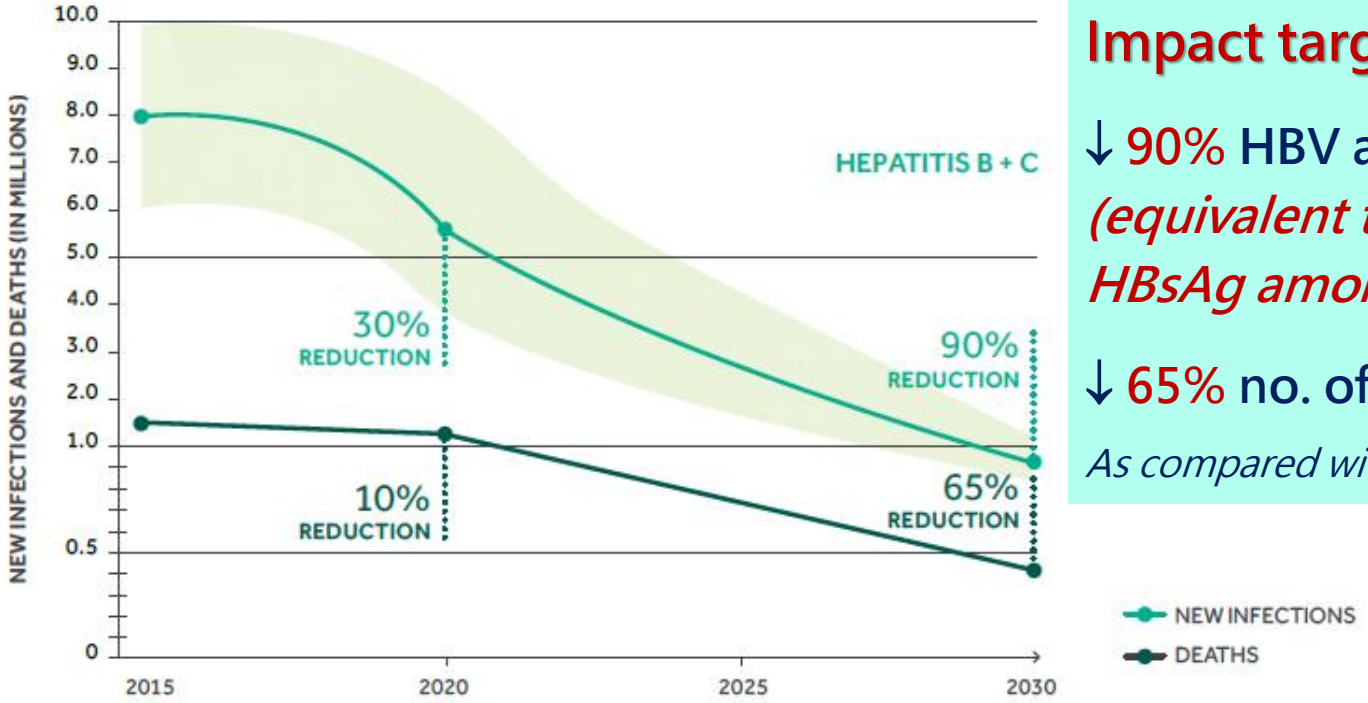
WHO Global health sector strategy on viral hepatitis, 2016 - 2021

Eliminate viral hepatitis as a major public health threat by 2030

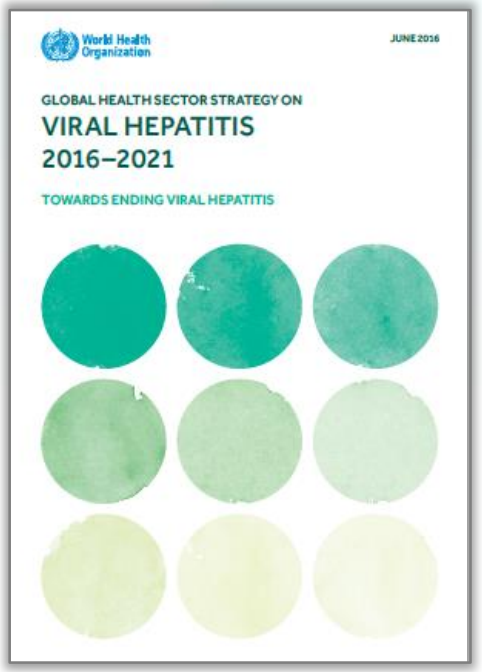


Impact targets in 2030

↓ 90% HBV and HCV incidence
(equivalent to 0.1% prevalence of HBsAg among children)

↓ 65% no. of HBV and HCV deaths

As compared with the baseline in 2015



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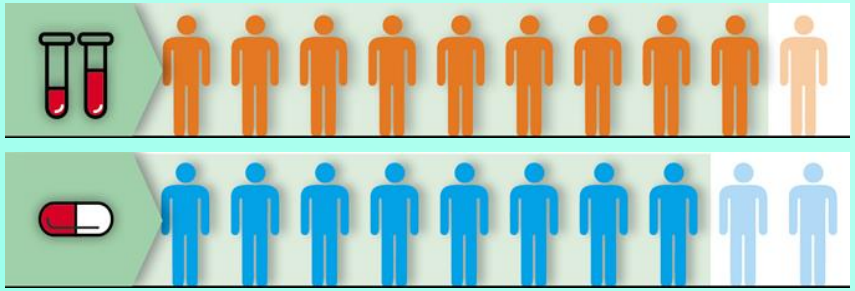
WHO Global health sector strategy on viral hepatitis, 2016 - 2021

