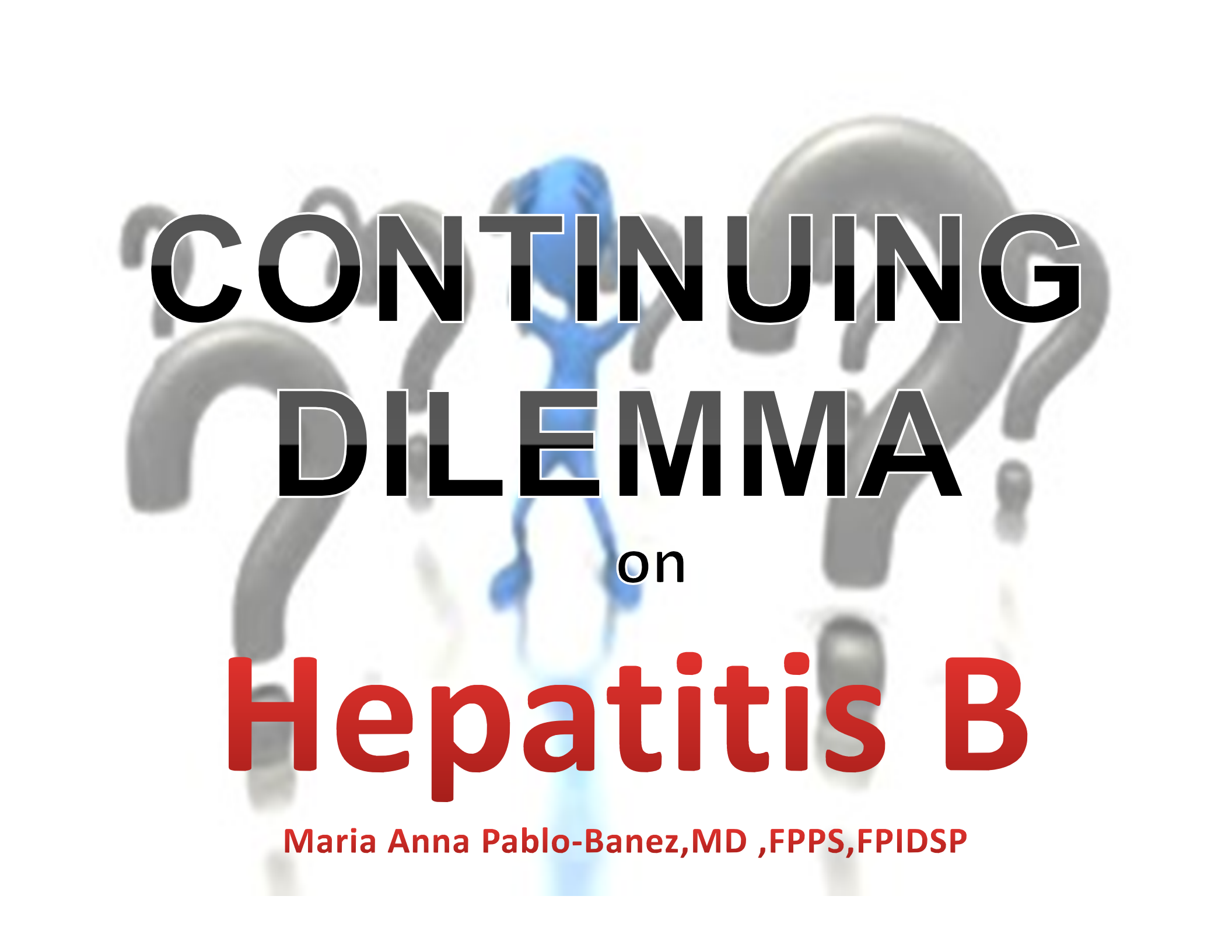


CONTINUING DILEMMA

on

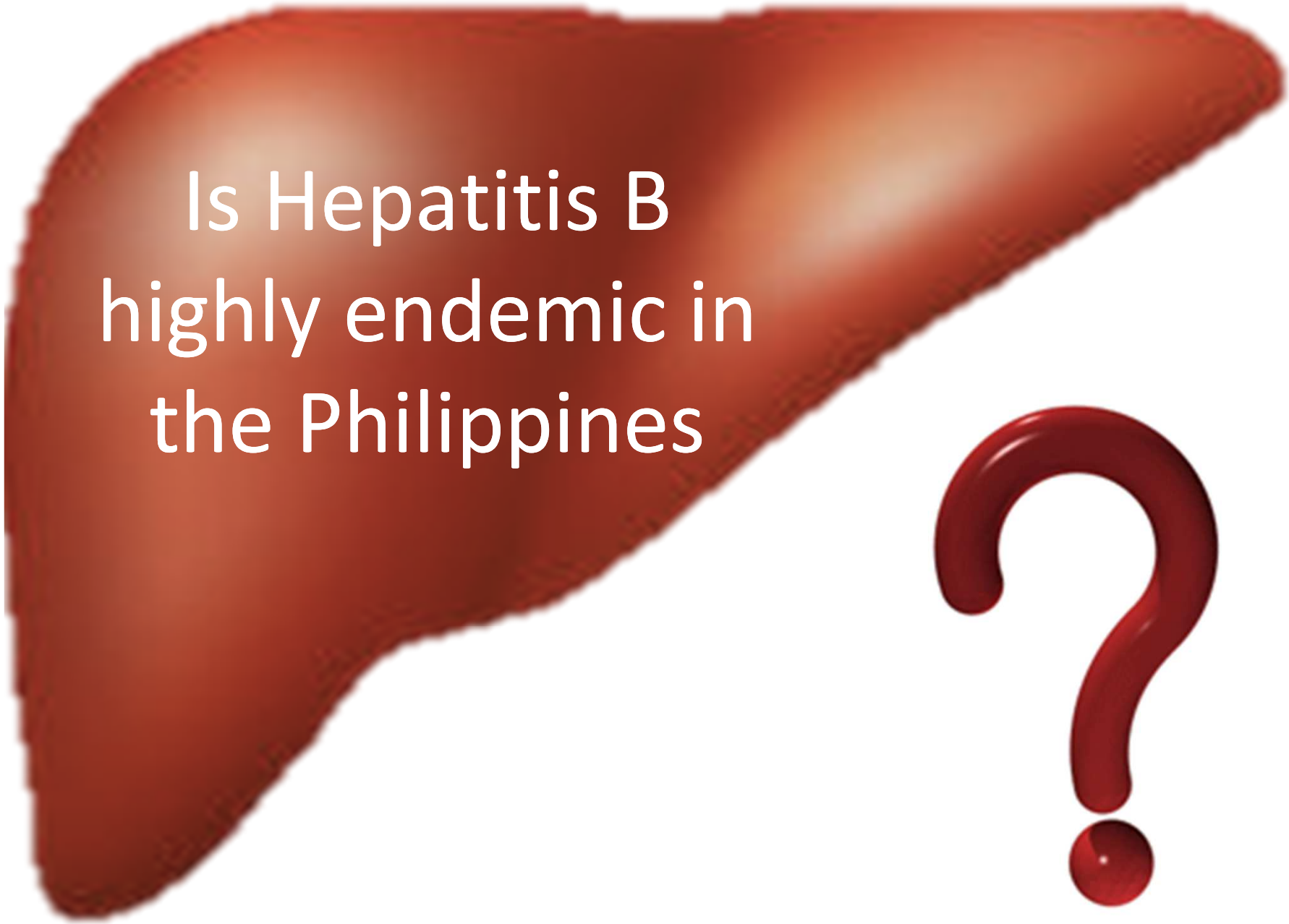
Hepatitis B

Maria Anna Pablo-Banez,MD ,FPPS,FPIDSP

Outline

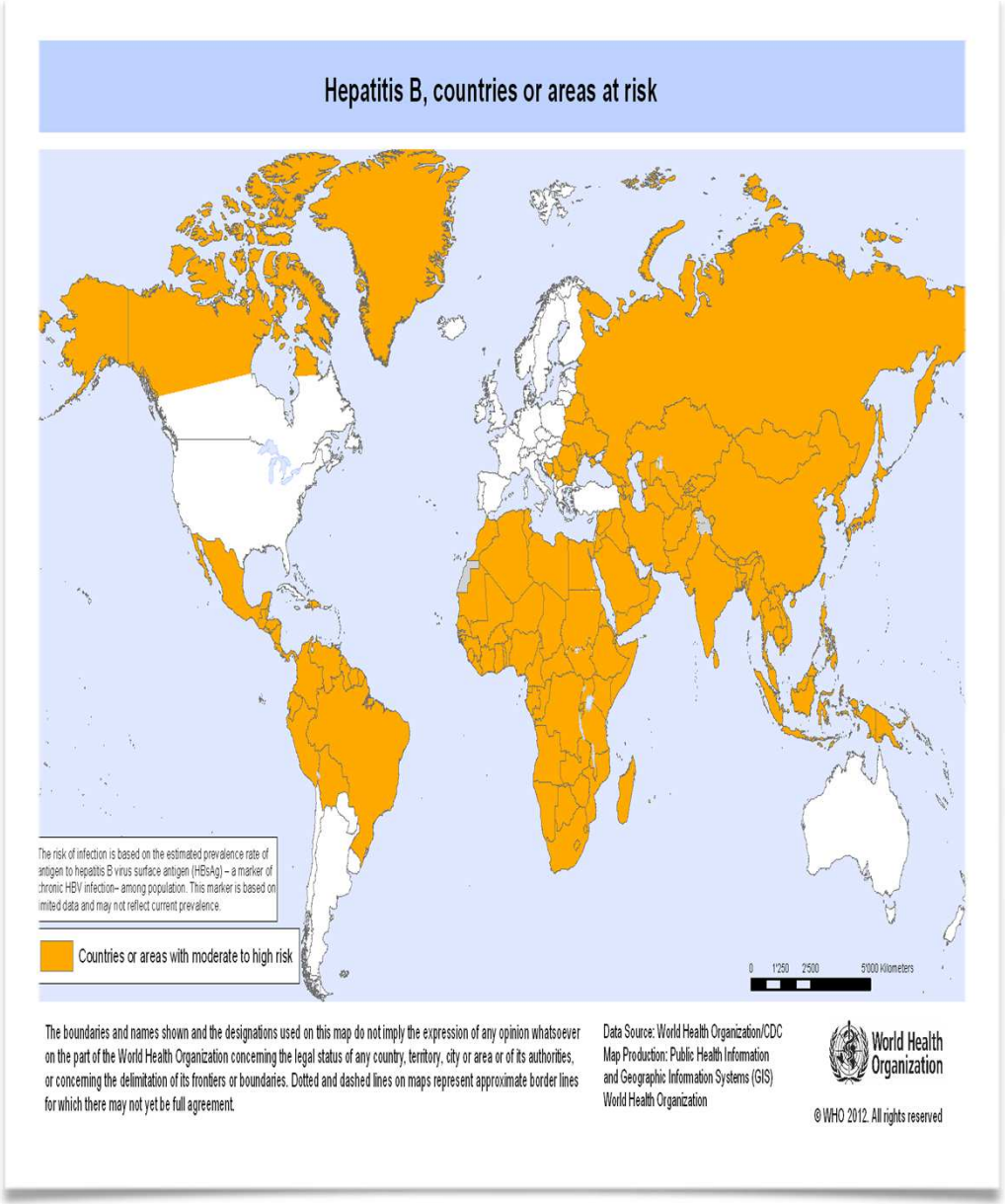
Frequently Asked Questions on:

