Asian Health Mini Medical School

HEPATITIS B AND LIVER DISEASE IN ASIANS

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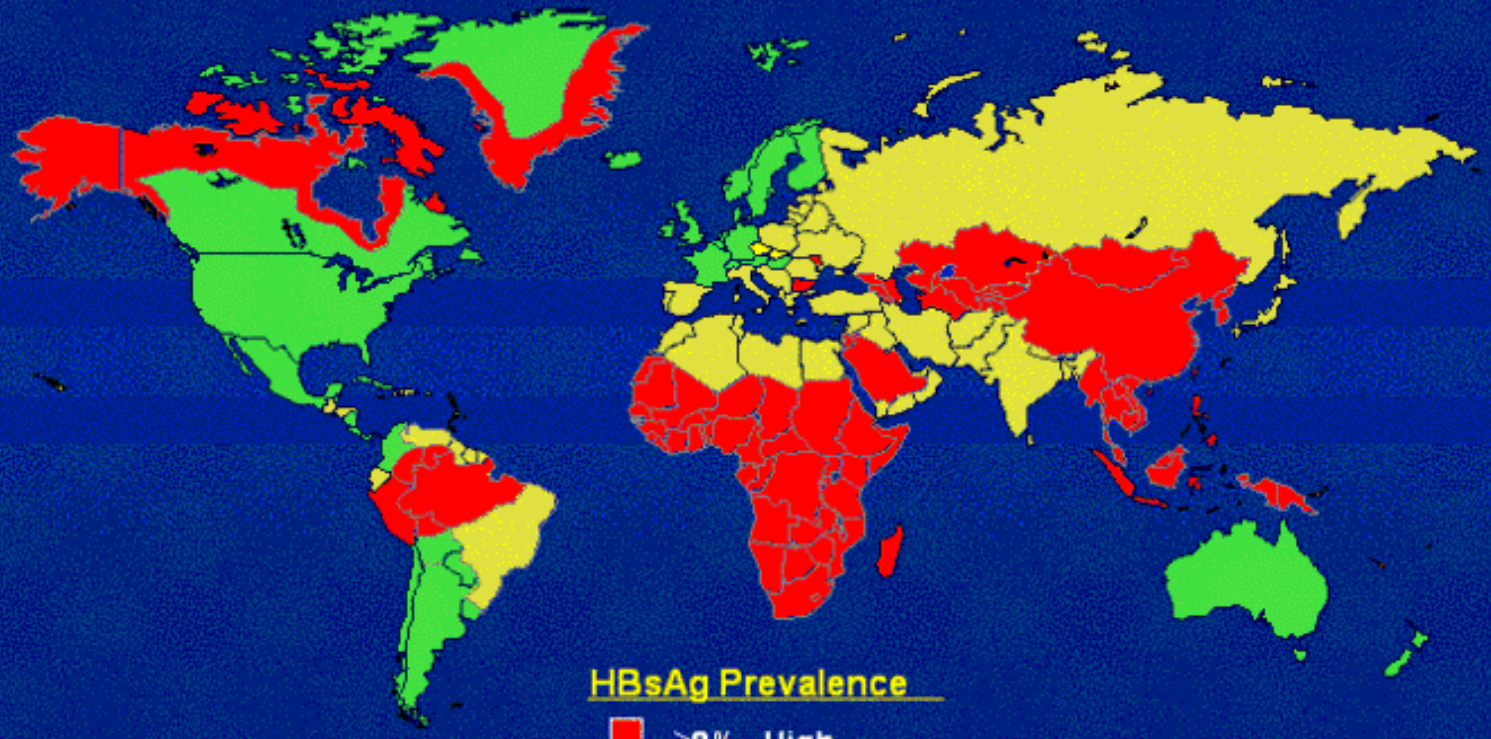
HEPATITIS B

- Who should be tested for HBV infection?
- Interpretation of hepatitis B and liver tests
- Subgroups and patterns of infection
- Who to treat
- Treatment options
- Screening for liver cancer (hepatocellular carcinoma) among hepatitis B patients

Geographic Distribution of Chronic HBV Infection



CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

POPULATION SCREENING FOR HBV

- All Asians and Pacific Islanders (>8% prevalence) should be tested. They account for 90% of HBV-infected individuals in the United States. Asians born in the United States should also be screened as many were born before universal vaccination in 1991
- Immigrants from areas with prevalence of 2-7%
- Household and sexual contacts of HBV-infected individual

WHO ELSE SHOULD BE SCREENED?

- Any history of IV drug use
- Multiple sexual partners or history of STD
- Homosexually active men
- Inmates of correctional facilities
- Individuals with chronically elevated ALT/ AST
- HCV or HIV-infected individuals
- Individuals on chronic hemodialysis
- All pregnant women

