VIRAL HEPATITIS

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PRIMARY VIRAL HEPATITIS

	HEPATITIS A	HEPATITIS B	HEPATITIS C	HEPATITIS D	HEPATITITS E
INCUBATION (DAYS)	**15-45, MEAN 30**	**30-180, MEAN 60-90**	15-160, MEAN 50	30-180, MEAN 60-90	14-60, MEAN 40
TRANSMISSION	**FECO-ORAL**	**BODY FLUIDS**	BODY FLUIDS	BODY FLUIDS	BODY FLUIDS
CHRONIC INFECTION	**NO**	**YES**	YES	YES	NO
PROGNOSIS	**EXCELLENT**	**WORSE WITH AGE, DEBILITY**	MODERATE	ACUTE: GOOD CHRONIC: POOR	GOOD
PROPHYLAXIS / PREVENTION	**VACCINE, IMMUNOGLOBULIN**	**VACCINE, IMMUNOGLOBULIN**	NO VACCINE AVAILABLE	HBV VACCINE	SAFE DRINKING WATER

HEPATITIS A

- RNA virus (Picornavirus)
- **Incubation period:** 15-45 days (~4 weeks)
- **Mode of Transmission:** feco-oral
- **Chronic infection:** none
- Replication is limited to the liver

A. **Acute Stage**(last for <6months):
    - Increased ALT
    - Antibody: IgM class
    - (+) fecal HAV shedding
B. **Convalescent Stage:**
    - Decreased ALT
    - Antibody: IgG class