- Disease Burden
- Transmission
- Clinical Spectrum
- Diagnosis
- Prevention


Is Hepatitis B
highly endemic in
the Philippines

Disease Burden

- >2 billion people infected worlwide
- ~ 360 million people chronically infected
- most prevalent in the Asia-Pacific region



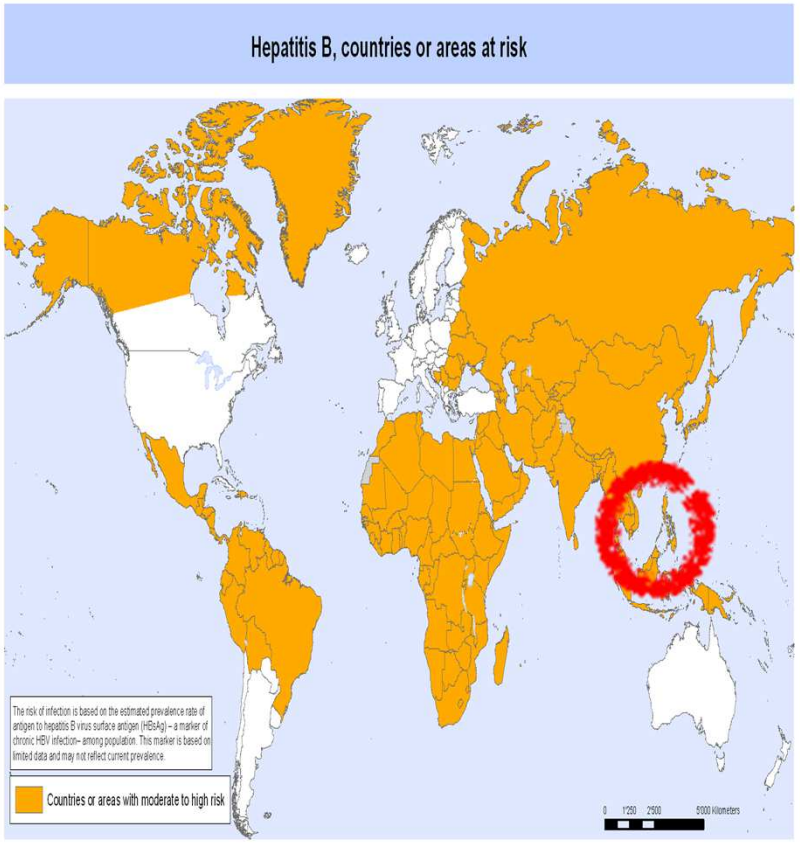
www.who.int/.../diseases/hepatitisB/new.../en/

WHO Level of Endemicity	Prevalence of Chronic HBsAg carriage
High	≥8%
Intermediate	2%-7%
Low	<2%

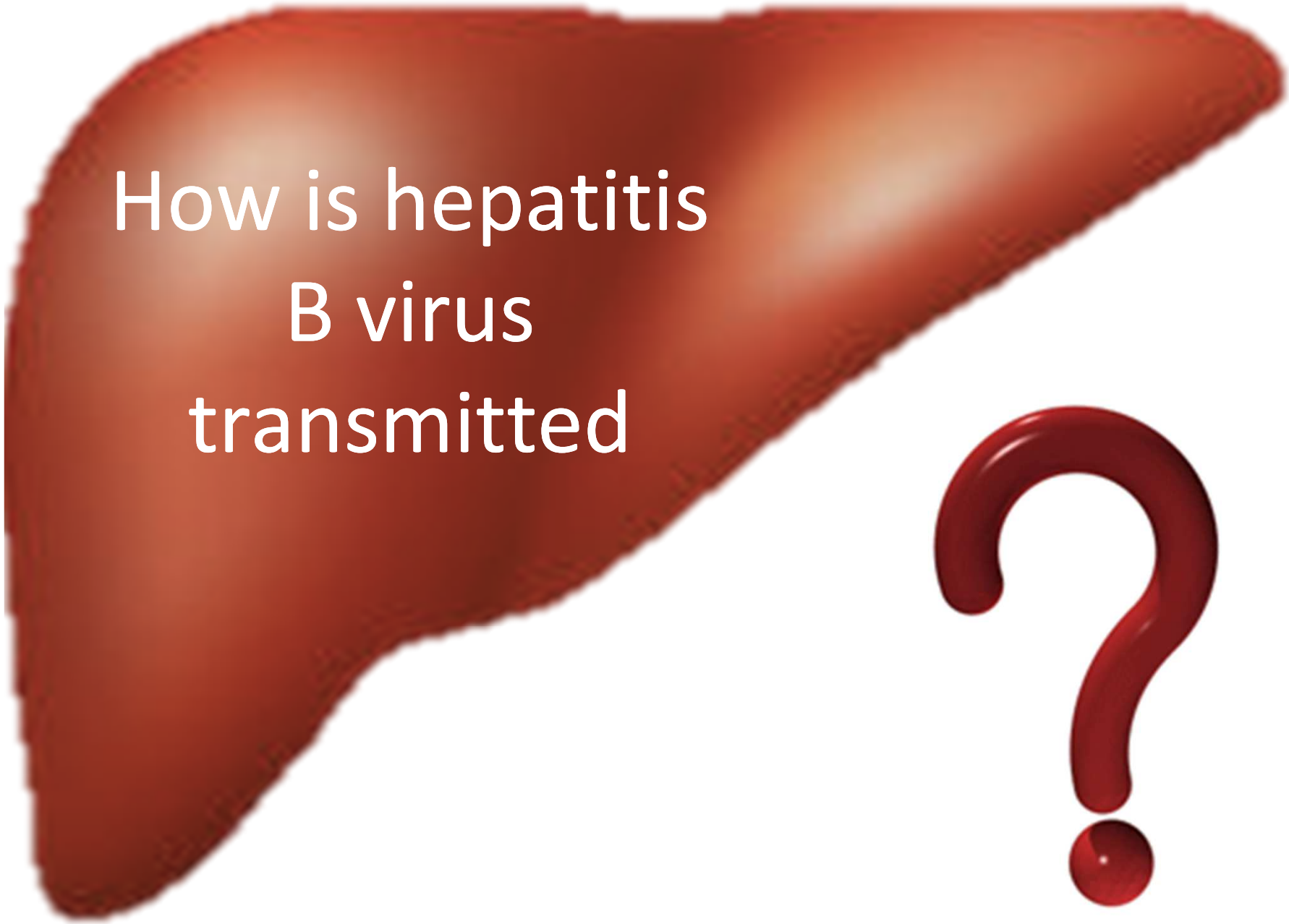
*www.cdc.gov/**vaccine**s/pubs/pinkbook/**hepb**.html,*
*www.who.int/**immunization**/topics/WHO_position_paper_**HepB**.pdf*

Disease Burden

- Prevalence of HBsAg Seropositivity Among Filipino Adults: 16.7% or ~7.3 million CHB adults
- Philippines is HIGHLY ENDEMIC for Hepatitis B



Wong SN, et al.World J Hepatol 2013 April 27; 5(4): 214-219


How is hepatitis
B virus
transmitted

Primary Sources of HBV Infection

Perinatal exposure from infected mothers at birth

- –most common mode of spread in highly endemic areas
- –WHO and DOH estimate 10% HBsAg positivity among Filipino women of childbearing age

CDC.MMWR.December 23, 2005 / 54(RR16);1-23
WHO Weekly Epidemiol Rec. 2009;84(40):405-20
WHO,WPRO, Manila;2006a
DOH, Republic of the Philippines.AO No. 2006-0015.

Risk of Vertical Transmission Without Prophylaxis

Maternal Status	Transmission Rate
HBsAg (+) , HBeAg (+)	70%-90%
HBsAg(+) , HBeAg (-)	10%-40%

CDC.MMWR.December 23, 2005 / 54(RR16);1-23
WHO. Weekly Epidemiol Rec. 2009;84(40):405-20

Primary Sources of HBV Infection

- **Nonsexual person-to-person contact**
  - inadvertent percutaneous or mucosal contact with blood or infectious body fluids of infected household member

In the WesternPacific Region, most CHB results from vertical transmission at birth or horizontal transmission in children under the age of 5 years (WHO)

V

survive in the environment ≥ 7 days)

CDC.MMWR.December 23, 2005 / 54(RR16);1-23
WHO Weekly Epidemiol Rec. 2009;84(40):405-20
Rani M, Yang B, Nesbit R. *Bull World Health Organ. 2009;* ***87: 707-13***

Primary Sources of HBV Infection

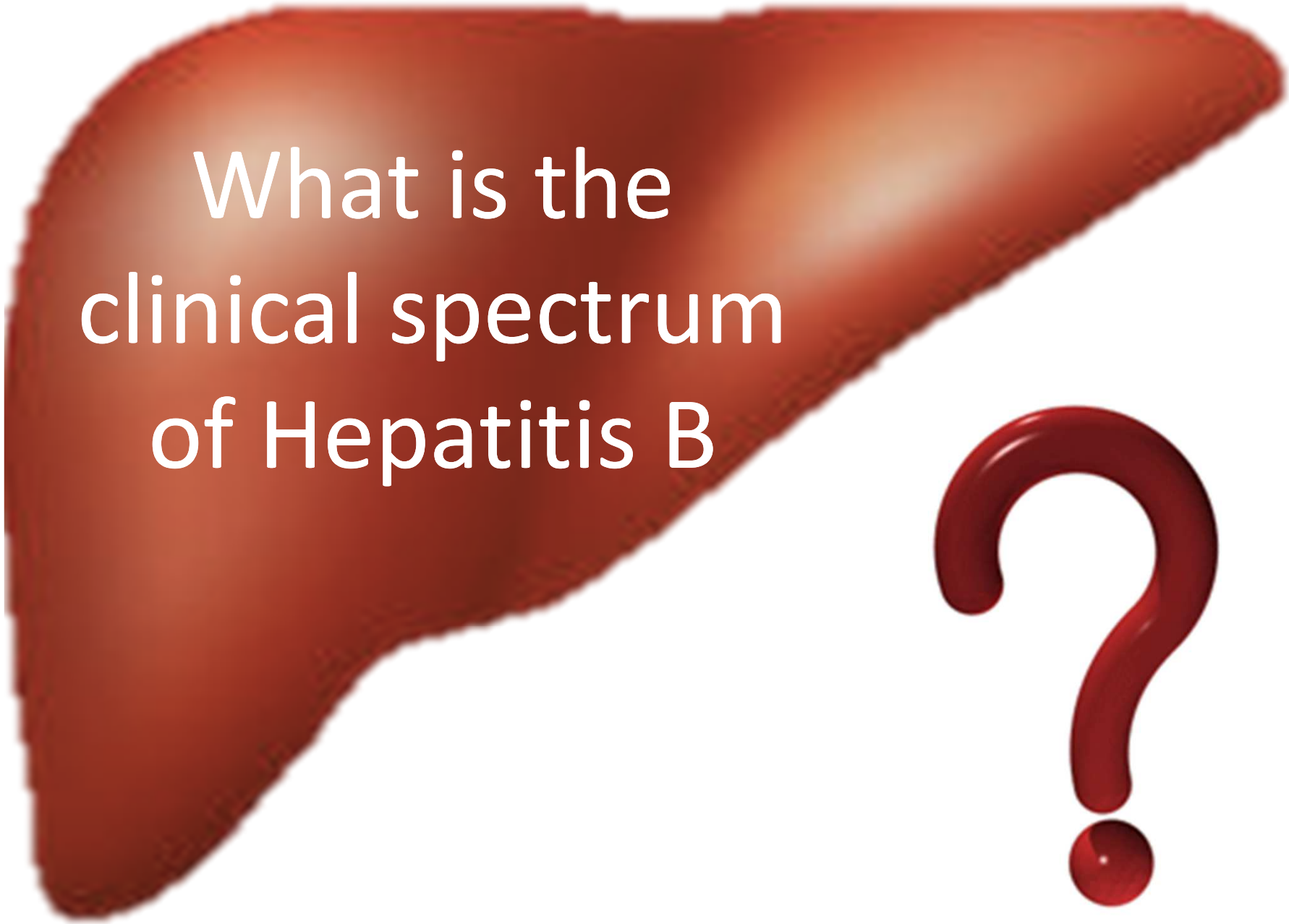
- **Sexual contact**
  - High risk sexual activity(i.e. multiple partners and male having sex with males)
- **Percutaneous exposure to blood or infectious body fluids**
  - Unsafe injection practices
  - Use of contaminated needles, syringes, sharps (acupuncture, tattooing, piercing, manicure/pedicure)
  - Cuts on skin
  - Sharing personal items (e.g. razor, toothbrushes)
  - Inadequately sterilized dental and surgical instruments