TRANSMISSION OF HBV

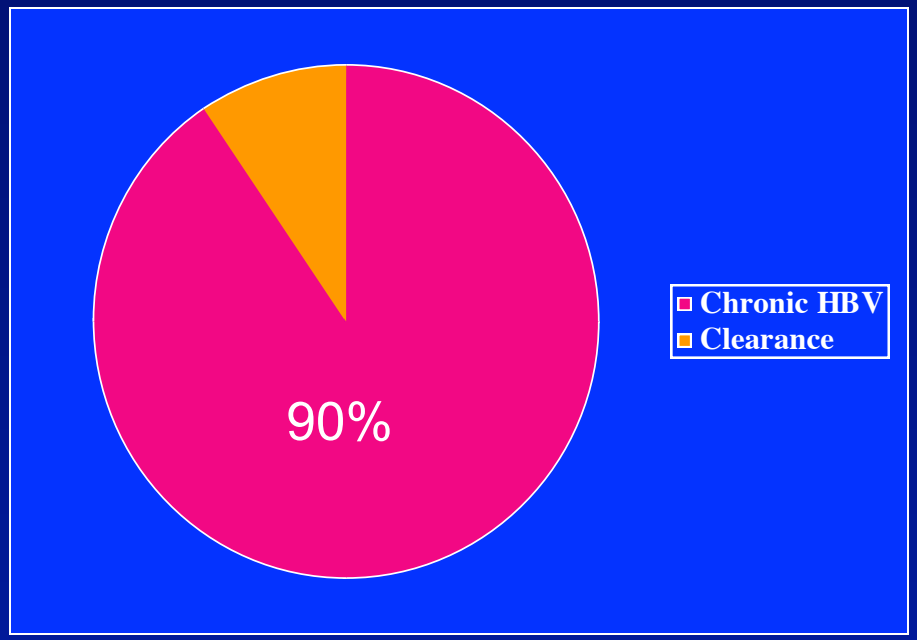
- Hepatitis B is transmitted through contact with body fluids, usually blood
- Hepatitis B is present in blood and other body fluids – semen, vaginal fluids, saliva and breast milk
- Transmission can therefore take place by sexual intercourse, body piercings and tattoos, blood transfusion (now very rare) and needle (injection drug use).

TRANSMISSION OF HBV

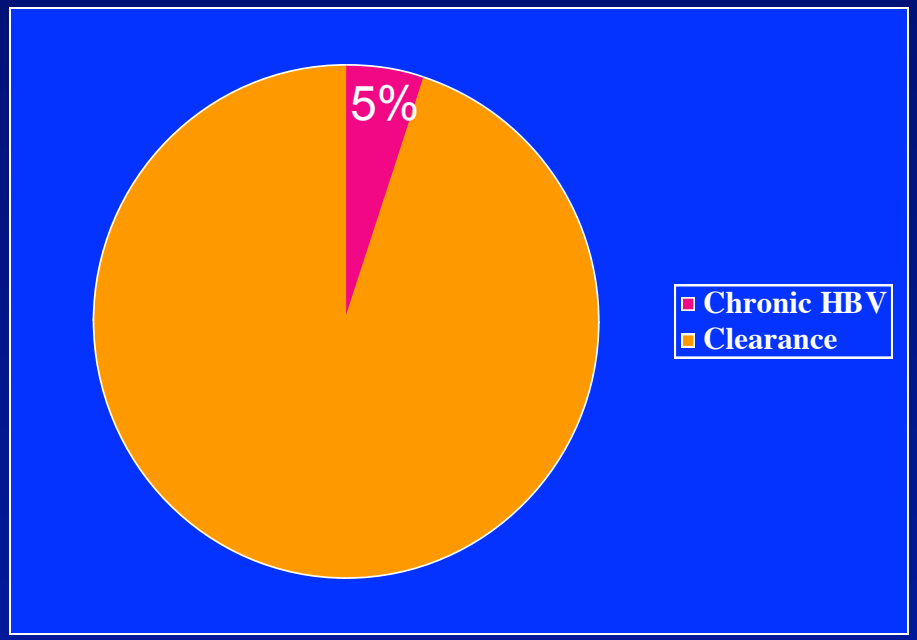
- In endemic areas such as Asia, many cases contracted hepatitis B via perinatal route from infected mother to newborn or "vertical transmission"

CHRONIC HBV AND AGE OF ACQUIRING INFECTION

NEONATAL INFECTION



ADULT INFECTION



DISEASE PRESENTATION

- Acute infection by hepatitis B may cause no symptoms, or mild to severe disease
- Common symptoms include body aches, loss of appetite, dark urine, jaundice, fever, nausea, or vomiting
- After acute infection, some clear the infection and become immune, others develop chronic infection/ hepatitis

DISEASE PRESENTATION

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- C
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Hepatitis B may be a silent disease

LIVER TESTS

- **MARKERS OF LIVER INJURY OR INFLAMMATION:**
  ALT (SGPT)　丙氨酸转氨酶
  AST (SGOT)

- **LIVER FUNCTION:**
  Bilirubin (degree of jaundice)
  Prothrombin time/ INR (clotting)
  Albumin