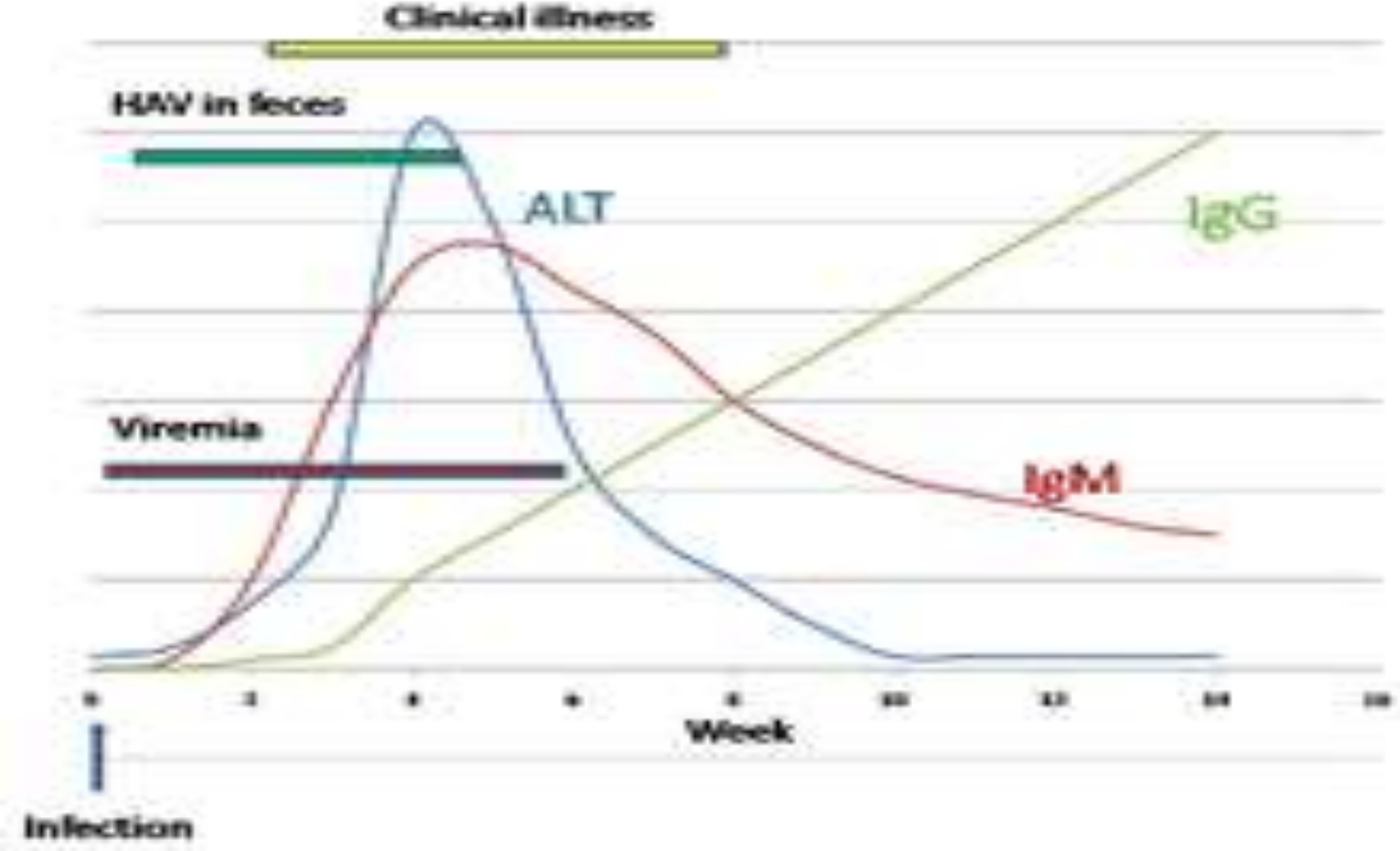
Serologic Markers of HAV

1. HA IgM

- –Indicates Acute HA infection
- –Fulminant if with signs of liver failure

2. HA IgG

- –Indicates immunity from HA infection


Clinical illness
HAV in feces
ALT
IgG
Viremia
IgM
Week
Infection

HEPATITIS B

- DNA Virus (Hepadnavirus)
- **Incubation period:** 30-180 days (~8-12 weeks)
- **Mode of Transmission:** Percutaneous Inoculation (body fluids from infected person)
- **Chronic infection:** Present
- Highest incidence of going into Hepatocellular Carcinoma

Serologic Markers of HBV

1. Hepatitis B surface antigen (HBsAg)

- present in the blood with acute and chronic HBV infections
- earliest indicator of acute hepatitis B
- undetectable in the blood during the recovery period

❑ <6 months = Acute

❑ >6 months = Chronic

(+) HBsAg , (+/-) IgM → HBV infection

2. Hepatitis B surface antibody (anti-HBs/HBsAb)

- **Indicates prior exposure and immunity from HBV**
- Antibody produced in response to HBV surface antigen
- Levels in the blood rise during the recovery phase
- Determines immunity from vaccination

3. Anti-hepatitis B core (anti-HBc/HBcAb)

- Produced in response to the core antigen and usually persists for life
- May represent **past** HBV infection