Service coverage targets in 2030

- ✓ 90% HBV vaccination coverage for the third dose
- ✓ 90% HBV vaccination coverage for birth dose (or other approach to prevent MTCT)
- ✓ 100% blood donations screened
- ✓ 90% safe injections (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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WHO Global progress report on HIV, viral hepatitis and STI, 2021

Global estimates as of 2019,

- Prevalence of HBV infection in the general population: 3.8%
  - ~ 296 million people living with chronic HBV infection
  - ~ 1.5 million new infections in 2019
- ~ 820 000 people died from hepatitis B in 2019, mostly from cirrhosis and hepatocellular carcinoma

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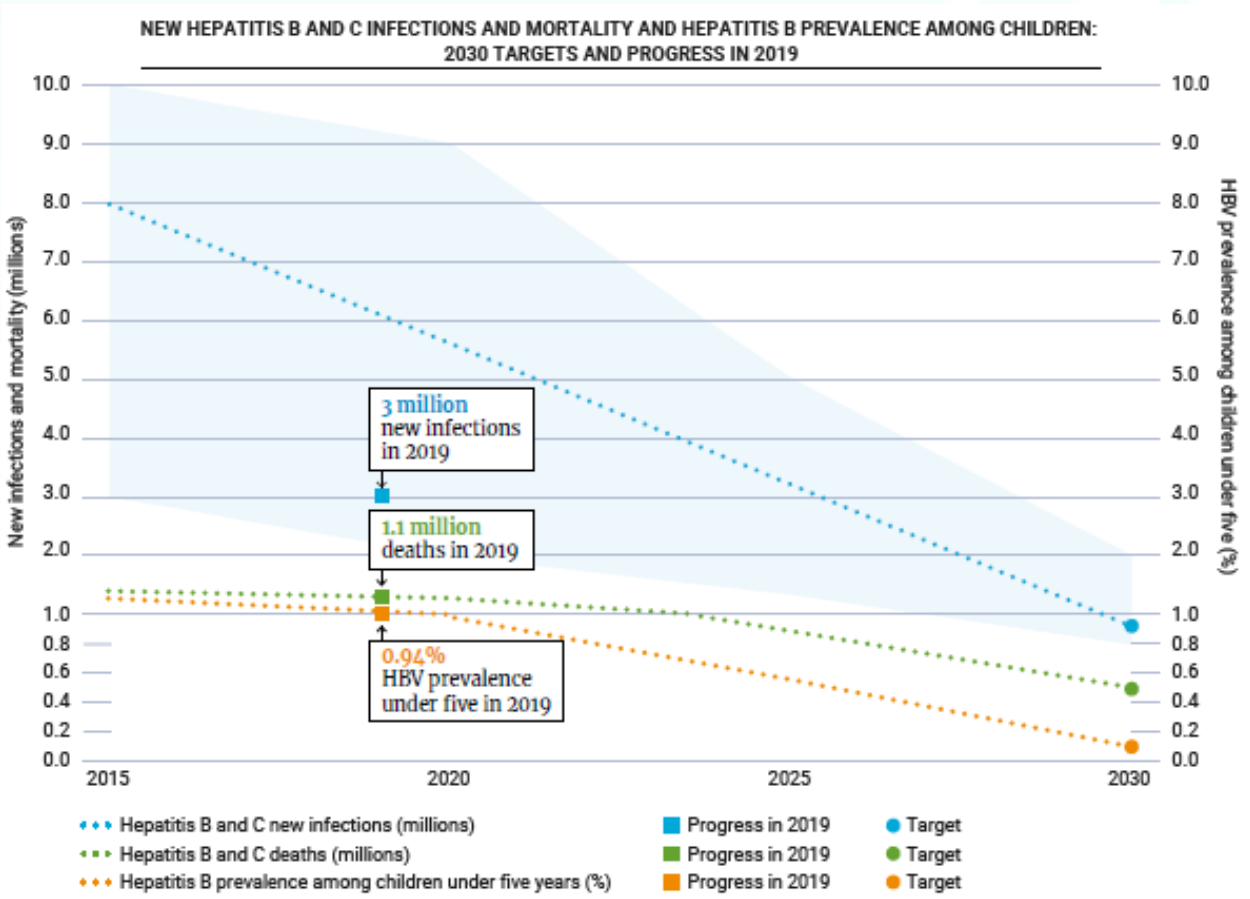
WHO Global progress report on HIV, viral hepatitis and STI, 2021



	2015	2019
HBV & HCV incidence	6-10 million	3 million
HBV & HCV deaths	1.34 million	1.1 million
HBV prevalence under 5	1.3%	0.94%
HBV prevalence	257 million (3.5%)	296 million [3.8%]*
HCV prevalence	71 million (1%)	58 million [0.8%]*

Scaled-up hepatitis B vaccination had steeply reduced the global prevalence of HBV infection among children under 5 to 0.94% in 2019,
from 4.7% in the pre-vaccination era (which, according to the year of introduction can range from 1980s to the early 2000s in different countries)

WHO Global progress report on HIV, viral hepatitis and STI, 2021
WHO Global Hepatitis Report 2017