CDC.MMWR.December 23, 2005 / 54(RR16);1-23.
WHO. Weekly Epidemiol Rec. 2009;84(40):405-20

- "HBV is **NOT SPREAD** through food or water, sharing eating utensils, breastfeeding, hugging, kissing, hand holding, coughing, or sneezing"

CDC.MMWR.December 23, 2005 / 54(RR16);1-23

CDC.Hamborsky J,Kroger A,WolfS,eds.13th ed.Washington,DC.Public Health Foundation.2015


What is the
clinical spectrum
of Hepatitis B

CLINICAL SPECTRUM

- Incubation period : 45 to 160 days (ave:120 days)

Acute infection

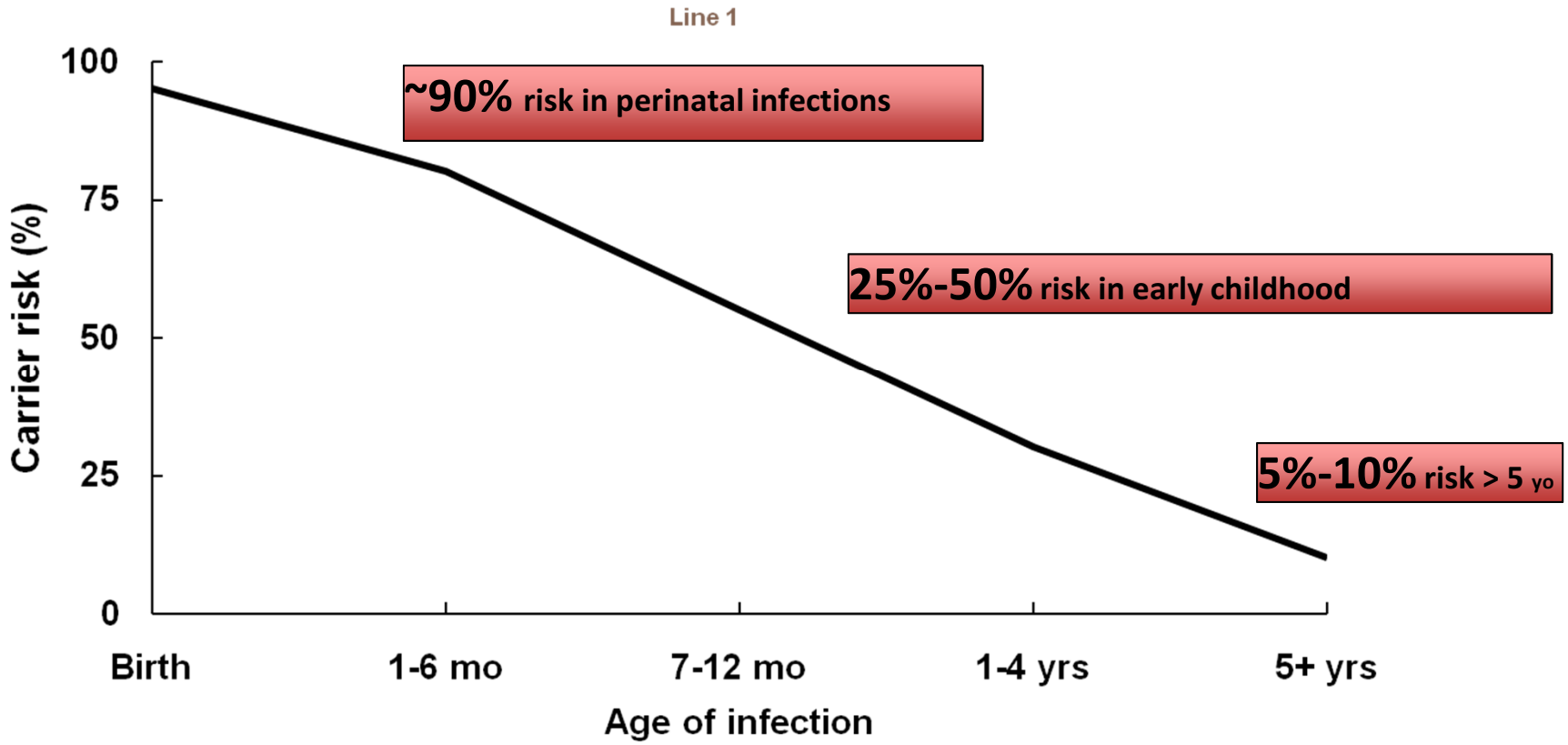
- Likelihood of symptoms is age-dependent:
  - < 1% of perinatal infections
  - 10% of early childhood infections
  - 30%-50% of late infections(>5 years old)
- Spectrum of signs and symptoms
  - Subacute illness with nonspecific signs and symptoms
  - Clinical hepatitis with jaundice
  - Fulminant hepatitis (0.1-0.6%) , ~70%mortality
  - Extrahepatic manifestations: arthralgia, arthritis, macular rashes, thrombocytopenia, polyarteritis nodosa, glomerulonephritis, papular acrodermatitis
- Most acute HBV infections in adults result in complete recovery

CDC.MMWR.December 23, 2005 /54(RR16);1-23

WHO. Weekly Epidemiol Rec. 2009;84(40):405-20

Chronic Infection

Risk of Chronic HBV Carriage by Age



CDC.MMWR.December 23, 2005
WHO. Weekly Epidemiol Rec. 2009;84(40):405-20

Chronic Infection

- **immunosuppression** or **chronic illness** at infection , also increase risk of chronic infection

- often asymptomatic & unrecognized in young children until a chronic liver disease,cirrhosis or hepatoma develops in mid-adulthood

- without monitoring and treatment , 25% of chronically infected infants and children will die prematurely from **HBV-related cirrhosis** or **hepatocellular carcinoma**

CDC.MMWR.December 23, 2005 / 54(RR16);1-23
WHO. Weekly Epidemiol Rec. 2009;84(40):405-20

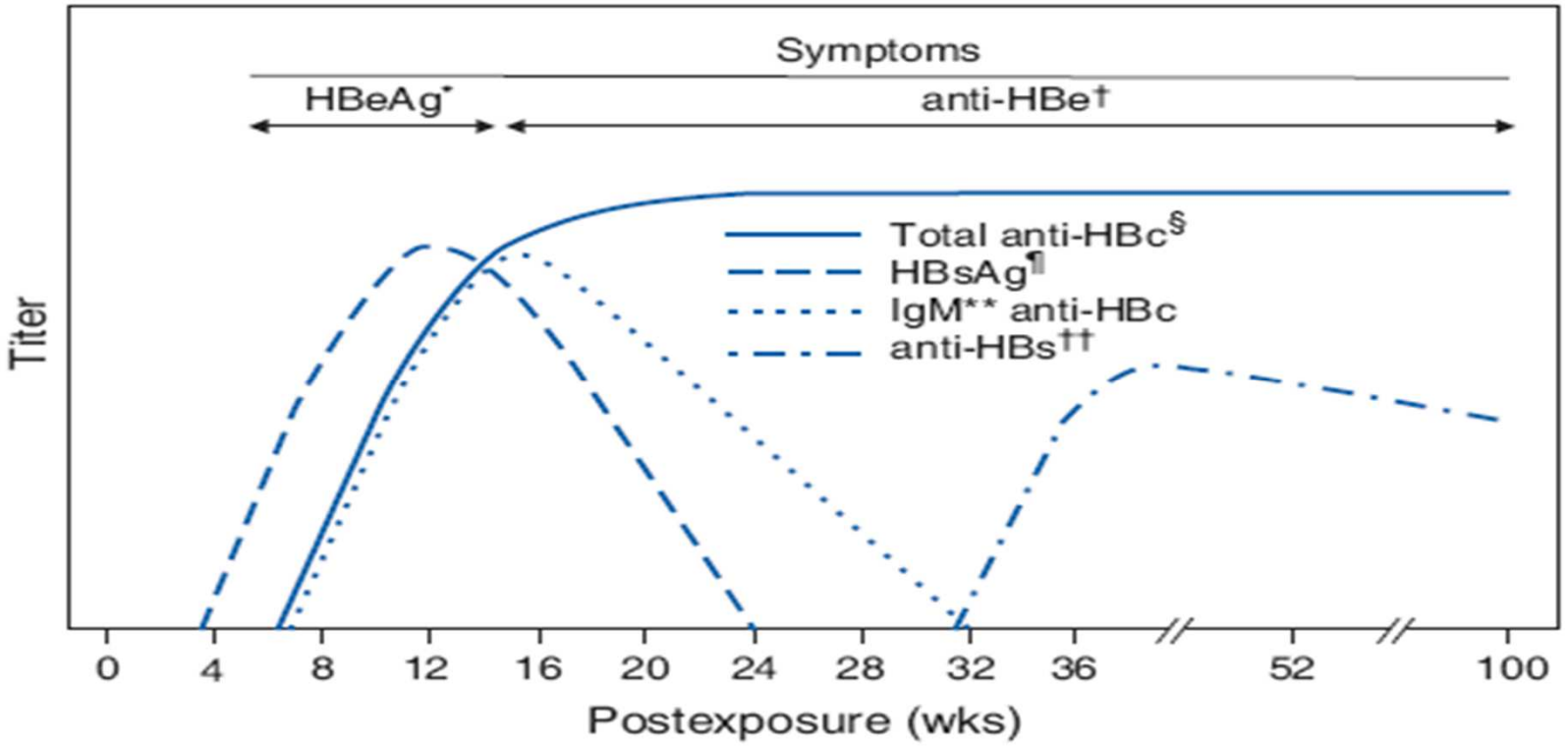
- In the Philippines, there is higher prevalence of chronic hepatitis B in patients with chronic liver disease (45.7%), hepatocellular carcinoma (70% to 74.8%), and cirrhosis (58.2%)