❑**HBcAb IgM** = acute, active HBV infection

❑**HBcAb IgG** = chronic, persistent HBV infection

4. Hepatitis B e-antigen (HBeAg)

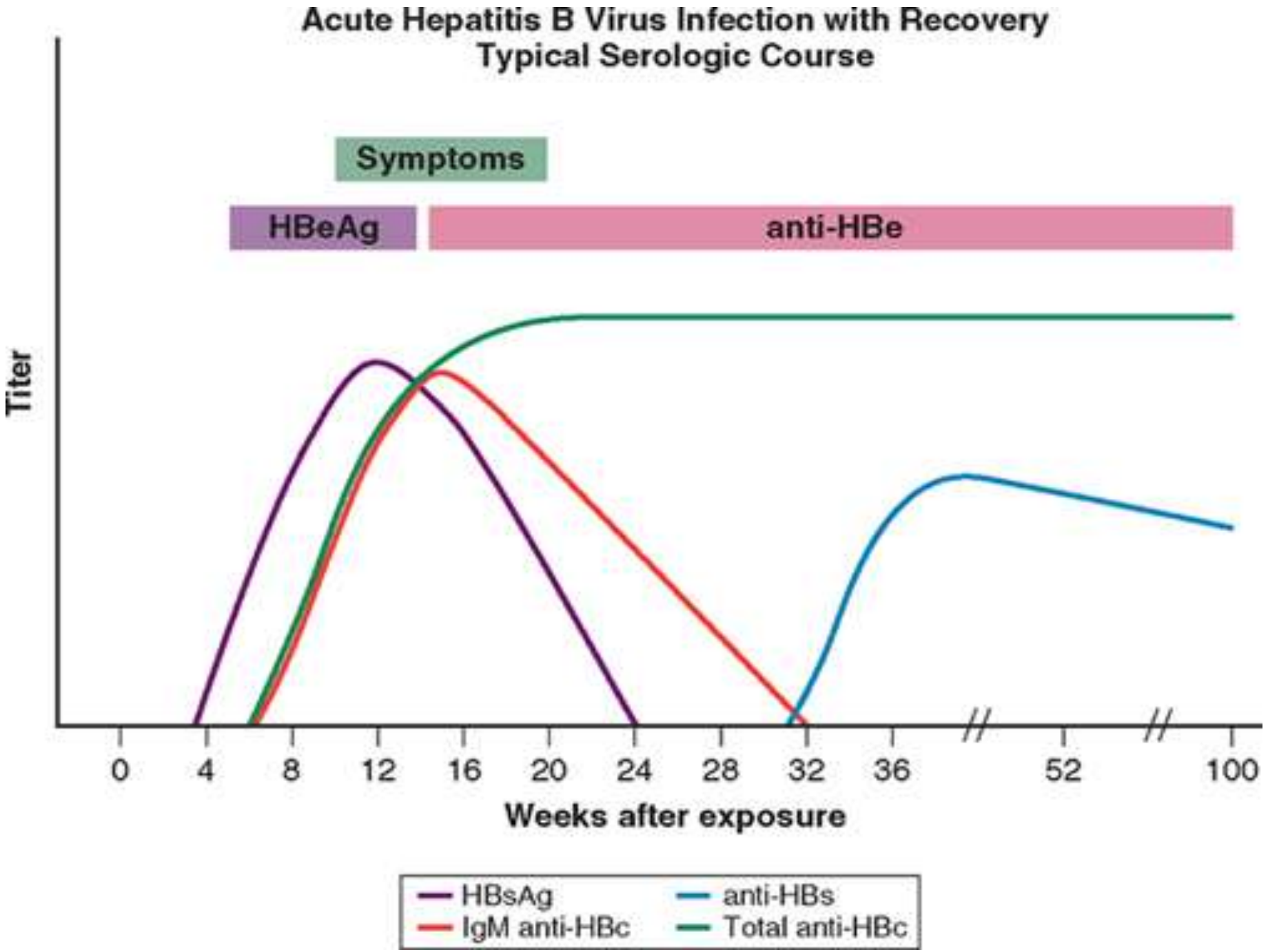
- Produced and released into the blood by actively replicating HBV
- e-antigen is found in the blood only when the HBV is actively replicating
- Used as a marker of **infectivity**