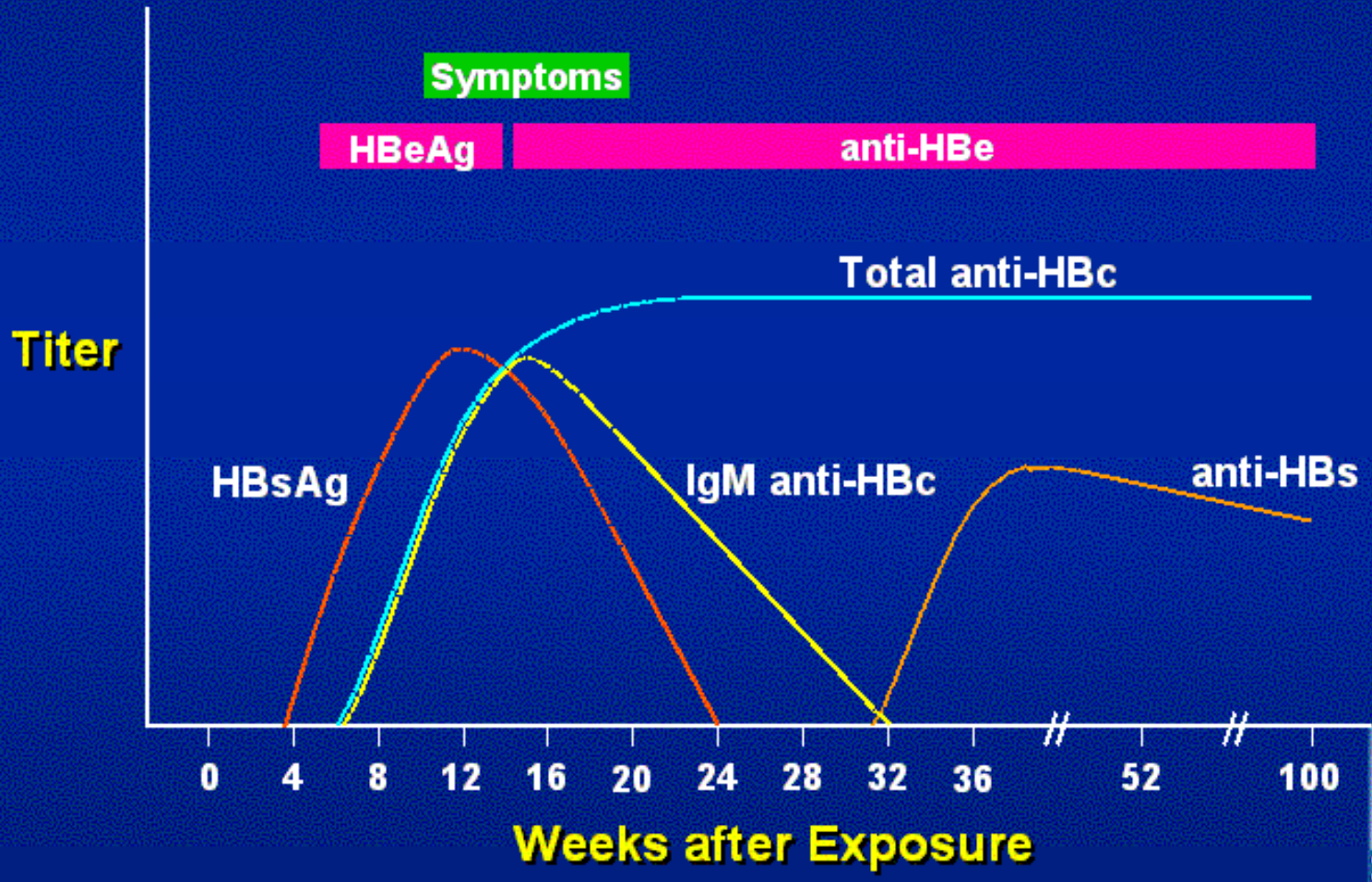
TESTING FOR CHRONIC HBV
SEROLOGIC MARKERS

- **DEFINITIONS:**
  - **Hepatitis B Surface Antigen (HBsAg) = Infection**
  - **Hepatitis B core Antibody (IgG) = Exposure**
  - **Hepatitis B Surface Antibody (HBsAb) = Immunity**

- **MARKERS OF VIRAL REPLICATION: ***
  - **Hepatitis B e Antigen (envelope)**
  - **Hepatitis B DNA by quantitative PCR**

* Do these tests only if HBsAg (+)