Gish RG, et al J Gastroenterol Hepatol. 2015 Dec 8. doi: 10.1111/jgh.13258


How is the diagnosis of hepatitis B established

Serologic course of acute HBV infections with recovery

CDC.*MMWR Recomm Rep.* 2008;57(RR-8):1-20



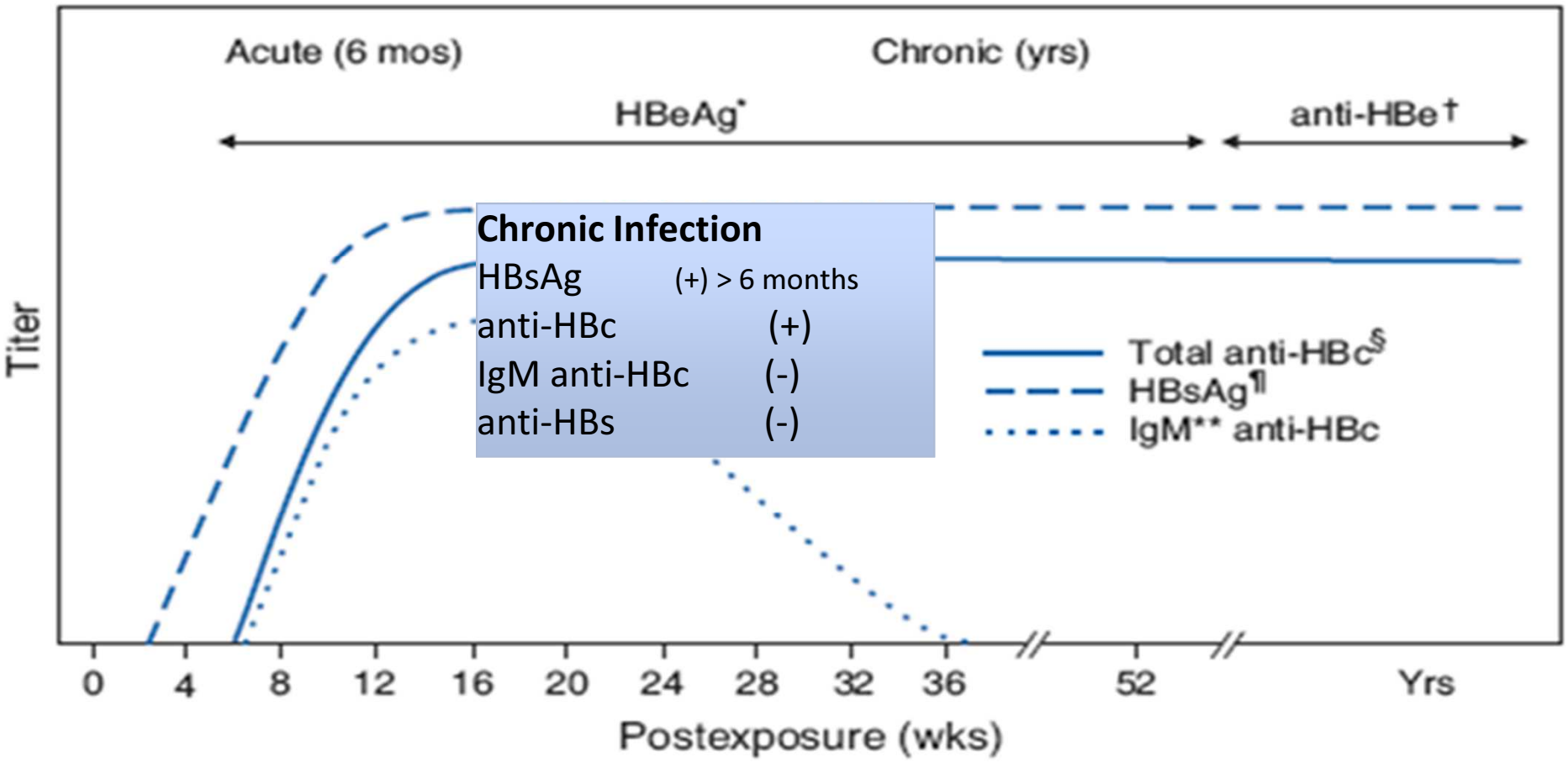
SUSCEPTIBLE
HBsAg (-)
anti-HBc (-)
anti-HBs (-)

Acute infection
HBsAg (+)
anti-HBc (+)
IgM anti-HBc (+)
anti-HBs (-)

Immune From Infection
HBsAg (-)
anti-HBc (+)
anti-HBs (+)

Immune from Vaccination
HBsAg (-)
anti-HBc (-)
anti-HBs (+)

Serologic course of acute HBV infection with progression to chronic HBV infection



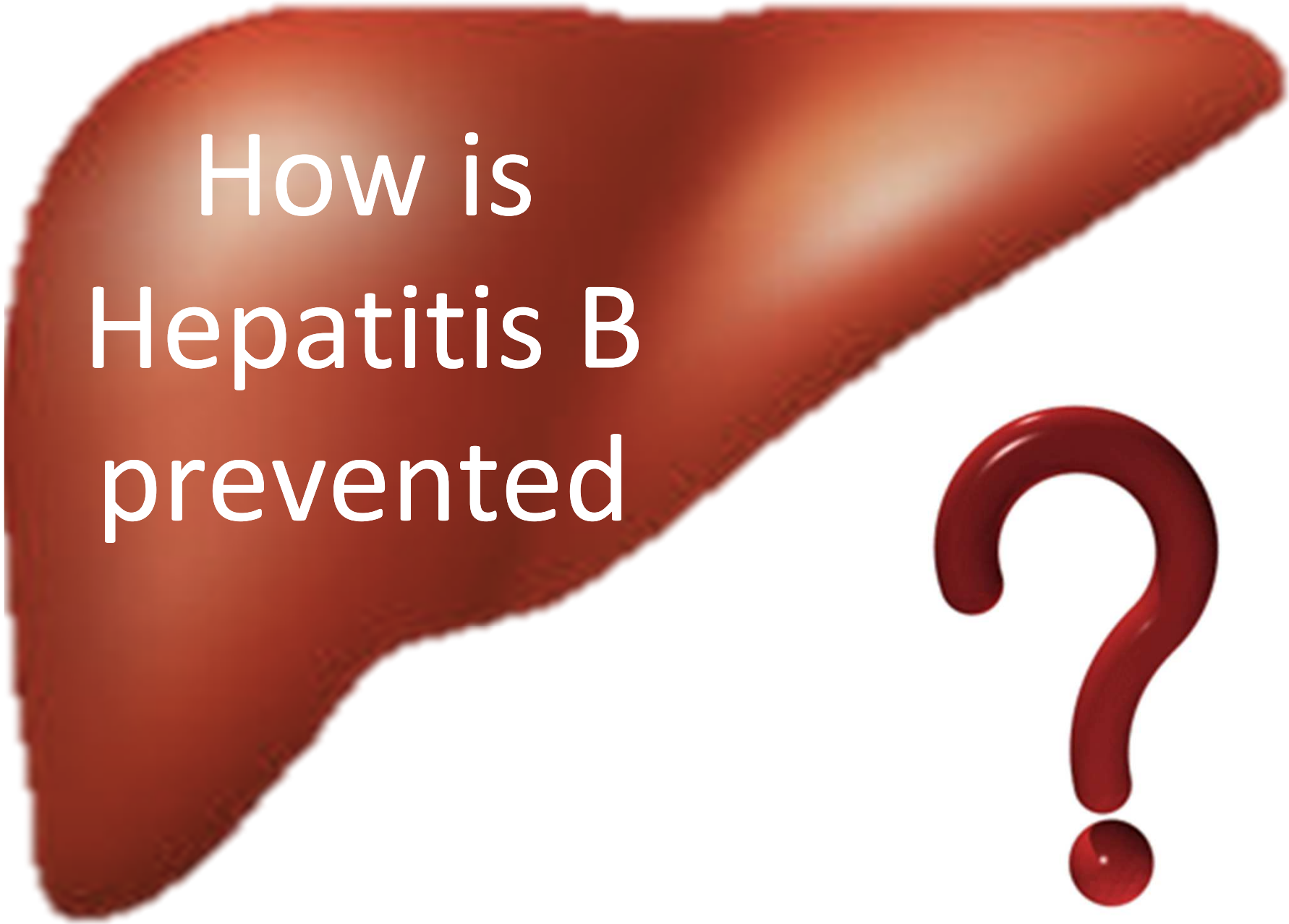
CDC.*MMWR Recomm Rep.* 2008;57(RR-8):1-20

What do the different serologic markers mean?

Factors to Be Tested	Use
HBs Ag	• acute or chronic infection
Anti-HBs	•resolved infection or immunity after immunization
Anti-HBc(total)	•acute, resolved or chronic HBV infection •single diagnostic test of choice for susceptibility
IgM anti-HBc	•acute or recent HBV infection (including HBsAg(-) people in“window”phase) • unreliable for perinatal infection
HBeAg	•marker of high degree of infectivity
Anti-HBe	•lower risk of infectivity
HBV DNA	•marker of viral replication; correlate with infectivity •assess/monitor treatment for chronic HBV

What do the different serologic markers mean?

Factors to Be Tested	Use
HBs Ag	• acute or chronic infection
Anti-HBs	•resolved infection or immunity after immunization
Anti-HBc(total)	•acute, resolved or chronic HBV infection •single diagnostic test of choice for susceptibility
IgM anti-HBc	•acute or recent HBV infection (including HBsAg(-) people in"window"phase) • unreliable for perinatal infection
HBeAg	•marker of high degree of infectivity
Anti-HBe	•lower risk of infectivity
HBV DNA	•marker of viral replication; correlate with infectivity •assess/monitor treatment for chronic HBV


How is
Hepatitis B
prevented

Vaccination :

- The best approach to HBV control
- Primary goal: eliminate transmission of HBV, thereby decreasing rates of chronic HBV infection and HBV-related cirrhosis& HCC

CDC.MMWR.December 23, 2005 / 54(RR16);1-23 WHO. Weekly Epidemiol Rec. 2009;84(40):405-20

Comprehensive immunization strategy to eliminate HBV transmission

Four components:

1) Universal immunization of infants at birth
2) Routine screening of all pregnant women and appropriate immunoprophylaxis of infants born to HBsAg (+) women and infants born to women with unknown HBsAg status
3) Routine immunization of children and adolescents not previously immunized
4) Immunization of previously unimmunized high risk adults

CDC.MMWR 2005;54[No. RR-16]:1--33).