*Mid-2019 world population = 7.7 billion

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Situation in Hong Kong

- Universal childhood hepatitis B vaccination programme since 1988
- Hepatitis B immunoglobulin (HBIG) given to neonates born to HBV-infected mothers
- Coverage for birth dose has been consistently > 99% over the years
- DH immunisation coverage surveys (ICS) among children aged 2 to 5 have shown a consistently high coverage for birth dose, second dose and third dose(> 99%)

Year	Number of first dose of hepatitis B vaccine administered in hospitals	Number of live births	Estimated birth-dose vaccination coverage
2014	61 813	62 305	99.2%
2015	59 520	59 878	99.4%
2016	60 522	60 856	99.5%
2017	56 403	56 548	99.7%
2018	53 506	53 716	99.6%
2019	52 603	52 856	99.5%
2020	42 876	43 031	99.6%

Year of ICS	Year of birth	Coverage of the third-dose vaccine
2015	2009	99.2%
	2010	99.2%
	2011	99.2%
	2012	99.2%
2018	2012	99.8%
	2013	99.5%
	2014	99.7%

*Estimated from statistics on administration of first dose of hepatitis B vaccine in public and private hospitals

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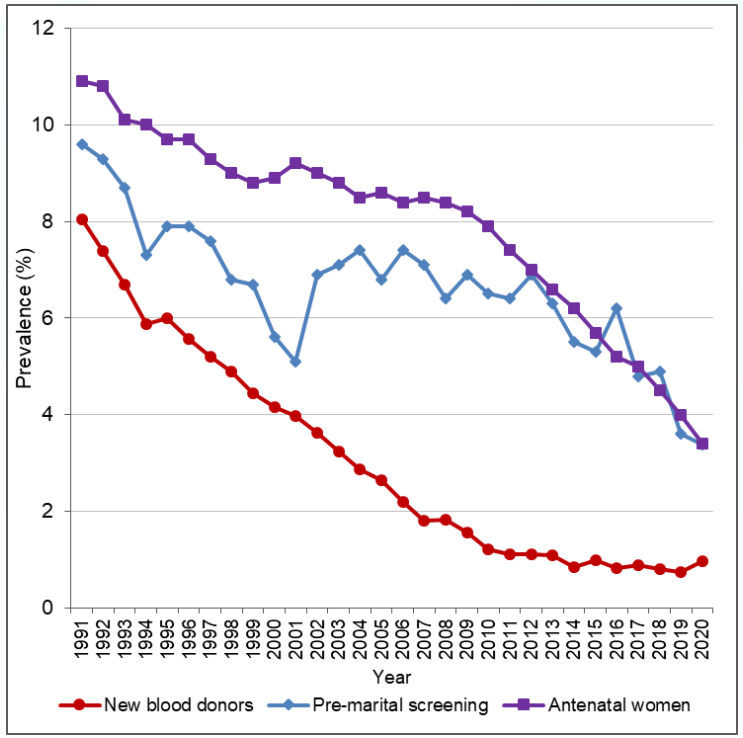
Situation in Hong Kong

- In 2016, a territory-wide prevalence study gave an age- and sex-adjusted HBsAg prevalence :
  7.2% (~ 540 000 HBV infection)[1]
- Mother-to-child transmission (MTCT) accounts for the prevalence of HBV infection in Hong Kong
- ↓ HBsAg prevelance in populations without specific HBV risk

	1991	2020
New blood donors	8.0 %	1.0 %
Pre-marital screening	9.6 %	3.4 %
Antenatal women	10.9 %	3.4 %



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

[1] Liu KS, Seto WK, Lau EH, et al. A Territorywide Prevalence Study on Blood-Borne and Enteric Viral Hepatitis in Hong Kong. J Infect Dis 2019; 219(12): 1924-33.