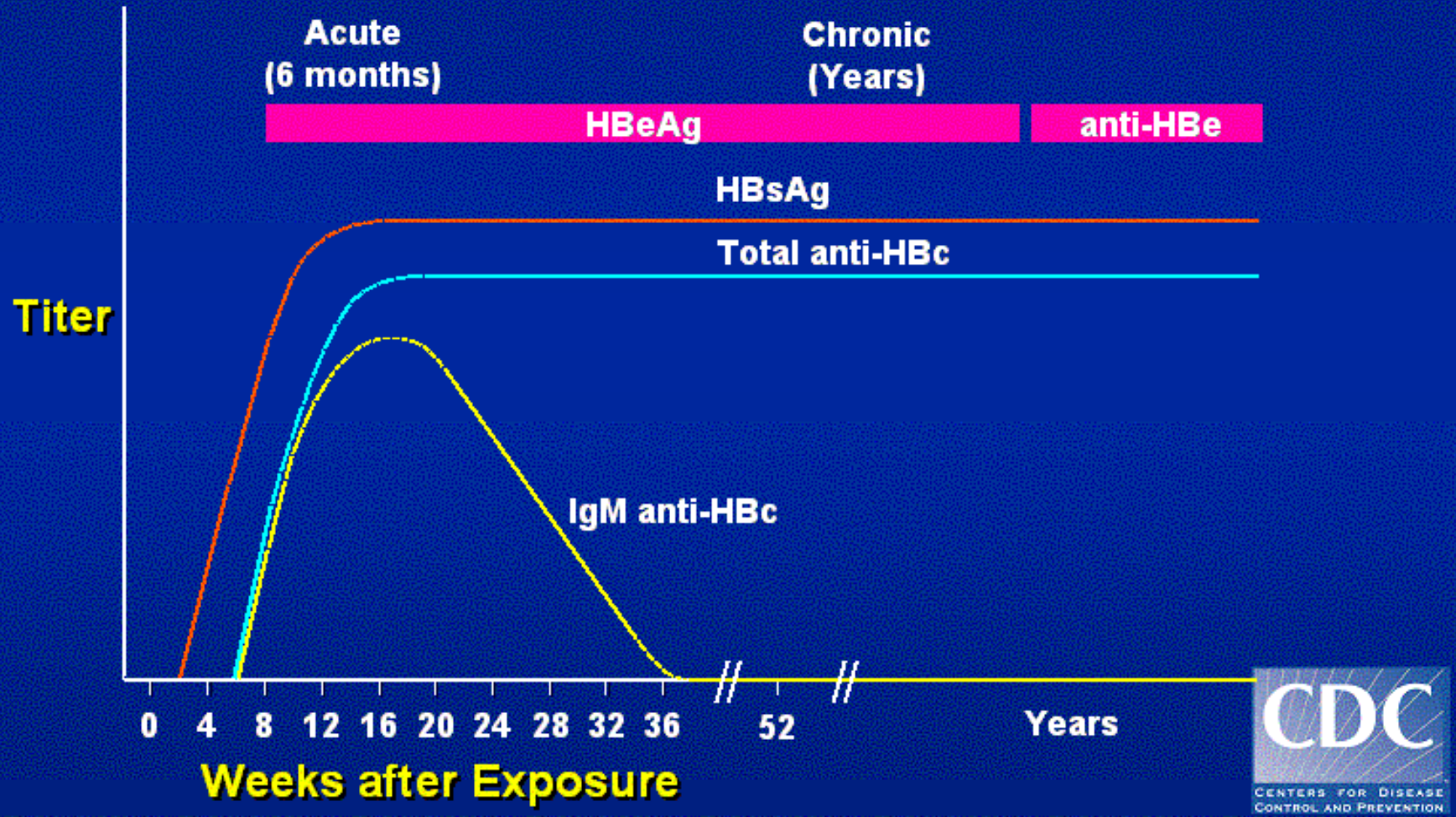
Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course



CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Progression to Chronic Hepatitis B Virus Infection

Typical Serologic Course



CDC
Centers for Disease Control and Prevention

Interpretation of Hepatitis B tests

HBsAg(+) HBcAb total (+) HBsAb (-)	Chronic hepatitis B infection
HBsAg(-) HBcAb total (+) HBsAb (+)	Immunity from previous infection