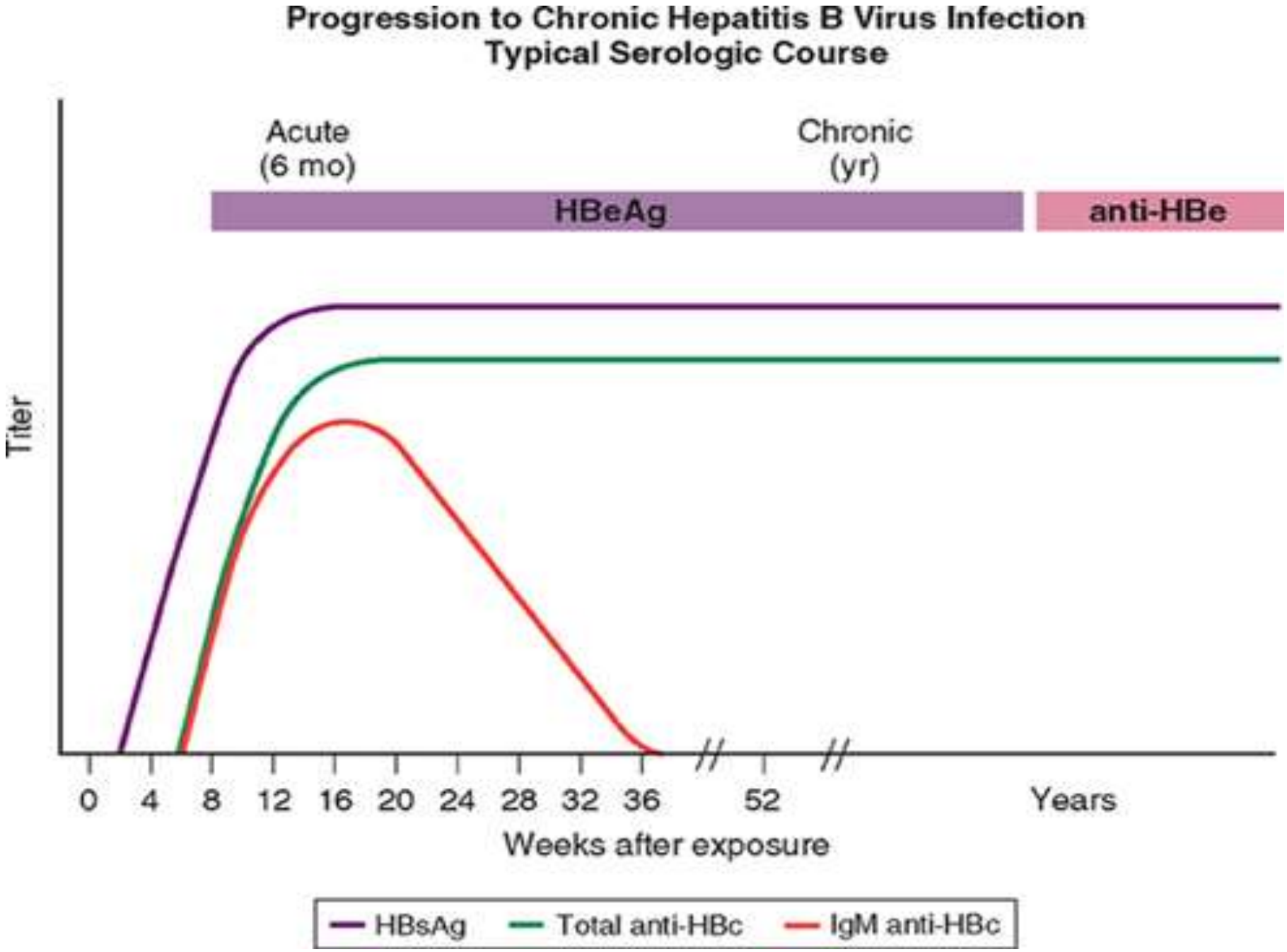
5. Anti-hepatitis Be antibody (Anti-HBe/HBeAb)

- Antibody produced in response to the HBeAg
- **No replication and infectivity**

6. Hepatitis B DNA (HBV DNA)

- Detects hepatitis B viral genetic material
- Indicator of HBV replication
- **Monitor antiviral therapy**


Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course
Symptoms
HBeAg
anti-HBe
Titer
0
4
8
12
16
20
24
28
32
36
52
100
Weeks after exposure
HBsAg
IgM anti-HBc
anti-HBs
Total anti-HBc


Progression to Chronic Hepatitis B Virus Infection
Typical Serologic Course
Acute
(6 mo)
Chronic
(yr)
HBeAg
anti-HBe
Titer
0
4
8
12
16
20
24
28
32
36
52
Years
Weeks after exposure
HBsAg
Total anti-HBc
IgM anti-HBc