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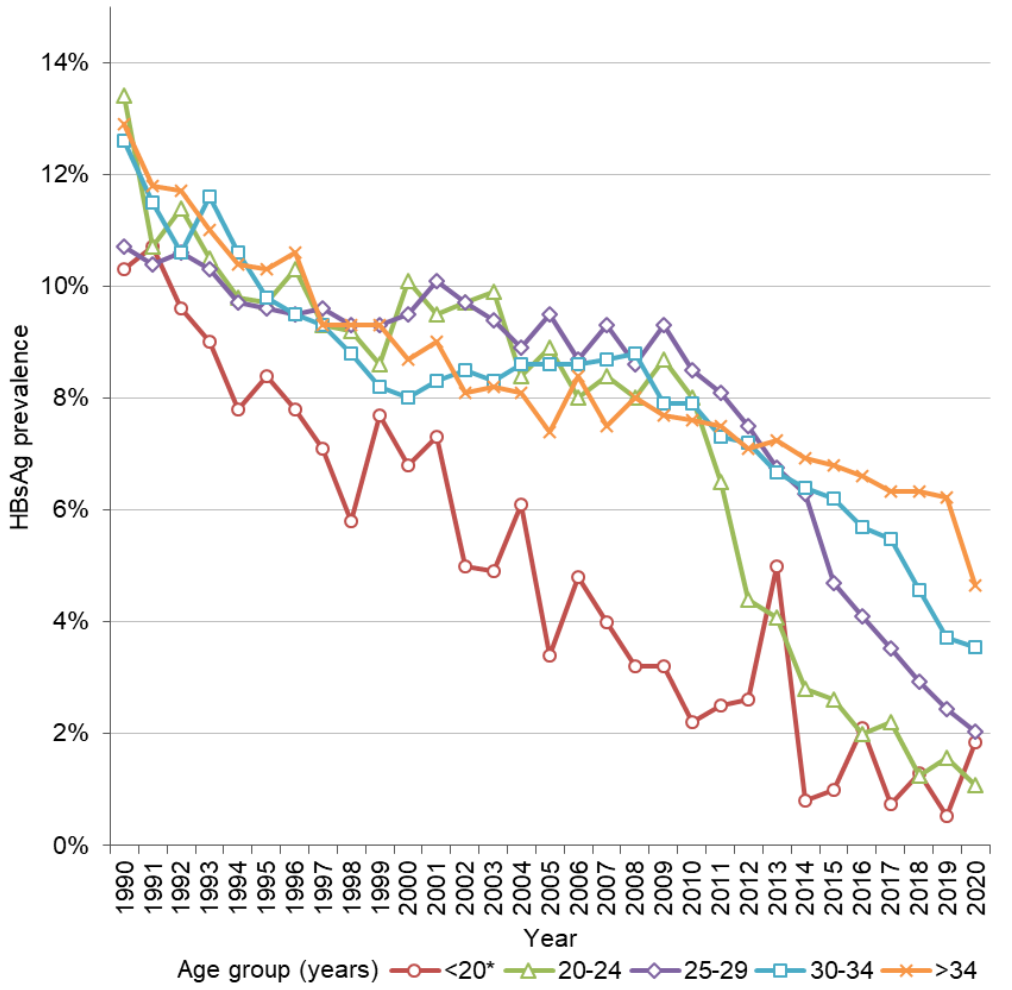
Situation in Hong Kong

- The prevalence of HBsAg among antenatal mothers varied significantly by age
  - dropping to a low level (< 2%) among those aged < 25
  - > 4% among those aged ≥ 35

	1991	2020
< 20	10.7 %*	1.9 %
20 - 24	10.7 %	1.1 %
25 - 29	10.4 %	2.0 %
30 - 34	11.5 %	3.5 %
> 34	11.8 %	4.7 %

* Figure refer to age group 15 - 19



Source: DH Family Health Service and Public Health Laboratory Service Branch

Situation in Hong Kong

- In 2009, DH conducted a biomarker survey on 1913 children aged 12 – 15 years who were born after the implementation of universal hepatitis B vaccination programme in 1988 → HBsAg seroprevalence at 0.78%
- In July 2011, Hong Kong was verified by the WHO Western Pacific Regional Office (WPRO) as having successfully achieved the goal of hepatitis B control.
- In 2013, Hong Kong was verified as having met the final regional control goal of achieving an HBsAg seroprevalence of less than 1% in children.

WHO targets

As compared with the baseline number in 2015:
By 2020: 30% reduction (equivalent to 1% prevalence of HBsAg among children)
By 2030: 90% reduction (equivalent to 0.1% prevalence of HBsAg among children)

Hong Kong achieves goal of hepatitis B control verified by the World Health Organization Western Pacific Region. Department of Health, Hong Kong; Communicable Diseases Watch 2011;8(15).

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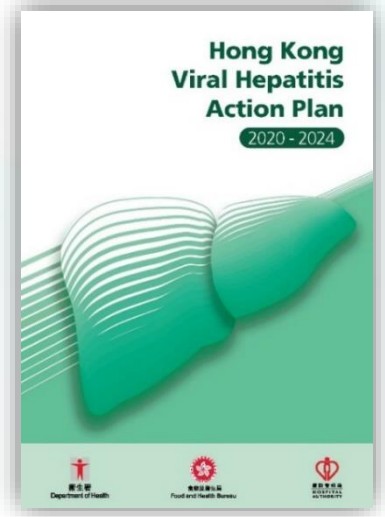
Hong Kong Viral Hepatitis Action Plan 2020 - 2024

- Progressing towards the WHO targets to eliminate viral hepatitis as a public health threat by 2030
  - 90% infected people diagnosed
  - 80% eligible patients treated
  - ↓ no. of new cases of chronic HBV and HCV by 90%
  - ↓ no. of deaths from HBV and HCV by 65%
- Specific actions under 4 strategic axes
- DH, HA and other community stakeholders
- Ultimate vision to render HK free of chronic viral hepatitis



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

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Hong Kong Viral Hepatitis Action Plan 2020 - 2024

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

Hong Kong Viral Hepatitis Action Plan 2020 - 2024

Use antivirals for preventing MTCT of HBV

- The initiative was rolled out to all birthing hospitals in August 2020
- Baseline HBV DNA done for all HBV-infected pregnant women
  - If high viral load > 200 000 IU/ml → referral to hepatology clinic for consideration of tenofovir (300mg daily by 28 week gestation)
  - Refer other HBV-infected pregnant women to appropriate level of care for long-term HBV management
- Hepatitis nurse clinics are set up to augment the capacity of hepatology clinic (education & counselling of antiviral use, monitor drug compliance, arrange assessment)