"In most countries the most feasible strategy for preventing perinatal HBV transmission involves giving a dose of hepatitis B vaccine to all infants at birth"

World Health Organization. Introduction ofhepatitis B vaccine into childhood immunizationservices. *WHO/V&B/01.31. 2001: 7-9.*

Schedule of Hepatitis B (HepB) and Pentavalent (DTP-Hib-hepB) vaccination

WHO position paper. Weekly Epidemiol Rec. 2009;84(40):405-20

Age**	Vaccine
At birth (within 24 hours)	HepB monovalent
6 weeks	DTP–HepB–Hib1
10 weeks	DTP–HepB–Hib2
14 weeks	DTP–HepB–Hib3

Four doses may be given for programmatic reasons (1 monovalent birth-dose followed by 3 monovalent or combined vaccine doses), administered according to the schedules of national routine immunization programmes.

balita

Linking Filipinos with news since 1994

THURSDAY, FEBRUARY 11, 2016

SEARCH: GO

HOME ABOUT ARCHIVES SUBSCRIBE

National Provincial Foreign Features /Tourism Lead Photo

DOH releases new 5-in-1 Vaccine(DTP-HiB-HepB) for babies in Western Visayas

DOH releases new 5-in-
Visayas

August 11, 2010 10:43 am

6-in-1 : DTaP + IPV + Hib + HepB

What is the importance of giving a **birth dose** of Hep B vaccine?

- A birth dose of Hepatitis B vaccine even without HBIG, a "**safety net**" to :
  - prevent perinatal infection among infants born to HBsAg-positive mothers who are not identified
  - provide early protection to infants at risk for infection after the perinatal period

CDC.MMWR.December 23, 2005 / 54(RR16);1-23
WHO. Weekly Epidemiol Rec. 2009;84(40):405-20

"Progress in HB control in the Philippines has been slow, erratic and to date inadequate, compounded by a high proportion of births not attended by a trained professional and inadequate immunization coverage"

Ruff TA, Bravo L,Gatchalian SR, and Bock HL .**PRIORITIES AND CHALLENGES FOR HEPATITIS B CONTROL IN THE PHILIPPINES AND THE IMPORTANCE OF A VACCINE DOSE AT BIRTH**. Southeast Asian J Trop Med Public Health .2009;40 (5) :972-90

Hepatitis B Control in th Philippines

Compulsory Hepatitis B immunization among infants and children less than 8 years old" (RA no. 7846, 1994)

EPI +Hepatitis-B vaccine within 24 hours after birth to newborns of women with Hepatitis-B

DOH, Republic of the Philippines.AO No. 2006-0015.
Implementing guidelines on hepatitis B immunization for infants. Manila
... **a vaccine dose at birth for all infants** +government funding for sufficient vaccine

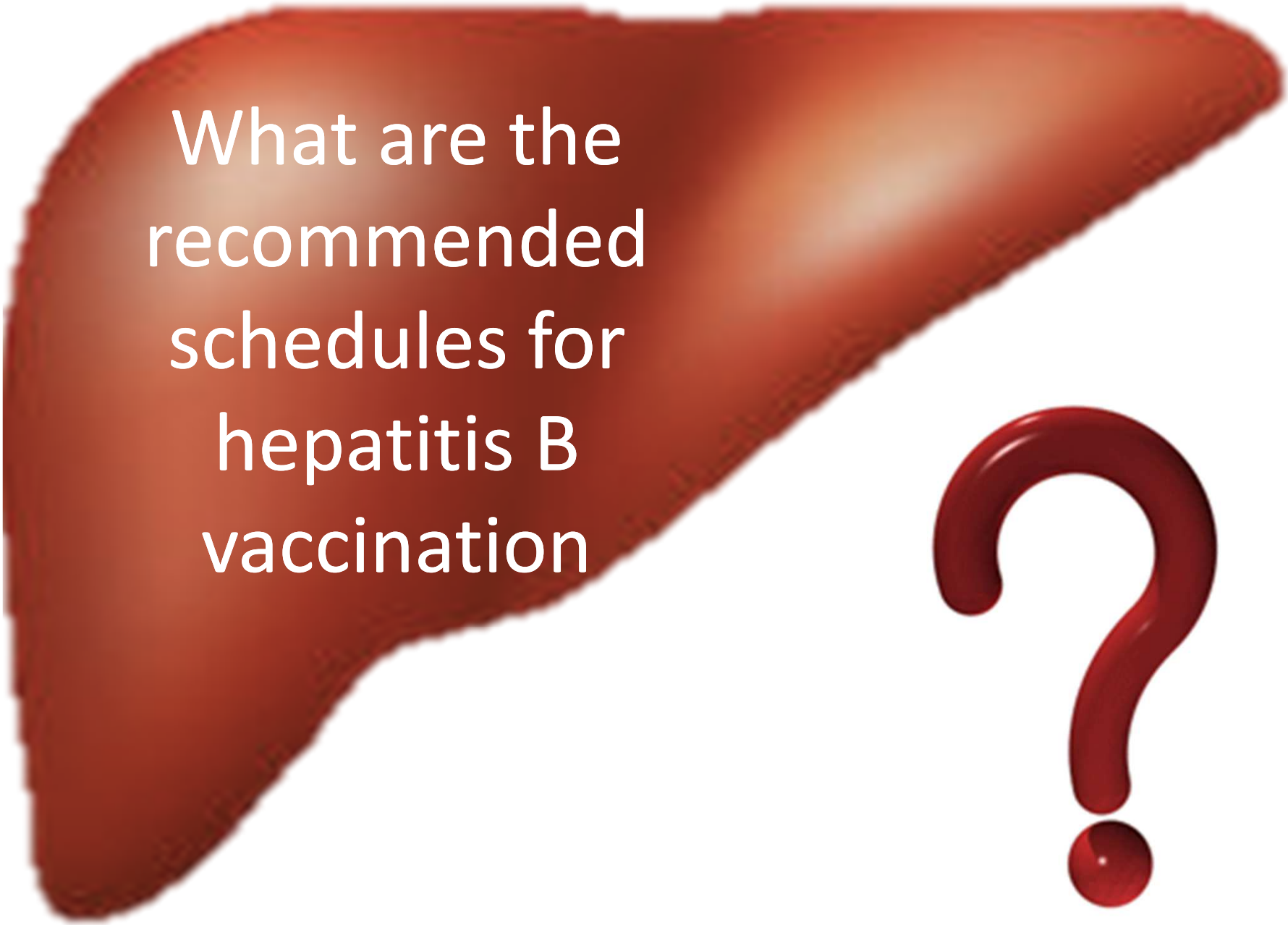
Unang Yakap, December 7, 2009

…BCG and Hep B vaccine after 1st breastfeed

Mandatory Infants and Children Health Immunization Act of 2011(RA No. 10152)
…all children <5 yo be given basic immunization against vaccine-preventable diseases including **a birth dose of the Hepatitis-B vaccine within 24 hours of birth**

PhilHealth Benefit for Mother and Child of 2013 RA No.10606)

Newborn Care Package (NCP) : PE, eye prophylaxis, Vit K , BCG , dose 1 Hep B vaccine newborn screening tests, and breastfeeding advice

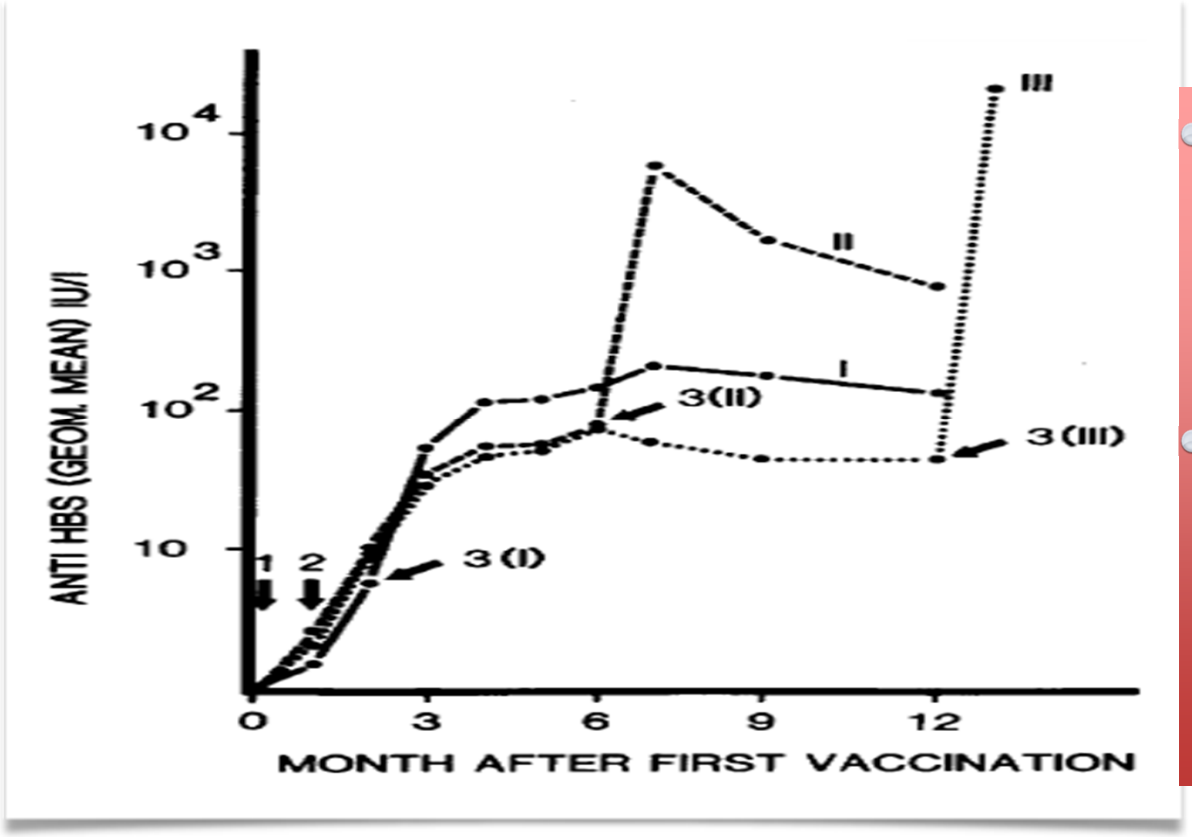

What are the recommended schedules for hepatitis B vaccination

CDC widely spaced interval (0,1,6 months)

- the final dose should be at 6 months old
- induce good antibody response
- longer interval between last 2 doses result in higher final antibody titer or longer duration of protective antibody