HBsAg(-) HBcAb total (-) HBsAb (+)	Immunity from vaccination

HBsAg = hepatitis B surface antigen, HBsAb = hepatitis B surface antibody
HBcAb = hepatitis B core antibody

TESTING FOR CHRONIC HBV
SEROLOGIC MARKERS

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CLASSIFICATION AND SPECTRUM OF DISEASE

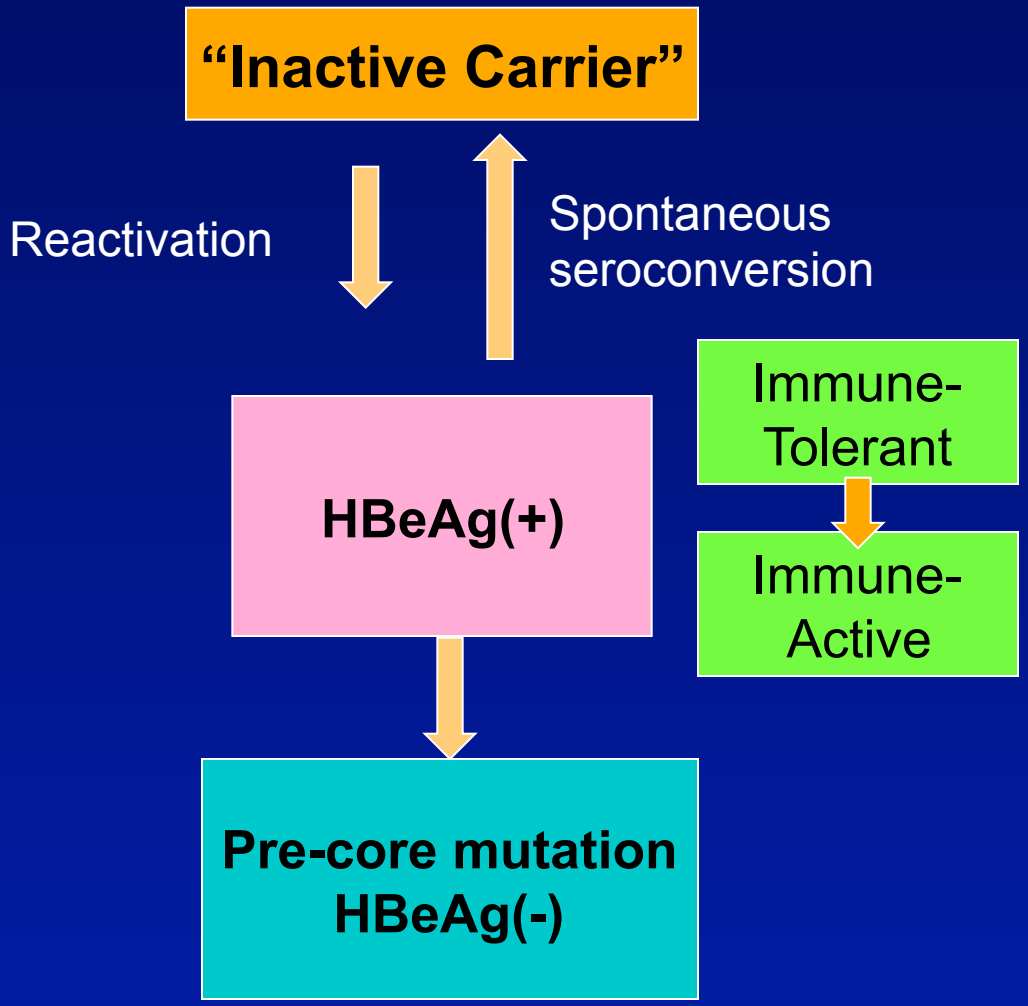
	HBeAg	HBV DNA	ALT
Inactive Carriers	(-)	(-) or low < 1000 IU/cc	Normal
"Wild type"	(+)	> 1000 IU/cc	Variable