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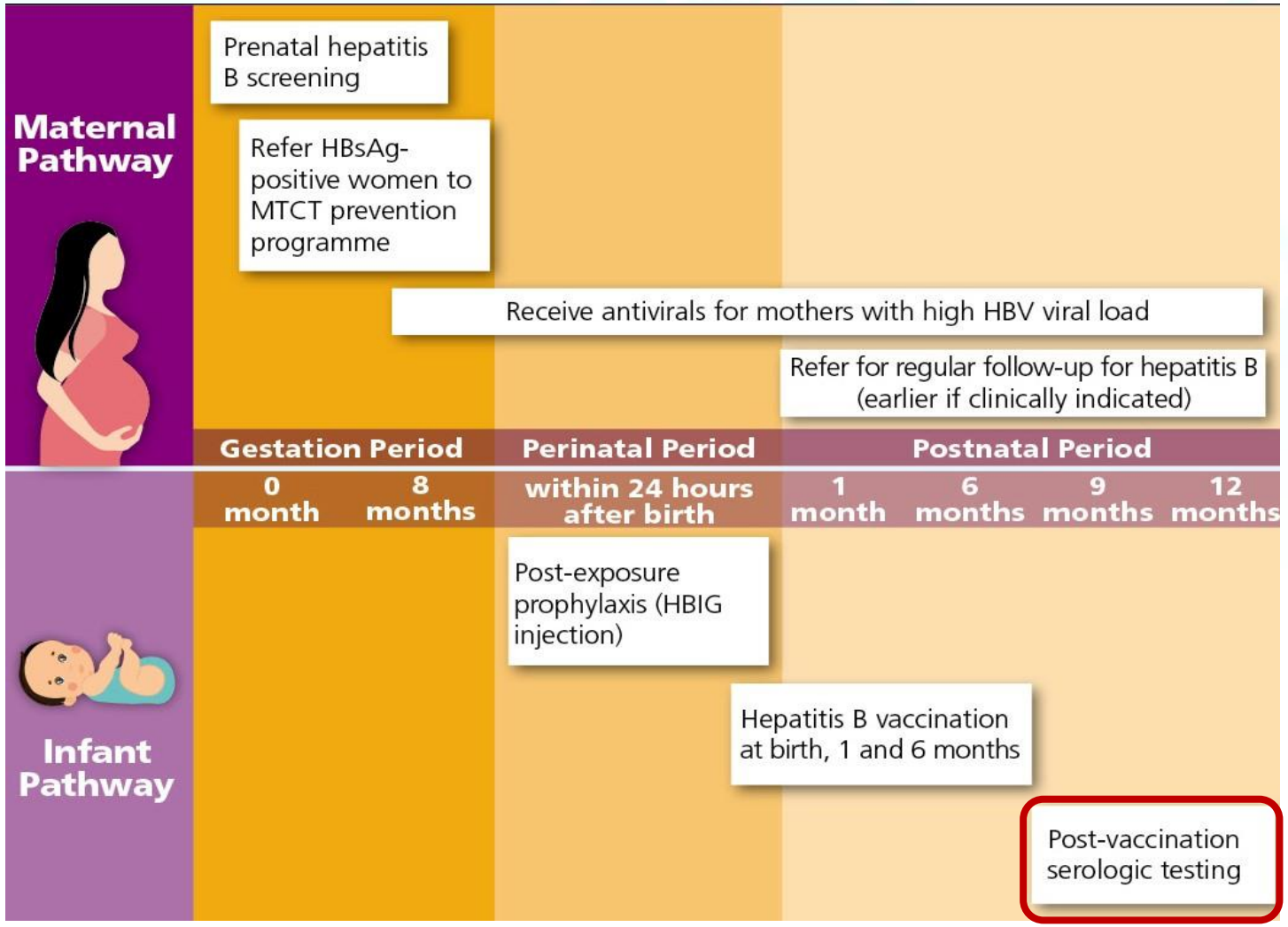

Post-vaccination serologic testing

WHO position paper – July 2017

Testing for immunity after HBV vaccination is recommended for individuals whose subsequent clinical management depends on knowledge of their immune status, such as

- persons at risk of occupational exposure to HBV infection, e.g. health-care workers
- infants born to HBsAg-positive mothers
- chronic haemodialysis patients
- HIV-positive and other immunocompromised persons
- sex partners or needle-sharing partners of persons who are HBsAg-positive

Post-vaccination serologic testing

WHO Regional Office for the Western Pacific (WPRO)

Hepatitis B control through immunization: a reference guide (2014)

PVST for babies born to HBsAg-positive mothers is useful in assessing the effectiveness of MTCT prevention programme, when antenatal hepatitis B screening and vaccination programme are in place

Post-vaccination serologic testing

Purposes of PVST

- to identify babies born to HBV-infected women who do not have an adequate immune response to the primary hepatitis B vaccination series and thus require re-vaccination
- to enable early identification of HBV-infected babies to ensure appropriate medical care for them
- to provide systematic information to monitor and evaluate the effectiveness of the MTCT prevention programme and strategy