CDC.MMWR.December 23, 2005 / 54(RR16);1-23

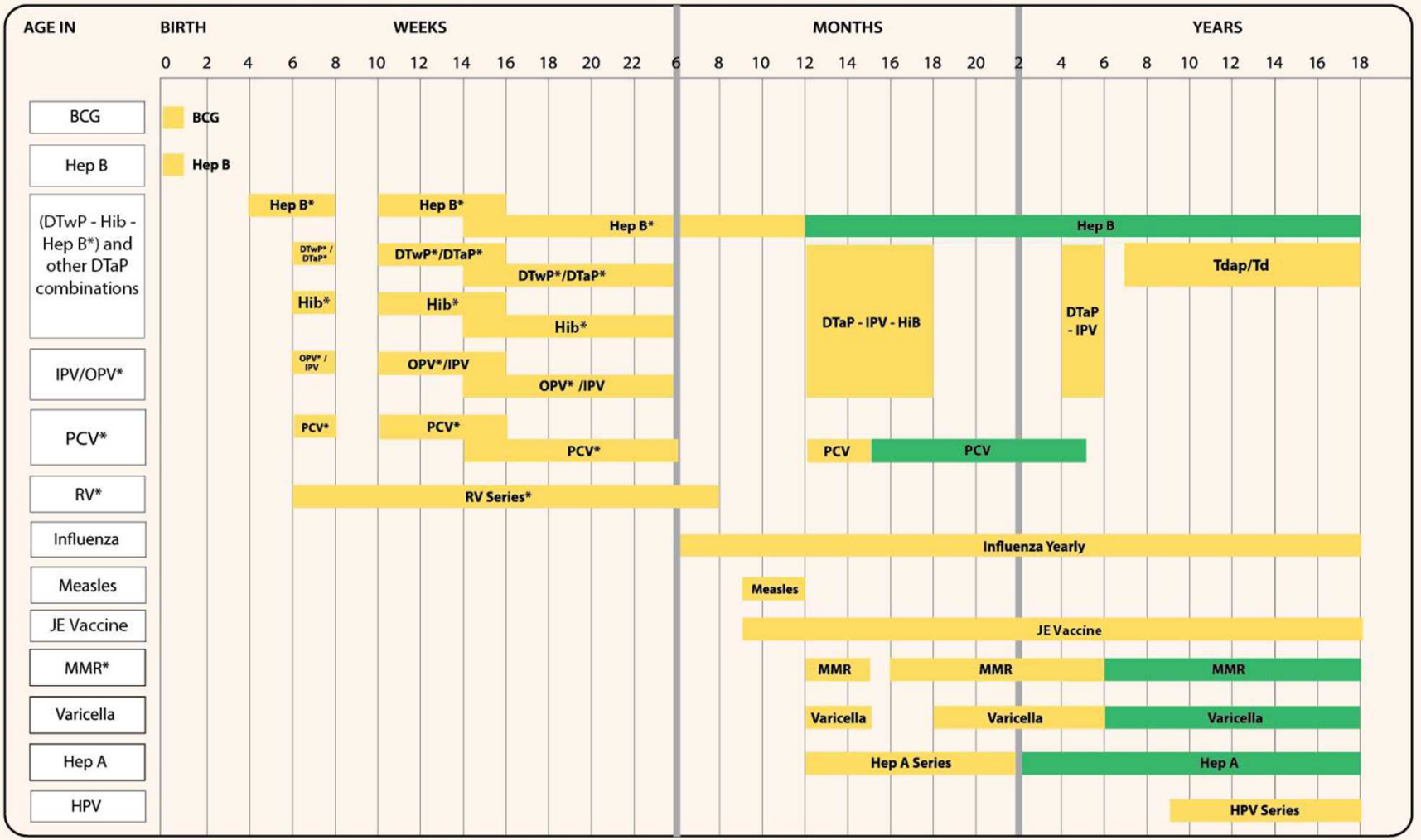
Immune responses to three doses of hepatitis B vaccine given at **months 0, 1, and 2** (group I), **0, 1, and 6** (group II), or at **0, 1, and 12** (group III)



- Increasing interval between dose 1 and dose 2 has little effect on final antibody titer.
- Longer interval between dose 2 and 3 results to a higher antibody titer and longer persistence of anti-HBs

Jilg W et al.THE JOURNAL OF INFECTIOUS DISEASES • VOL. 160, NO.5. NOVEMBER 1989

Childhood Immunization Schedule 2016



Hepatitis B Vaccine (HBV)

Given intramuscularly (IM)

The first dose is given at birth or within the 1st 12 hours of life. The minimum interval between doses is 4 weeks.

The final dose is administered not earlier than age 24 weeks. Another dose is needed if the last dose was given at age < 24 weeks.

For preterm infants:

- If born to HBsAg (-) mothers and medically stable, the 1st dose of HBV may be given at 30 days of chronological age regardless of weight, and this can be counted as part of the 3-dose primary series.
- Another dose of HBV is needed for those < 2 kgs whose 1st dose was received at birth

For infants born to HBsAg (+) mothers, administer HBV and HBIG (0.5ml) within 12 hours of life. HBIG should be administered not later than 7 days of age, if not immediately available.

For infants born to mothers with unknown HBsAg status:

- With birth weight ≥ 2 kgs, administer HBV within 12 hours of birth and determine mother's HBsAg as soon as possible. If HBsAg (+) administer HBIG not later than 7 days of age.
- With birth weight < 2 kgs, administer HBIG in addition to HBV within 12 hours of life.

WHO minimal interval (0-6-10-14 weeks)

- induce good antibody response, with lower final antibody titer
- preferred for rapid protection, and better compliance

WHO.Weekly Epidemiol Rec.2009; 84(40):405-20

Long Term protection for schedules with shorter interval

- limited data , but alternative schedules often not feasible.
- “concerns about long -term protection are of less practical significance in countries of high endemicity where most HBV infections are acquired in childhood "

Plotkin S, Orsenstein W, Offit P. Vaccines. Philadelphia: Elsevier, 2013

Three or Four-Dose Hepatitis B Series (monavalent + combination vaccine)

Birth	1.5 mos	2 mos	2.5mos	3.5mos	4 mos	6 mos	15-18 mos
	6 weeks	8weeks	10weeks	14 weeks			
Hep B1 monovalent	5-in-1 (LHC)		5-in-1 (LHC)	5-in-1 (LHC)			
Hep B1 monovalent	5-in-1 + Hep B monovalent 6-in-1				5-in 1 5-in-1	5-in-1 + Hep B monovalent 6-in-1	5-in-1 5-in-1 or 6-in-1
Hep B1 monovalent		6-in-1			6-in-1	6-in-1	5-in-1

5-in-1 (LHC) : DTwP + Hib + HepB
5-in-1(private practice) : DTaP + IPV + Hib
6-in-1(private practice) : DTaP + IPV + Hib + HepB

If there is an interruption between doses of hepatitis B vaccine, does the vaccine series need to be restarted

NO, the series does not need to be restarted.

WHO

- The minimum interval between dose s is 4 weeks

WHO.Weekly Epidemiol Rec.2009; 84(40):405-19

CDC

- The minimum interval between dose 1 and dose 2 is 4 weeks
- The minimum interval between dose 2 and dose 3 (3-dose series) **OR** dose 3 and dose 4 (4-dose series) is 8 weeks
- The minimum age for the final (3rdor 4th) dose of HepB vaccine is 24 weeks

CDC.MMWR.December 23, 2005 / 54(RR16);1-23

How can perinatal transmission be prevented in infants born to HBsAg (+) mothers

Hepatitis B Immunoprophylaxis Scheme for Infants Based on Maternal HBsAg Status

At Birth

Maternal Status	Infants ≥ 2000 g	Infants < 2000 g
HBsAg (+)	• ***HepBvaccine+HBIG ,**w/in12hrs of birth * HBIG not later than 7 days	
HBsAg unknown	•**Hep B vaccine** ,w/in 12 hr of birth •determine maternal HbsAg status •if (+), give HBIG ASAP , not later than 7 days	•**Hep B vaccine+HBIG**,within 12 hrs of birth
HBsAg (-) After Birth	•Hep B vaccine at birth or before hospital discharge Complete 3-4 dose vaccine series,starting 6 weeks old (monovalent or combination vaccine)	• **Hep B vaccine dose 1 at 30 days of chronologic age** or at hospital discharge if discharge occurs before 30 days of age counted as 3-dose primary series Birth dose not counted, as immune response less reliable Complete 4 –dose vaccine series (monovalent or combination) at 6 months old

Centers for Disease Control and Prevention.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: Course Textbook - 13th Edition (*2015*)

For a baby born to an HBsAg (+) mother, Hepatitis B vaccine and HBIG should be given preferably within 12hours (CDC) or 24 hrs (WHO) after birth to prevent perinatal transmission.

What if HBIG is not available?

Would Hepatitis B vaccine alone be protective?

Protective Efficacy of Immunoprophylaxis to infants born to HBsAg (+) mother

Immunoprophylaxis	Protective efficacy in preventing perinatal HBV infection
Hepatitis B Vaccine + HBIG (birth dose +2 doses)	85-95%
Hepatitis B Vaccine (birth dose + 2-3 doses)	70-95%

CDC.MMWR.December 23, 2005 / 54(RR16);1-23
WHO. Weekly Epidemiol Rec. 2009;84(40):405

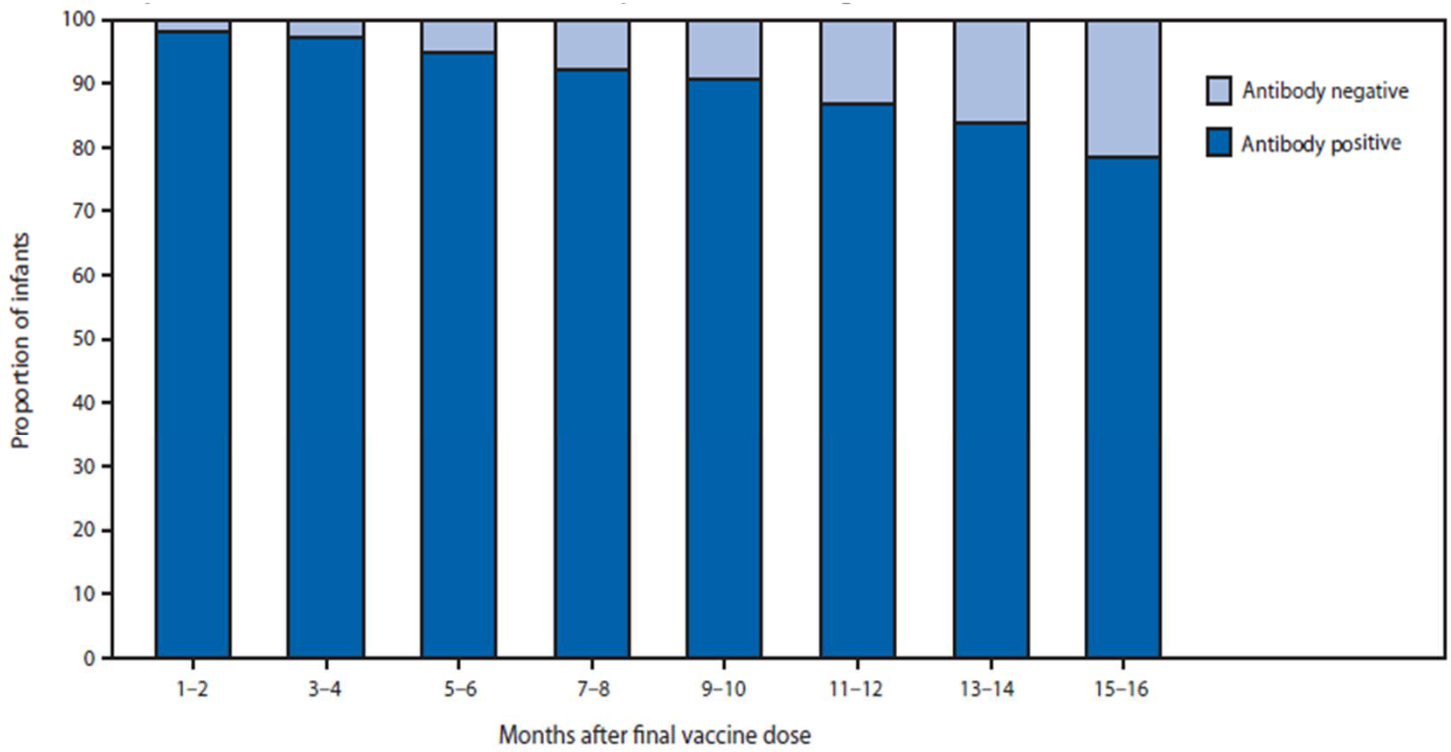
When should postvaccination serologic testing be done on infants born to HBsAg(+) mothers

New Recommendation:

- Check for **HBsAg** and **anti-HBs** after ≥3 doses of HepB vaccine , at **age 9–12 months old** (or 1–2 months after the final dose of the vaccine series, if delayed)

CDC .*MMWR* **October 9, 2015 / 64(39);1118-20**

Proportion of infants with anti-HBs ≥10mIU/ml with increasing interval from final vaccine dose



Source: Reprinted with permission of publisher from: Ko SC, Schillie SF, Walker T, et al. Hepatitis B vaccine response among infants bo surface antigen-positive women. Vaccine 2014;32:2127–33.