Serologic Markers Summary

HEPATITIS A MARKERS

**no hepatitis A antigen markers because when you look at the clinical course of hepatitis A, it is short-lived, and by the time you are symptomatic, the virus is already excreted in the feces.*

- **HA IgM**
  - Indicative of acute HA infection
  - *Fulminant if with signs of liver failure (treated with transplantation)*
- **HA IgG**
  - Indicative of immunity from HA infection
  - **NO CHRONIC HEPATITIS A**

HEPATITIS B MARKERS

**no hepatitis core antigen because the antigen always stays in the nucleus of the hepatocytes throughout the whole course.*

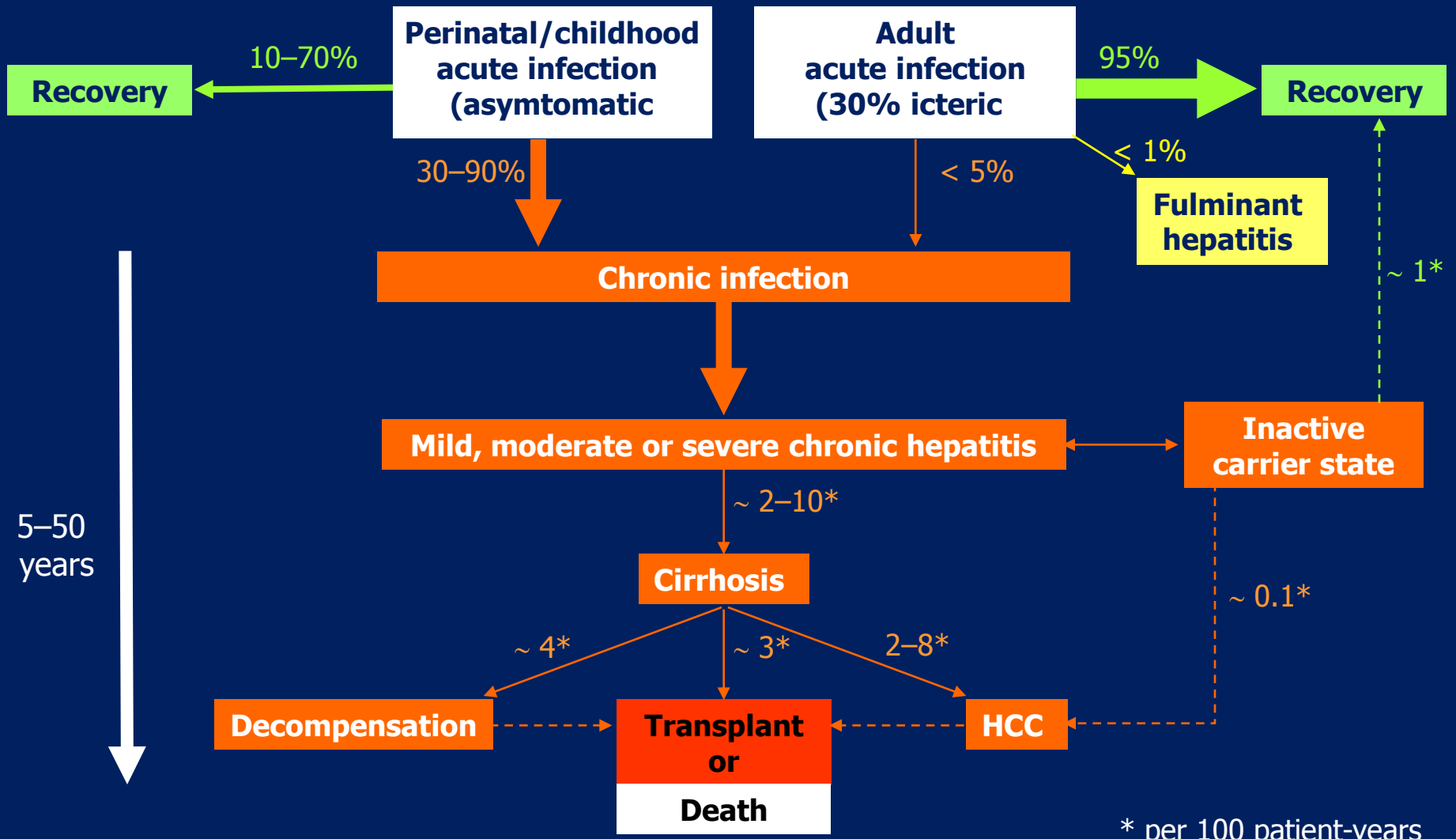
- **HBsAg**
  - Presence of HBV infection
- **HBsAb**
  - Immunity from HBV
- **HBeAg**
  - Viral Replication
  - Infectivity
- **HBeAb**
  - *No replication and infectivity*
- **HBc IgM**
  - Active HBV infection *(presence of necrosis of hepatocytes)*
- **HBc IgG**
  - Recovery from acute HBV infection
  - Chronic persistent HBV infection