Immune-tolerance = young age when HBV DNA very high but ALT normal
Immune activation = ALT elevated with immune-mediated injury

Pre-core mutant	(-)	> 1000 IU/cc	Variable

HBV DNA fluctuates over time, may be associated with periodic flares with very high ALT preceded by a rise in HBV DNA

Hepatitis B – A dynamic disease



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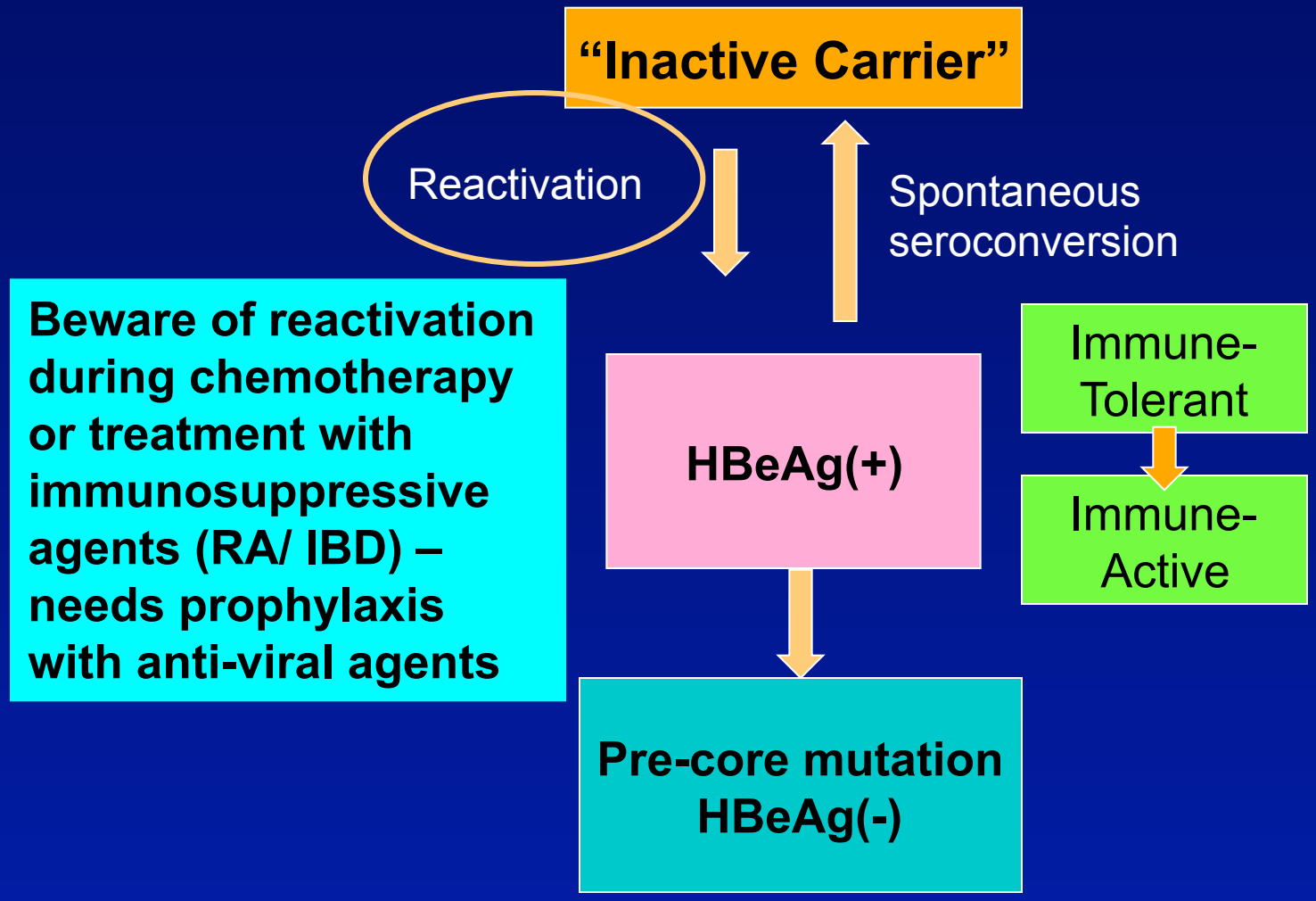
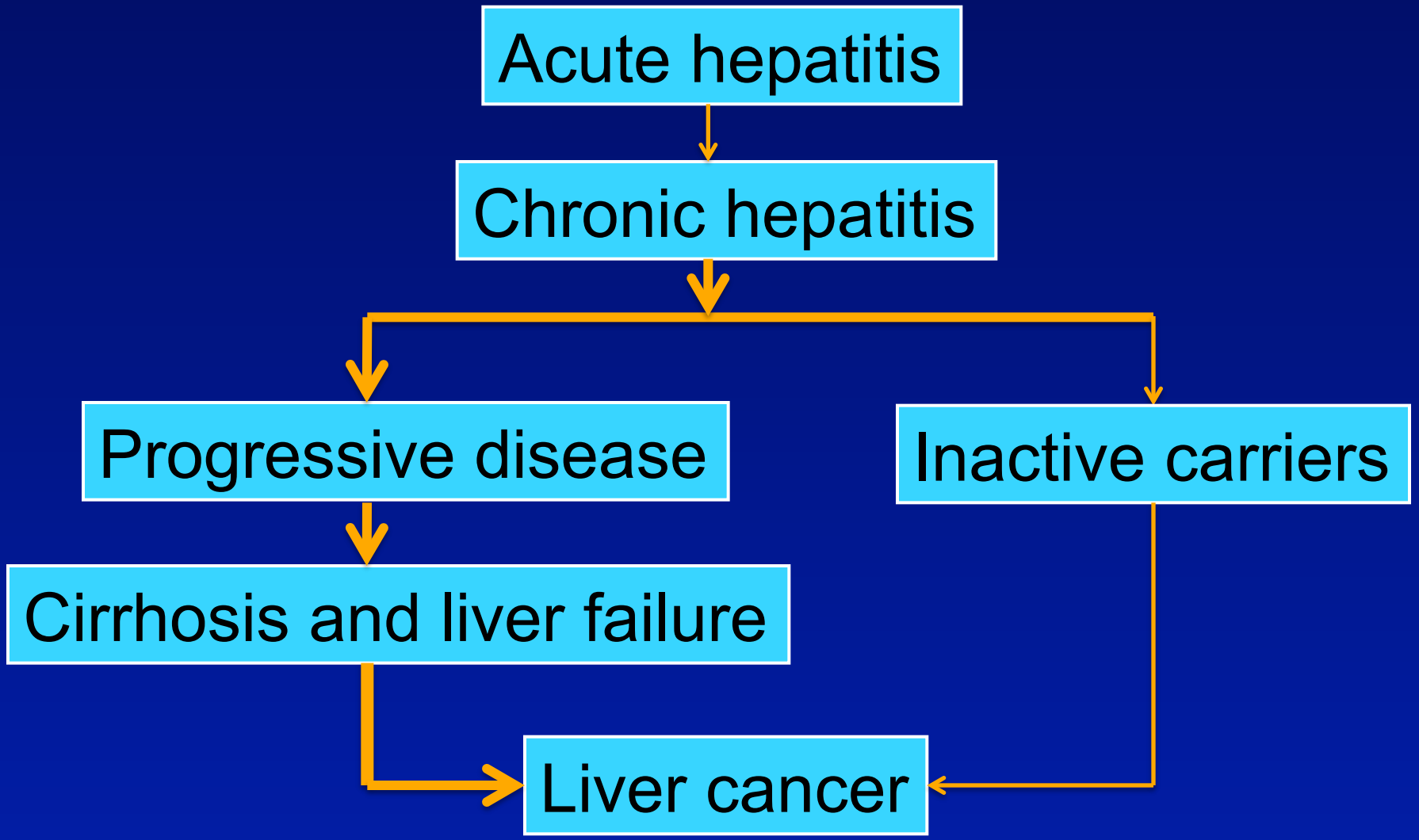