* p<0.01, Mantel-Haenszel chi square.

*Levels of anti-HBs decreased with increasing intervals from the last dose of HepB vaccine

Postvaccination Serology on infants born to HBsAg (+) mothers:

It should **NOT be done before 9mos old as** hepatitis B immune globulin (HBIG) may still be present

AND

NOT done until ≥4 weeks after last dose of HepB vaccine due to possible transient (<21 days) HBsAg-positivity related to the vaccine

CDC .*MMWR* **October 9, 2015 / 64(39);1118-20**

Postvaccination serologic testing (HBsAg and Anti-HBs)

- **NOT ROUTINE** following vaccination of infants, children, adolescents, or most adults
- **Recommended 1-2 months after the last vaccine dose**

  (3rd or 4th) for the following specific groups:
  - chronic hemodialysis patients
  - Immunocompromised persons
  - persons with HIV infection
  - sex partners of HBsAg+ persons
  - healthcare personnel who have contact with blood/body fluids of patients who might be infected with HBV or at risk for sharp/needlestick injuries

Centers for Disease Control and Prevention.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: Course Textbook - 13th Edition (*2015*)

What will you do if the anti-HBs level of a baby baby born to an HBsAg (+) mother , 1 month after completing a primary series, is less than 10 mIU/ml

Seroprotection against HBV infection:

Anti-Hbs = 10 mIU/ml

after complete hepatitis B vaccine series

Management of Nonresponse (anti-HBsAg < 10 mIU/ml) to a Primary Series of Hepatitis B Vaccine

- Revaccinate with a second series of three doses
- Given at 0, 1 and 6 months (or 0, 1, and 4 month or 0, 2 and 4 month schedule)
- Retest 1-2 months after completing the second series

CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: 13th Edition (*2015*)

Nonresponder or Hyporesponder

- Persistent nonresponse (anti-HBs <10 mIU/ml) after a second 3-dose HepB vaccine series (6 valid doses)
  - in less than 5% of vaccinees
- Request for HBsAg to check for chronic infection as cause
- If exposed, treat with postexposure prophylaxis

CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: Course Textbook - 13th Edition (*2015*)

Recommended postexposure prophylaxis for percutaneous or permucosal exposure to hepatitis b virus

ACIP,USA

Vaccination and antibody response status of exposed person	Treatment		
	Source HBsAg-positive	Source HBsAg-negative	Source not tested or status unknown
Unvaccinated	HBIG x 1; Initiate HB vaccine series	Initiate HB vaccine series	Initiate HB vaccine series
Previously vaccinated:			
· Known responder	No treatment	No treatment	No treatment
· Known nonresponder: - After 3 doses	HBIG x 1 and initiate revaccination	No treatment	- If known high-risk source, treat as if source were HBsAg-positive.
- After 6 doses	HBIG x 2 (separated by 1 month)	No treatment	- If known high-risk source, treat as if source were HBsAg-positive.
· Antibody response unknown	Test exposed person for anti-HBs - If adequate,* no treatment - If inadequate,* HBIG x 1 and vaccine booster	No treatment	Test exposed person for anti-HBs - If adequate,* no treatment - If inadequate,* HBIG x 1 and vaccine booster

HBIG dose: .06 ml/kg IM

CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: Course Textbook - 13th Edition (*2015*)

Can a mother who is HBsAg(+) breastfeed her baby

Safety of breastfeeding in case of chronic hepatitis B virus infection of mothers

Author	No. of infants	Population	Prophylaxis	Infected or failed seroconversion to antiHBs		*P*
				BF (%)	FF (%)	
Beasley et al[56]	147	USA, Taiwan (China)	No	53	60	NS
Tseng et al[57]	170	Hong Kong (China)	HBIG + Vx	7	6	NS
de Martino et al[58]	85	Italy	Vx	4.6	3.2	NS
Hill et al[59]	369	USA	HBIG + Vx	0	3	0.06

BF: Breastfeeding; FF: Formula feeding; HBIG: Hepatitis B immune globulin; NS: Nonsignificant.

CONCLUSION:

With appropriate immunoprophylaxis (birth dose of hepatitis B vaccine ± HBIG) ,breast-feeding of infants of chronic HBV carriers poses no additional risk for the transmission of the hepatitis B virus.

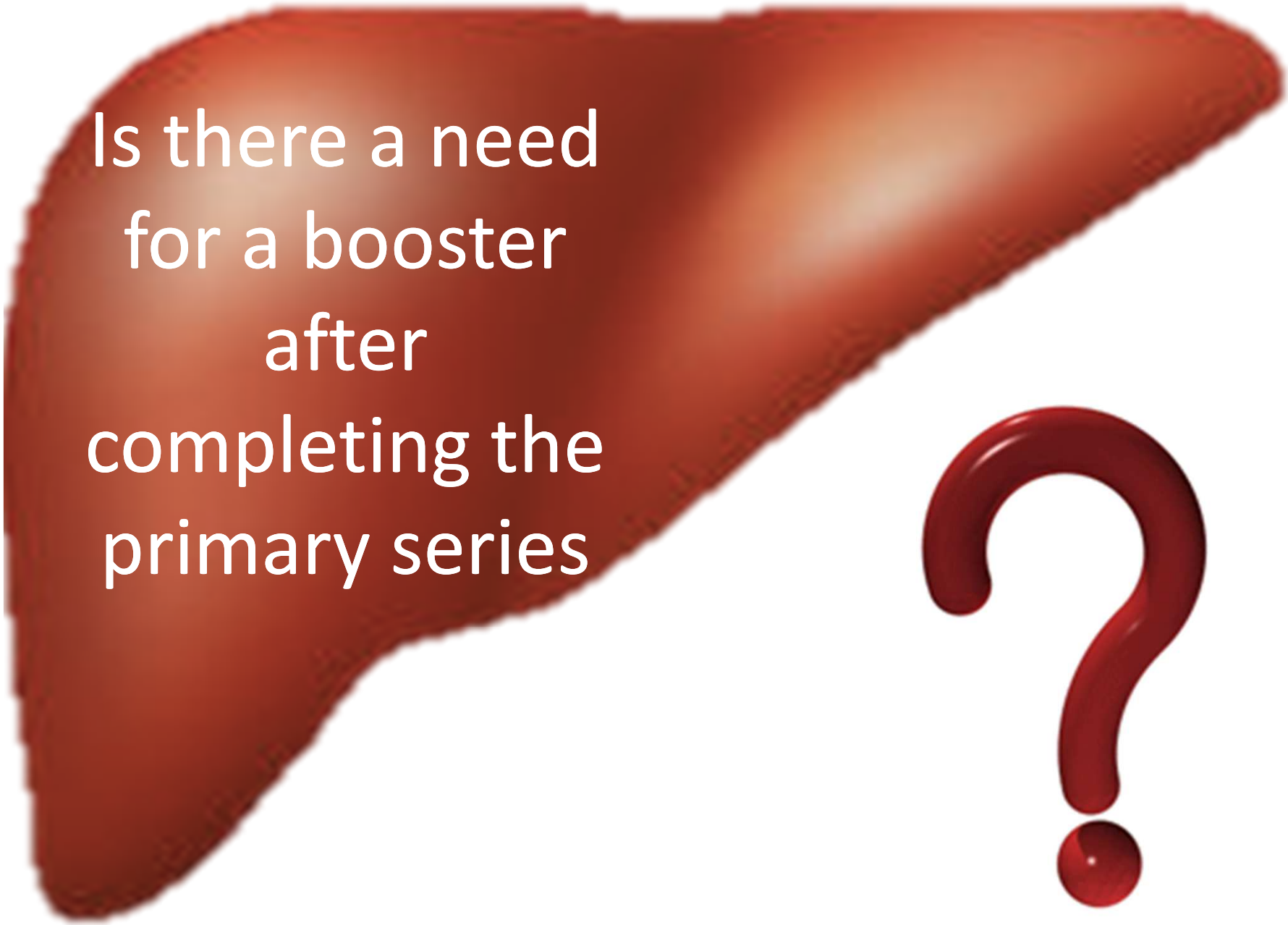
World J Gastroenterol. 2010 Oct 28; 16(40): 5042–5046

Recommendations on Breastfeeding

- YES, a mother who is HBsAg (+) can breastfeed her baby for as long as the baby is given appropriate immunoprophylaxis (birth dose of hepatitis B vaccine ± HBIG) and vaccine series completed.
- carrier mothers should not participate in donating breast milk
- breastfeeding mothers with chronic hepatitis B should also exercise care to prevent bleeding from cracked nipples

CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: - 13th Edition (*2015*)

Hepatitis B and breastfeeding. *www.who.int/**child**.../**hepatitis_b**_and_**breastf**...*


Is there a need
for a booster
after
completing the
primary series

- NO,

  booster vaccination is not recommended for long term protection,for immunocompetent children and adults who responded to a primary series especially if the last dose was given at 6months old and at least 8 weeks interval from previous dose

CDC.MMWR.December 23, 2005 / 54(RR16);1-23 .WHO.Weekly Epidemiol Rec.2009; 84(40):405-420
CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: - 13th Ed (*2015*)

Protective Efficacy and Induction of Anti-HBs Antibodies

- The primary 3-dose vaccine series induces protective antibody concentrations (anti-HBsAg ≥ 10 mIU/ml) in >95% of healthy infants, children and adolescents and in 90% of healthy adults.

CDC.MMWR.December 23, 2005 / 54(RR16);1-23 .WHO.Weekly Epidemiol Rec.2009; 84(40):405-420.

CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: Course Textbook - 13th Edition (2015)

Protective Efficacy and Induction of Anti-HBs Antibodies

- After primary hepatitis b immunization, anti-HBs levels rapidly decline within the first year and more slowly thereafter
  - child vaccine responders : 15%-50% with low or undetectable anti-HBs levels, 5-15 years after vacccination
  - Adult vaccine responders: 7%-%50% have anti-HBs <10mIU/ml , 5-15 years after vaccination

- The higher the peak of vaccine-induced anti-HBs concentration , the longer for antibody levels to decline to ≤10 mIU/ml.