Clinical Manifestations (both HA and HB)

- **Constitutional Prodromal Symptoms/ Preicteric Phase**
  - Anorexia, nausea and vomiting, fatigue, malaise, arthralgias, myalgias, headache, photophobia, pharyngitis, cough, and coryza: 1-2 weeks before jaundice
  - Low grade fever (38-39^{o}C): more often in HA than in HB
  - Dark urine and clay-colored stools: 1-5 days before icteric phase

- **Clinical Jaundice/ Icteric Phase**
  - Mild weight loss may still continue
  - Hepatomegaly with tenderness
  - RUQ pain and discomfort
  - Splenomegaly and cervical adenopathy
  - Spider Angioma
- **Recovery/Posticteric Phase**
  - constitutional symptoms disappear
  - Hepatomegaly may still be present
  - HA & HE: 1-2 months after onset of jaundice
  - HB & HC: 3-4 months

Clinical Outcomes of HBV



Adapted from EASL Consensus Statement. *J. Hepatol*. 2003; **39** (S1):S3–25

Prophylaxis

Hepatitis A

- Passive and active immunization options
- Pre-exposure: IG is effective in preventing clinically apparent HepA ; also during incubation period
  - For travel: 0.02mL/kg for travel lasting <3mos

    0.06mL/kg for every 4-6 months
- Post-exposure: 0.02mL/kg as early after exposure as possible
- Unnecessary: with HepA vaccine, casual contacts, for most elderly persons likely to be immune
- Hepatitis A vaccines: at least 1 yr old; adequate protection beginning 4 wks after inoculation
  - Preferred preexposure immunoprophylaxis
  - IG + vaccine

Prophylaxis

Hepatitis B

- Preexposure prophylaxis in settings of frequent exposure: 3 IM (deltoid) injections of HepB vaccine at 0,1,6 mos.
- Pregnancy is not a contraindication to vaccination.
- Dosage and schedule dependent on recombinant vaccine available and target group. See table 298-6 p1947.

Prophylaxis

Hepatitis B

- Postexposure
  - Unvaccinated persosns sustaining exposure to HBV: HBIG + hepatitis B vaccine
  - Perinatal exposure (from (+)HBsAg mothers): single dose of HBIG 0.5mL IM in the thigh, immediately after birth + complete course of 3 injections of rHepB vaccine started within the first 12h of life
  - direct percutaneous inoculation or transmucosal exposure to (+)HBsAg body fluids/blood: single IM dose of HBIG 0.06mL/kg ASAP + complete course within first week
  - by sexual contact: single IM dose of HBIG 0.06mL/kg within 14 days of exposure + complete course within first week

Protection

- ~80-90% of immunocompetent vaccinees retain protective levels of anti-HBs – at least 5 yrs; 60-80% - 10yrs
- Booster immunizations:
  - immunocompromised persons who lost detectable anti-HBs or immunocompetent persons who sustain percutaneous (+)HBsAg inoculations after losing detectable antibody
  - Hemodialysis patients – annual anti-HBs testing after vaccination; booster when anti-HBs <10mIU/mL