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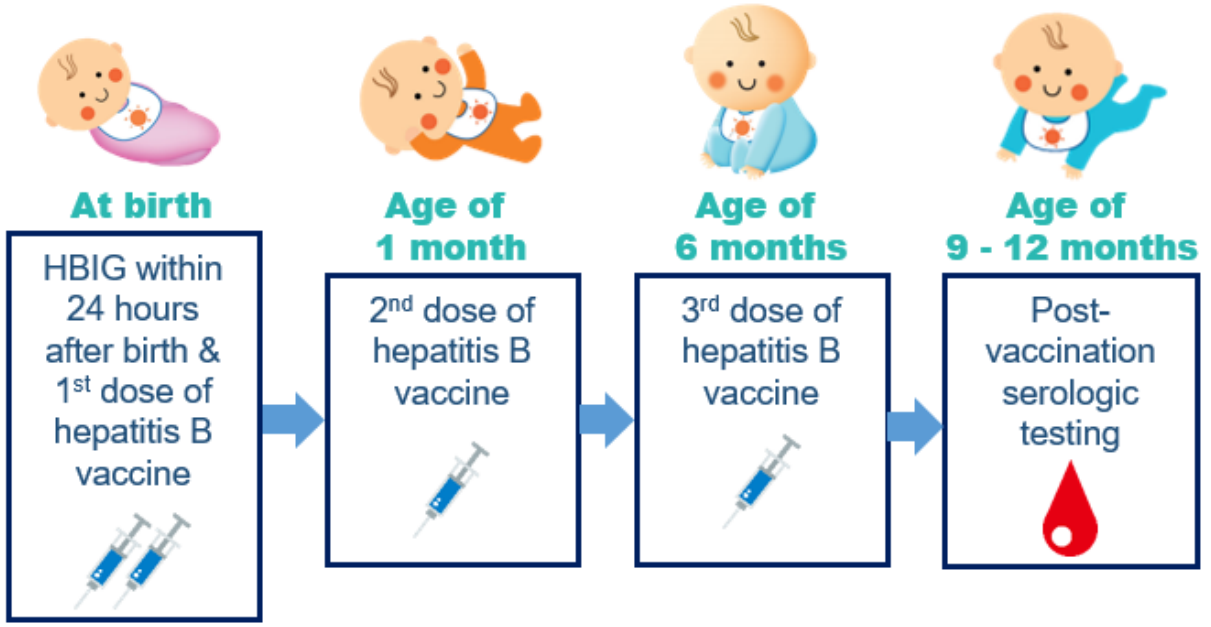
Post-vaccination serologic testing

- testing on HBsAg and anti-HBs
- Infants born to HBV-infected women
- at age 9 –12 months
- If primary vaccination series is delayed, 1 – 2 months after the final dose



PVST

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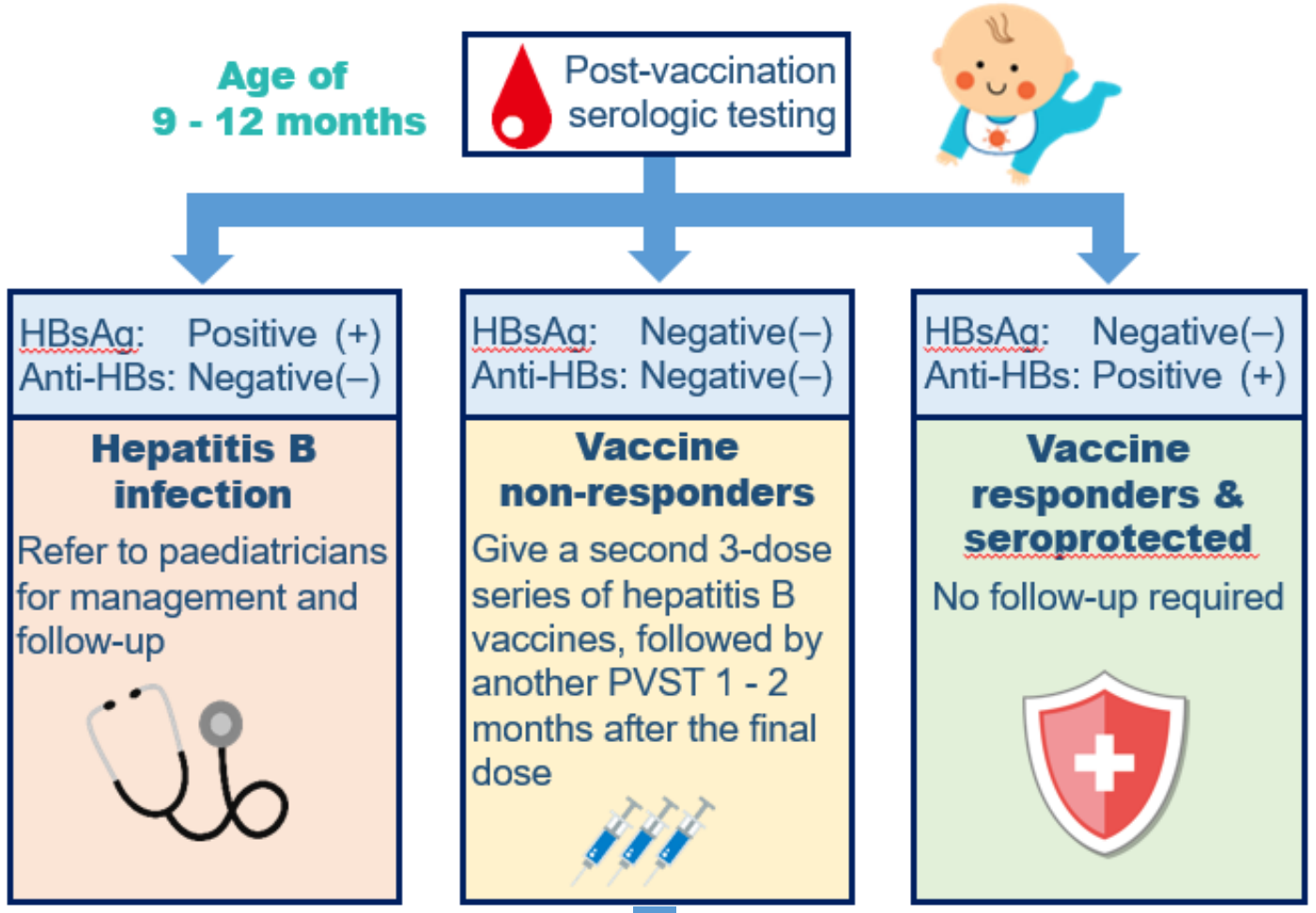
The timing of PVST is critical to guide appropriate follow-up actions