NATURAL HISTORY



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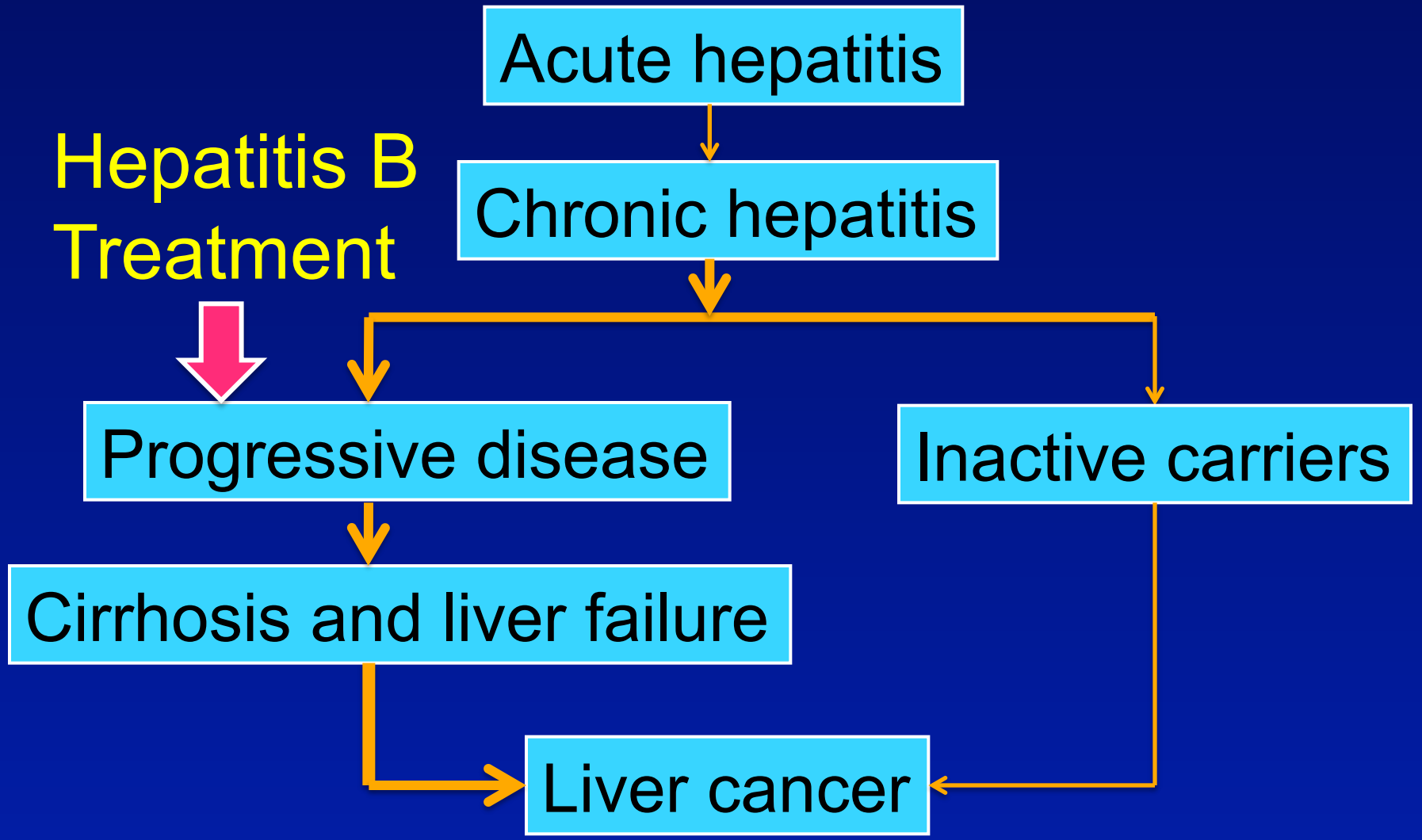

AASLD CHB Guidelines: Recommended Treatment Endpoints

HBeAg(+):

- Seroconversion from HBeAg(+) to HBeAb(+) potential endpoint
- Duration of therapy: Continue until at least 6-12 months after HBeAg seroconversion but relapse rate high after stopping

HBeAg(-):

- Undefined endpoint (under active investigation) *
- Duration of therapy = long-term in most cases

* The optimal duration of treatment is not known (many recommended indefinite treatment or until loss of hepatitis B surface antigen)

Treatment Guidelines: Recommended criteria for treatment

HBeAg(+):

- Abnormal ALT (> 2 times ULN per AASLD) * or advanced disease on liver biopsy or Fibroscan
- Hepatitis B DNA > 20,000 IU/mL

HBeAg(-):

- Abnormal ALT * or advanced disease on liver biopsy or Fibroscan
- Hepatitis B DNA > 2,000 IU/mL

* Normal ALT defined as > 35 for male and > 25 for female latest AASLD guideline

Not all guidelines agree on criteria for treatment

HEPATITIS B GENOTYPES (A to J)

Genotype	Significance
A	Higher response to Interferon
B	Asia – Lower risk for cirrhosis and HCC
C	Asia – Higher risks for cirrhosis and HCC
D	Higher risks for cirrhosis and HCC

- No difference in response to oral nucleoside analogues among genotypes
- Utility in clinical practice not established

ADVANCES IN HEPATITIS B TREATMENT
NUCLEOSIDE/ NUCLEOTIDE ANALOGUES

Treatment	Key points
Lamivudine	High risk for drug resistance (20%/yr)
Adefovir	Low potency, drug resistance (25% at 4 yrs)
	Nephrotoxicity * in 5-10% long-term
Telbivudine	High risk for drug resistance (10-20%/yr)
Entecavir	Low resistance (1% after 6 years)
	Excellent potency and safety
	Avoid if history of lamivudine-resistance
Tenofovir	No resistance reported
	Excellent potency and safety
	Kidney toxicity (< 1% new prodrug)

* Proximal renal tubular acidosis, phosphorus wasting, may not be completely reversible after stopping treatment

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Entecavir	Low resistance (1% after 6 years)
	Excellent potency and safety
	Avoid if history of lamivudine-resistance
Tenofovir	Low resistance (0% after 3 years)
	Excellent potency and safety
	Potential nephrotoxicity * (1-3%)

Current first line therapy

HEPATITIS B TREATMENT

Treatment	Key points
PEG-Interferon	Short duration - 48 weeks Significant side effects Contraindicated in decompensated HBV Better response with genotype A Long-term sustained response Hepatitis B e antigen (+) 30-40% Hepatitis B e antigen (-) 20%

Marcellin P et al. N Eng J Med 2004;35:1206-17

Lau GK et al. N Eng J Med 2005;352:2682-95

CASE #1

- Mr. C is a 56 year-old man with chronic hepatitis B, negative hepatitis B e antigen on prior testing
- ALT 84, hepatitis B DNA 150,000 IU/mL
- ALT 32, hepatitis B DNA 400 IU/mL
- ALT 100, hepatitis B DNA 77,000 IU/mL

To treat or not to treat?

CASE #1

- Mr. C is a 56 year-old man with chronic hepatitis B, negative hepatitis B e antigen on prior testing
- ALT 84, hepatitis B DNA 150,000 IU/mL
- ALT 32, hepatitis B DNA 400 IU/mL
- ALT 100, hepatitis B DNA 77,000 IU/mL

ACTIVE DISEASE, TREAT!