*Those at risk for both Hep A and B: combined vaccine with 720ELISA units of inactivated HAV + 20ug of recombinant HBsAg (0,1,6 mos)

Guidelines on the Evaluation of Hepatitis B Surface Antigen (HBsAg) Positive Workers for Employment (2007)

By the Hepatology Society of the Philippines

Objectives of the Guidelines

The guidelines aim to…

1) Help physicians recognize the implications of the different phases of chronic HBV infection on the risk of transmission in the workplace, eligibility for treatment and the risk of developing complications
2) To serve as guide in categorizing the risk of HBV transmission in the workplace according to type of occupation and the individual's infectivity

Policy Statements

Policy Statement 1:

- Serum HBsAg positivity alone ***should not*** be a basis for discrimination, work restriction, and subsequent disqualification from employment

  (Level of Evidence III)

Policy Statement 2:

- Minimum requirements for a confirmed HBsAg-positive person undergoing pre-employment evaluation should include:
  - * Serum HBeAg and Anti-HBe
  - * Serum ALT
  - * Ultrasound of the liver

(Level of evidence of III)

Policy Statement 3

> If the HBsAg is positive, HBeAg is positive, and ALT is normal, the person is likely to have chronic HBV infection **(Immune Tolerant Phase)**

(Level of Evidence II-2)

Policy Statement 3

- Monitoring of **ALT** levels should be performed **every 3-6 months**. Referral to a specialist may be considered for further evaluation and management

  (Level of Evidence III)

Policy Statement 4

- If the HBsAg is positive, HBeAg is positive, and the ALT is greater than normal, the person is likely to have **HBeAg positive chronic hepatitis B** (**Immune Clearance Phase**)

  (Level of Evidence II-2)

- **Serum HBV DNA** determination using a PCR-based assay is recommended. Other causes of elevated ALT levels should be considered. Those persons with high HBV DNA levels and abnormal ALT may be eligible for treatment. Referral to a specialist may be an option

  (Level of Evidence III)

Policy Statement 5

- If the HBsAg is positive, HBeAg is negative, anti-HBe is positive and ALT is greater than normal, then the person is likely to have **HBeAg negative chronic hepatitis B** *(Level of Evidence II-2)*
- **Serum HBV DNA** determination using a PCR-based assay is recommended. Other causes of elevated ALT levels should be considered. Those persons with high HBV DNA levels and abnormal ALT may be eligible for treatment. Referral to a specialist may be an option

  (Level of Evidence III)

Policy Statement 6

> If the HBsAg is positive, HBeAg is negative

and the anti-HBe is positive, and ALT is normal, this person is likely to have **chronic HBV infection, inactive HBsAg carrier state**. A serum HBV DNA **<2,000 IU/mL** strongly supports the diagnosis. **(Level of Evidence II-2)**

> Monitoring of the serum ALT every 6-12 months is recommended. Referral to a specialist should be considered. (Level of Evidence III)

Policy Statement 7

> If the ultrasonographic finding of the liver is abnormal, appropriate management should be instituted *(Level of Evidence III)*

Categories of Occupations According to Risk of HBV Exposure from Infected Workers

Category 1	Category 2	Category 3
➢ Health care workers (HCWs) who are performing or who have a reasonable expectation of performing **exposure-prone procedures (EPPs)** ➢ Other workers whose occupation involves potential for exchange of body fluids **(eg. Commercial sex workers)**	> HCWs who are not performing or who do not have reasonable expectation of performing EPPs	➢ Non-HCWs ➢ All other occupations that do not fall into Categories 1 or 2

Exposure Prone Procedures

A. Surgery

1) Abdominal Surgery (ie. Open surgical procedures)
2) Cardiothoracic Surgery
3) Neurosurgery (ie. Neurocraniotomy)
4) Obstetrics and gynecology (ie. All open surgeries)
5) Orthopedic surgery (ie. Open surgical procedures)
6) Ophthalmology
7) Orbital Surgery
8) Otorhinolaryngology surgery (ie. insertion of ventilation tubes)
9) Plastic surgery (ie. extensive cosmetic surgery)
10) Podiatric surgery (Any surgery where part of the operator's finger will be inside the wound and out view)
11) Transplantation surgery