Jilg W,Schmidt M,Deinhardt F.J Infect Dis.1989;160:766-9CDC.MMWR.December 23, 2005 / 54(RR16);1-23 .
WHO.Weekly Epidemiol Rec.2009; 84(40):405-420.Leuridan E, Van Damme P. Clin Infect Dis.2011;53:68–75.
Centers for Disease Control and Prevention.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: Course Textbook - 13th Edition (*2015*)

Protective Efficacy and Immune Memory after Vaccination

- While vaccine induced antibody levels decline with time, majority of immunocompetent children and adults are still protected against acute disease and chronic HBsAg carriage due to **IMMUNE MEMORY** that remains intact for more than 20 years following immunization

Banatvala J, Van Damme P, Oehen S. Vaccine 2000; 19:877–885.Banatvala JE, Van Damme P. J Viral Hepat 2003; 10:1–6. Jilg W, Schmidt M, Deinhardt F. Lancet 1990; 335:173–174.West DJ, Calandra GB.Vaccine 1996; 14:1019–1027.Hall AJ. Hepatology 2010; 51:1485–1486. Leuridan E and Van Damme E.Clinical Infectious Disease,2011;53(1):68-75

Protective Efficacy and Immune Memory after Vaccination

- Persistence of vaccine-induced immune memory has been demonstrated by an **anamnestic increase** after an additional vaccine dose

- Exposure to HBV results in an anamnestic anti-HBs response that prevents clinically significant HBV infection.

CDC.MMWR.December 23, 2005 / 54(RR16);1-23 .WHO.Weekly Epidemiol Rec.2009; 84(40):405-420.
CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: Course Textbook - 13th Edition (*2015*)

Medscape

Hepatitis B Vaccine Booster Unnecessary

Ricki Lewis,Phd

January 27, 2016

Antibody Levels and Protection After Hepatitis B Vaccine:Results of a 30-Year Follow-up Study and Response to aBooster Dose

Bruce MG,Bruder D,Hurlburt D et al.J Infect Dis .Jan,2016 available at http://jid.oxfordjournals.org/

THE LATEST NEWS AND CLINICAL VIEWS

Hepatitis B vaccine protection lasts 30 years

RICHARD PIZZI, ID Practitioner

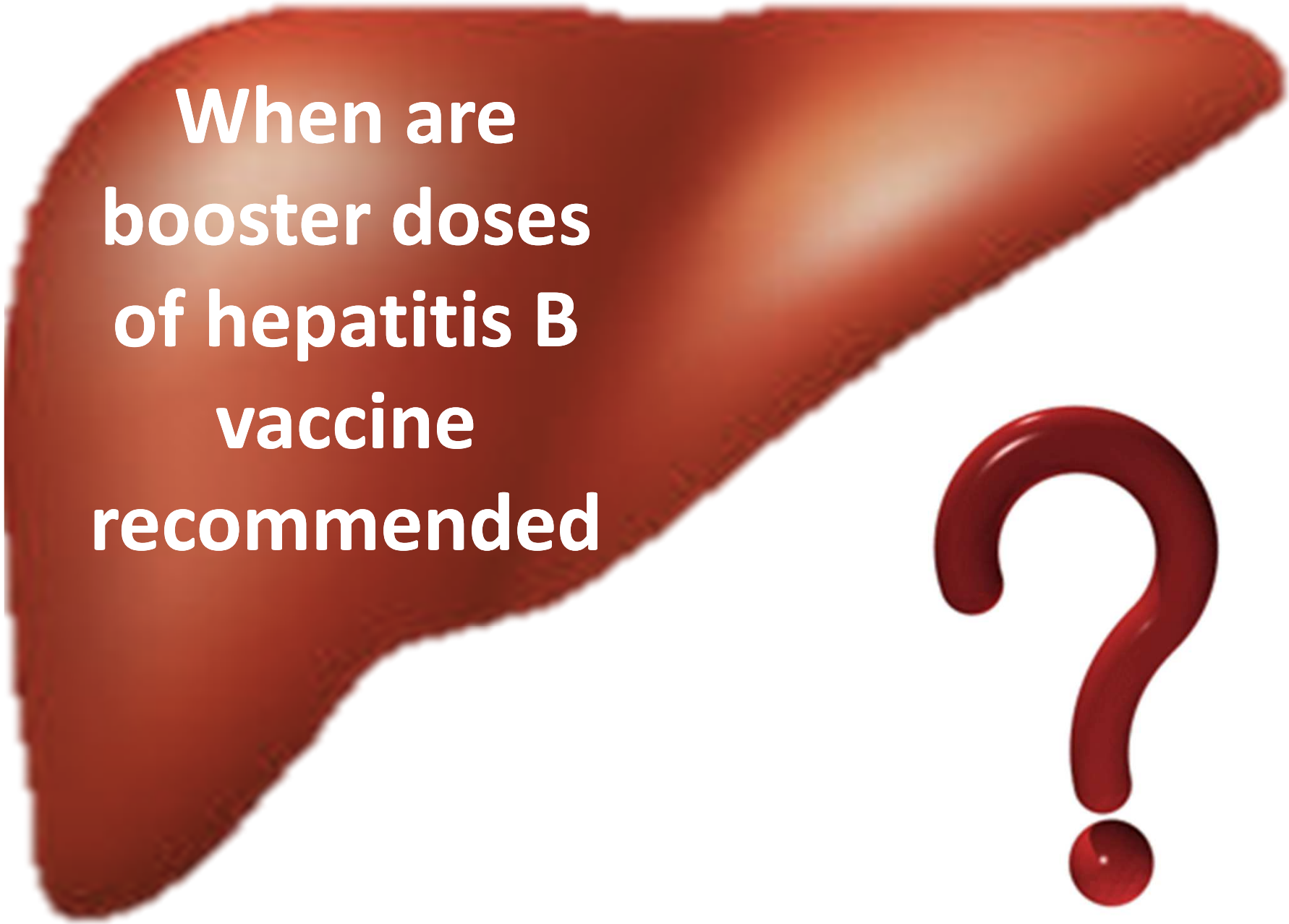
February 2, 2016

Antibody Levels and Protection After Hepatitis B Vaccine: Results of a 30-Year Follow-up Study and Response to a Booster Dose

Bruce MG,Bruder D,Hurlburt D et al.J Infect Dis .Jan,2016 available at http://jid.oxfordjournals.org/

- Follow up study : 243 Alaska native adults and children ≥6 months old,who responded to 3 –dose hepatitis B vaccine given in 1981,but without subsequent booster
- No significant breakthrough infections
- **CONCLUSION**: Based on anti-HBs level ≥10 mIU/mL in 51% of the 243 responders to the primary series ,at 30 years and an 88% booster dose response**, at least 90% of participants had evidence of protection 30 years later**, and thus HBV vaccine booster doses are not needed for persons 30 years out from a primary HBV vaccine series

For babies given hepatitis b vaccination using the accelerated schedule (0-6-10-14 weeks)or or a schedule where the last dose was given at age < 24 weeks, an additional dose is recommended to increase final antibody titer


When are booster doses of hepatitis B vaccine recommended

Booster doses of HBV vaccine are recommended ONLY for:

hemodialysis patients :

- need for booster assessed by annual testing for anti-HBs.
- a booster dose should be administered when anti-HBs levels decline to <10 mIU/mL.

other immunocompromised persons (HIV-infected persons, hematopoietic stem-cell transplant recipients, and persons receiving chemotherapy):

- the need for booster not determined.
- When anti-HBs levels decline to <10 mIU/mL, annual anti-HBs testing and booster doses considered if with ongoing risk for exposure.

CDC.MMWR.December 23, 2005 / 54(RR16);1-23 .WHO.Weekly Epidemiol Rec2009; 84(40):405-420
CDC.Hamborsky J,Kroger A,Wolfe S,eds.13th ed.Washington,DC.Public Health Foundation.2015

What does a negative anti-HBs serologic response mean if previously vaccinated (≥3 doses), but not tested after vaccination?

- Distinguish true vaccine failure (lack of protection) or response to the initial vaccination series with waning of antibody (protected).
- Give a "challenge dose" of hep B vaccine to assess protection
  - Protected if anti-HBs≥ 10 mIU/ml("memory" response)
  - If no response (anti-HBs ≤10 mIU/ml), complete revaccination and retest for anti-HBs
  - Or give 3 doses ; do anti-HBs testing 1--2 months after the third dose (more practical)

CDC.Epidemiology and Prevention of Vaccine-Preventable Diseases. The *Pink Book*: - 13th Edition (*2015*)

A high school graduate who is planning to take up a nursing course consults you because of a laboratory exam with this result:

HBsAg- reactive
anti HBS- non reactive
anti HBc – reactive

He is asymptomatic , but is requesting for a "medical certificate" prior to college entry.

What will you do

- Chronic HBV infection in itself should not prohibit the practice or study of medicine, surgery, dentistry, or allied health professions.

- An applicant who is HBsAg(+) should not be declared unfit to enroll/work and denied enrollment/employment without appropriate medical evaluation and counseling

Guideliness on the Evaluation of Hepatitis B Surface Antigen (HBsAg) Positive Workers for Employment - Revised Edition 2011 ***liverphil****.org/docs/****HepaB****-2011-HSP.pdf*

2014 HSP Consensus Statements on the Management ofChronicHepatitisB.*www.****liverphil****.org/.../****HEP****%20B%20GUIDELINES%20-%20BOOKLET*

MMWR.Updated CDC Recommendations for the Management of Hepatitis B Virus–Infected Health-Care Providers and Students. *July 6, 2012* / *Vol*. *61* / *No*. RR--*3* / Pg. 1 – 12

Medical Evaluation and Counseling of HBsAg(+) Student or Healthcare worker

- Determine status of Hep B :
  - HBeAg, anti-Hbe,and HBV DNA, repeat HbsAg and anti-HBs after 6 months
  - *HBV DNA serum levels preferred to monitor infectivity*
    - *Threshold value "safe" for practice <1,000 IU/ml*
- Asses status of liver : ALT ,liver ultrasound
- Evaluate for HBV risk factors & co-infections :
  - HCV,HIV,alcohol intake, family history of HBV infection or HCC
- Avoidance of high-risk behavior and prevention of HBV transmission

May do the initial work-up, but refer to a gastroenterologist!

Guideliness on the Evaluation of Hepatitis B Surface Antigen (HBsAg) Positive Workers for Employment - Revised Edition 2011 ***liverphil****.org/docs/****HepaB****-2011-HSP.pdf*
2014 HSP Consensus Statements on the Management of Chronic Hepatitis B.*www.****liverphil****.org/.../****HEP****%20B%20GUIDELINES%20-%20BOOKLET*
MMWR.Updated CDC Recommendations for the Management of Hepatitis B Virus–Infected Health-Care Providers and Students. *July 6, 2012* / *Vol*. *61* / *No*. RR--*3* / Pg. 1 – 12

Key Messages

- Hepatitis B is highly endemic in the Philippines
- Perinatal transmission from an infected mother ,at birth, is the most important mode of spread
- Up to 90% of infants infected perinatally or in the first year of life will develop chronic HBV infection without immunoprophylaxis
- Vaccination is the best approach to HBV control


Thank You!