CASE #1

- Mr. C believes that his wife and children have all received vaccination, but wants to make sure that they are immune. He wants to know which tests he should request from the doctor

Interpretation of Hepatitis B tests

HBsAg(+) HBcAb total (+) HBsAb (-)	Chronic hepatitis B infection
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HBsAg(-) HBcAb total (-) HBsAb (+)	Immunity from vaccination

HBsAg = hepatitis B surface antigen, HBsAb = hepatitis B surface antibody
HBcAb = hepatitis B core antibody

CASE #2

- Ms. L is a 46 year-old woman with chronic hepatitis B, negative hepatitis B e antigen on prior testing
- ALT 18, hepatitis B DNA 100 IU/mL
- ALT 20, hepatitis B DNA < 10 IU/mL
- ALT 19, hepatitis B DNA 40 IU/mL

To treat or not to treat?

CASE #2

- Ms. L is a 46 year-old woman with chronic hepatitis B, negative hepatitis B e antigen on prior testing
- ALT 18, hepatitis B DNA 100 IU/mL
- ALT 20, hepatitis B DNA < 10 IU/mL
- ALT 19, hepatitis B DNA 40 IU/mL

"Inactive Carrier", no treatment needed but continued monitoring important

CASE #3

- Mr. W is a 66 year-old man with chronic hepatitis B, negative hepatitis B e antigen on prior testing
- ALT 18, hepatitis B DNA 2500 IU/mL
- ALT 20, hepatitis B DNA 7680 IU/mL
- ALT 19, hepatitis B DNA 9880 IU/mL

To treat or not to treat?

CASE #3

- Mr. W is a 66 year-old man with chronic hepatitis B, negative hepatitis B e antigen on prior testing
- ALT 18, hepatitis B DNA 2500 IU/mL
- ALT 20, hepatitis B DNA 7680 IU/mL
- ALT 19, hepatitis B DNA 9880 IU/mL

Borderline case, what to do?

- Estimate degree of fibrosis (scarring) based on liver stiffness (shear wave velocity)
- Non-invasive
- Nearly as accurate as liver biopsy
- Help guide treatment decision

CASE #3

- His Fibroscan showed mild disease with F0-1 fibrosis (stage 4 means cirrhosis).
- The recommendation is to follow blood tests every 3-6 months, and treat if increase in ALT and higher hepatitis B DNA > 2000 IU/mL

CASE #3

- Mr. W also reports that he has been taking a "magic liver pill" that he bought 3 months ago and has been feeling better overall
- He drinks on average 2 glasses of wine or 2 cans of beer 3-4 times a week


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MILK THISTLE
supports liver repair**
ORANGE GRAPE
encourages proper liver and gallbladder function**
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60 Vegetarian Capsules
NOW
Liver Refresh
Liver Support*
• Promotes Optimal Liver Health*
• Supports Healthy Detoxification Processes*
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A Dietary Supplement
OMEGA ALPHA
Liver Flush
Supports Normal Liver Function*
Apoya una función hepática normal
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• Supports Healthy Detoxification Processes*
90 Veg Capsules
A Dietary Supplement
OMEGA ALPHA
Liver Flush™
Supports Normal Liver Function*
Apoya una función hepática normal
SUPPLEMENT • SUPLEMENTO DIETÉTICO

DISPELLING MISCONCEPTIONS

Remember:

- Do not go by how you feel! Liver disease may be “silent” for many years
- It is safe to take acetaminophen (Tylenol) up to 2 grams a day in divided doses even in patients with cirrhosis
- Avoid herbs and supplements
- Avoid alcohol

LIVER CANCER SCREENING IN HBV

- Patients at high risk for liver cancer should be screened with Ultrasound (+ AFP) every 6 months

  1) Cirrhosis
  2) Family history of liver cancer (first degree relative)
  3) Age ≥ 40 for male and ≥ 50 for female
  4) Hepatitis D co-infection

  Consider screening for those with a history of active replication (HBV DNA+) and or active inflammatory activities

HEPATITIS B VACCINATION

- A nationwide program of vaccination implemented in 1984 in Taiwan have reduced the HBsAg carrier rate in children from 10% to < 1% 10 years later.[1]
- In the U.S., universal vaccination of newborns was implemented by the CDC in 11/1991.
- All newborns to HBsAg (+) mothers also receive HBIG in addition to vaccination and should be tested for response to vaccination.

[1] *Chen HL et.al. JAMA 1996;276:906-908*

SUMMARY – HEPATITIS B

- **ALL** Asians and Pacific Islanders should be screened for hepatitis B infection - The first and most important step
- Chronic hepatitis B may be a silent disease – do not go by how you feel, regular monitoring is essential
- Understand guidelines for treatment based on liver enzymes (markers of liver injury) and hepatitis B activities (hepatitis B DNA)

SUMMARY – HEPATITIS B

- Advances in the development of oral anti-viral agents that are potent, safe and well tolerated, with low risks for drug resistance
- Early treatment (if indicated) may prevent complications of liver disease due to hepatitis C – cirrhosis, liver failure and liver cancer
- Screening for liver cancer with ultrasound + AFP every 6 months in hepatitis B-infected individuals to diagnose liver cancer at an early, curable stage

Thank You

"Is life worth living? It all depends on the liver."
William James, American philosopher (1842)