- The optimal timing of PVST is 1 – 2 months after the final dose of hepatitis B vaccine due to the lower levels of measured anti-HBs with increasing time after vaccination.
- PVST undertaken at increasing intervals after the final vaccine dose could result in misclassification of some seroprotected infants as vaccine non-responders and therefore lead to unnecessary re-vaccination.
- PVST should not be performed earlier than the age of 9 months to avoid detection of passive anti-HBs from HBIG administered at birth and maximise the likelihood of detecting late HBV infection.

PVST



HA Paed with ID unit
(QEH, QMH, PMH & PWH)

If inadequate immunity after 2 series of hepatitis B vaccination → HKCH

Positive anti-HBs result refers to ≥ 10 mIU/mL

Post-vaccination serologic testing

Seroconversion after re-vaccination

- WHO position paper (2017): Most individuals who do not respond to a primary 3-dose series with anti-HBs antibody concentrations < 10 mIU/mL do respond to an additional 3-dose vaccination series.
- A systematic review and meta-analysis of management options for adults who responded poorly to hepatitis B vaccination found that seroconversion rate after additional 3 doses could reach 80% or above.
- Other studies or PVST programmes showed a seroconversion rate > 90% after reimmunisation of infants or children who did not respond to the primary hepatitis B vaccination.

PVST

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Post-vaccination serologic testing

Action	Action Party	Timeline	Progress
3.1.2.1 Establish a policy initiative to provide PVST to babies born to HBsAg-positive mothers	SCVH	Completed	✓
3.1.2.2 Establish the implementation plan and resources implication of PVST	DH & HA	2020Q4	✓
3.1.2.3 Provide professional training about PVST programme to obstetricians and paediatricians	DH & HA	2021Q3	✓
3.1.2.4 Establish the logistics and workflow of PVST	DH & HA	2021Q4	✓
3.1.2.5 Implement PVST programme	DH & HA	2022Q1	
3.1.2.6 Review the acceptance of PVST programme	DH & HA	2023Q2	

PVST

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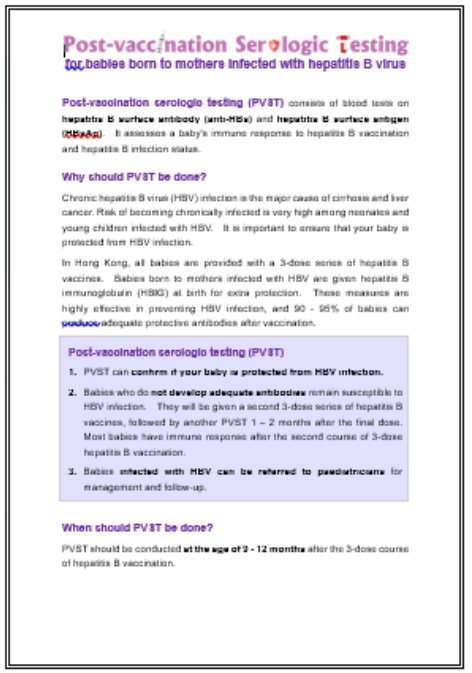
Post-vaccination serologic testing

- DH and HA collaborate to provide PVST service
- Plan to implement the service in Q1 of 2022
- DOB as eligibility cut-off:
  Infants born to hepatitis B mothers in and after April 2021 will be included in the initiative
- Interim review will be conducted on clinical and service outcomes
- PVST will provide systematic information to assess the effectiveness of the MTCT prevention strategies


Post-vaccination Serologic Testing
for babies born to mothers infected with hepatitis B virus

Post-vaccination serologic testing (PVST) consists of blood tests on hepatitis B surface antibody (anti-HBs) and hepatitis B surface antigen (HBsAg). It assesses a baby's immune response to hepatitis B vaccination and hepatitis B infection status.

Why should PVST be done?

Chronic hepatitis B virus (HBV) infection is the major cause of cirrhosis and liver cancer. Risk of becoming chronically infected is very high among neonates and young children infected with HBV. It is important to ensure that your baby is protected from HBV infection.