Exposure Prone Procedures

B. Trauma (ie. open head injuries)

C. Anesthesia (ie. insertion of chest tubes)

D. Cardiology (ie. placement of pacemakers)

E. Nursing (ie. nurses performing first assist)

F. Dentistry

G. Psychiatry (ie. care of violent and/or biting patient)

Policy Statement 8

A. For Category 1 Occupations

- All HBsAg-positive persons should have **mandatory HBV-DNA testing** (Level of Evidence II-2)

a) If HBV DNA **> 2,000 IU/mL**, they are cleared for employment with work restrictions (Level of Evidence II-3).

> They are not allowed to perform EPPs (Level of Evidence III).

a) If HBV DNA **< 2,000 IU/mL**, they are cleared for employment with no work restrictions due to low risk of HBV transmission (Level of Evidence III).

> In all HBsAg positive HCWs performing EPPs, annual HBV D DNA testing is recommended. If HBV DNA becomes > 2,000 IU/mL, they should not be allowed to perform EPPs

B. For Category 2 and 3 Occupations

a) All HBsAg-positive persons are cleared for employment with no work restrictions due to neglible risk of HBV transmission. (Level III)

b) Serum HBV DNA testing is **not** a prerequisite for pre-employment. (Level III)

C) Further work restrictions based on the clinical status of the infected person should be made on a **case to case basis** by the attending physician in consultation with a specialist (Level of Evidence III)

Policy Statement 9

- HBsAg-positive job applicants should be issued a **medical certificate** which must include

A) Complete diagnosis *(Level of Evidence III)*

B) Risk of transmission *(Level of Evidence III)*

C) Recommendation for Employability *(Level of Evidence III)*

1) Cleared for employment with work restrictions
2) Cleared for employment with NO work restrictions
3) Not cleared for employment

Policy Statement 10

> The attending physician should educate the patient on the following: current status of hepa B infection, modes of transmission, adherence to standard precautions, risk of transmission/for complications, the need for monitoring, screening of first degree relatives, close personal and household contacts; options for treatment

Recommendations for Application of Standard Precautions

- Hand hygiene
- Personal Protective Equipment (PPE) – gloves, gown, mask, eye protection, or face shield; soliled patient care equipment; environmental control; textile and industry; injection practices; needles and other sharps; patient resuscitation; cough etiquette

Policy Statement 11

- The hepatitis B status of a job applicant or employee should be kept confidential.

Policy Statement 12

- Each healthcare institution is encouraged to form an Advisory Panel to discuss issues on Hepatitis B and employment particularly those not covered by these guidelines.

Terms and Diagnostic Criteria in Chronic HBV Infection

CHRONIC HEPATITIS B	
HBeAg-**positive** Chronic Hepatitis B	HBeAg-**negative** Chronic Hepatitis B
➢ HBsAg positive > 6 months ➢ HBeAg positive, anti-Hbe negative ➢ Serum HBV DNA >20,000 IU/mL, or 112,000 copies ➢ Persistent or intermittent elevation in ALT levels ➢ Liver biopsy showing HAI >4	➢ HBsAg positive > 6 months ➢ HBeAg negative, anti-HBe positive ➢ Serum HBV DNA >2,000 IU/mL or 11,200 copies/mL ➢ Persistent or intermittent elevation in ALT levels ➢ Liver biopsy showing HAI>4

Terms and Diagnostic Criteria in Chronic HBV Infection

Acute Exacerbation or Flare of Hepatitis B	Resolved Hepatitis B
> Intermittent elevations of ALT to more than 10 times ULN or more than two times the baseline value	> Previous HBV infection without further virologic, biochemical or histologic evidence of active infection or disease

Thank you!