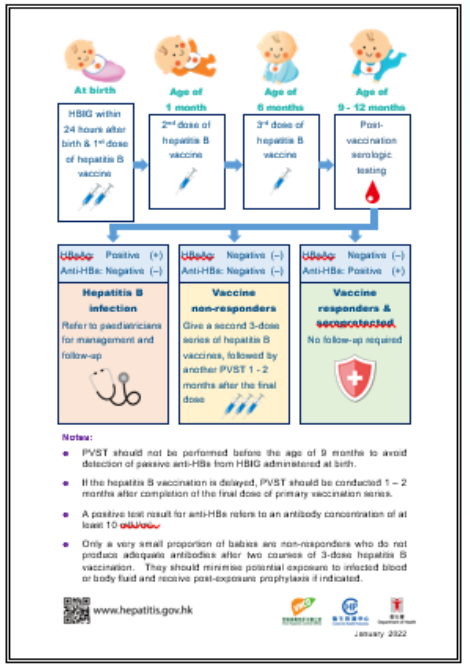
In Hong Kong, all babies are provided with a 3-dose series of hepatitis B vaccines. Babies born to mothers infected with HBV are given hepatitis B immunoglobulin (HBIG) at birth for extra protection. These measures are highly effective in preventing HBV infection, and 90 - 95% of babies can produce adequate protective antibodies after vaccination.

Post-vaccination serologic testing (PVST)

1. PVST can confirm if your baby is protected from HBV infection.
2. Babies who do not develop adequate antibodies remain susceptible to HBV infection. They will be given a second 3-dose series of hepatitis B vaccines, followed by another PVST 1 – 2 months after the final dose. Most babies have immune response after the second course of 3-dose hepatitis B vaccination.
3. Babies infected with HBV can be referred to paediatricians for management and follow-up.

When should PVST be done?

PVST should be conducted at the age of 9 - 12 months after the 3-dose course of hepatitis B vaccination.



www.hepatitis.gov.hk/english/health_professionals/files/iCE_PVST.pdf
www.hepatitis.gov.hk/english/hepatitis_elimination/maternal_transmission_of_hepatitis_b.html

Experience of PVST programmes in other places

Macau (2009 – 2013)

- 74.5% (980/1315) had completed hep B vaccination and PVST according to protocol
  - 88% (864/980) seroprotected
  - 9.6% (94/980) inadequate immunity → 74 re-vaccinated
    → 29 repeated PVST (all with adequate anti-HBs)
  - 2.24% (22/980) tested positive for HBsAg (MTCT rate)

Chinese Mainland

- uptake rate at 65.6% in some provinces (Henan, Sichuan, Jilin and Gansu) in 2014

Choi KC, Wong CL, Ieong KM. Effectiveness of Macau hepatitis B vaccination programme for newborns from hepatitis B carrier mother. HK J Paediatr (New Series) 2019; 24:76-9.

Wang F, Zhang G, Zheng H, et al. Post-vaccination serologic testing of infants born to hepatitis B surface antigen positive mothers in 4 provinces of China. Vaccine 2017; 35(33):4229-35.

Key facts of PVST

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1. The development of chronic HBV infection is common in infants infected from their mothers or before the age of 5 years
2. Post-vaccination serologic testing is recommended for all infants born to mothers infected with HBV
3. PVST on HBsAg and anti-HBs is conducted at age of 9 - 12 months
4. Those without adequate immunity should be re-vaccinated and retested

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Video – Stop MTCT to realise a hepatitis B-free generation

https://www.youtube.com/watch?v=5_FFuOKVVb4

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Video – Hong Kong Viral Hepatitis Action Plan 2020-2024

English

Chinese

https://www.youtube.com/watch?v=WqeRtCNtDk0

Useful resources

Category	Title	Link	Cover
Factsheet	Post-vaccination Serologic Testing (PVST)	https://www.hepatitis.gov.hk/doc/pdf/PVST_factsheet.pdf	
iContinuing Education (iCE)	Serologic testing after hepatitis B vaccination for babies born to mothers infected with hepatitis B virus	https://www.hepatitis.gov.hk/english/health_professionals/files/iCE_PVST.pdf	
iContinuing Education (iCE)	Prevention of mother-to-child transmission of hepatitis B virus	https://www.hepatitis.gov.hk/english/health_professionals/files/iCE_PMTCT_of_HBV.pdf	

Useful resources

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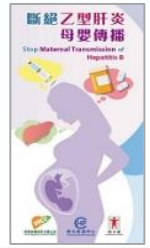
Category	Title	Link	Cover
Health Talk	Prevention of mother-to-child transmission of hepatitis B	https://www.hepatitis.gov.hk/english/health_professionals/files/Prevention_of_MTCT_of_HBV_web.pdf	
Health Talk	Stop mother-to-child transmission of hepatitis B	https://www.hepatitis.gov.hk/tc_chi/news_activities/files/mother2child_Hepatitis_B.pdf	
Video	Hong Kong Viral Hepatitis Action Plan 2020-2024	https://youtu.be/VaHs-DZWXEM	
Video	Stop mother-to-child transmission to realise a hepatitis B-free generation	https://youtu.be/5_FFuOKVVb4	

Useful resources

Category	Title	Link	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	Hepatitis B Vaccination	https://www.hepatitis.gov.hk/tc_chi/resources/files/leaflet2020_2.pdf	

控制病毒性肝炎辦公室 Viral Hepatitis Control Office
衞生防護中心 Centre for Health Protection
衞生署 Department of Health

Useful resources

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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	
Poster	Hepatitis B Vaccination	https://www.hepatitis.gov.hk/tc_chi/resources/files/poster2020_2.pdf