

Hepatitis B

**What Students Should Know Before They
Go Out to Educate the Public**

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What is Hepatitis B?

- Hepatitis B is an infection of the liver caused by the hepatitis B virus

How common is hepatitis B?

Worldwide

- 350 million people are chronic carriers
- About 75% of HBV carriers live in Asia
- 0.5-1 million deaths per year due to HBV

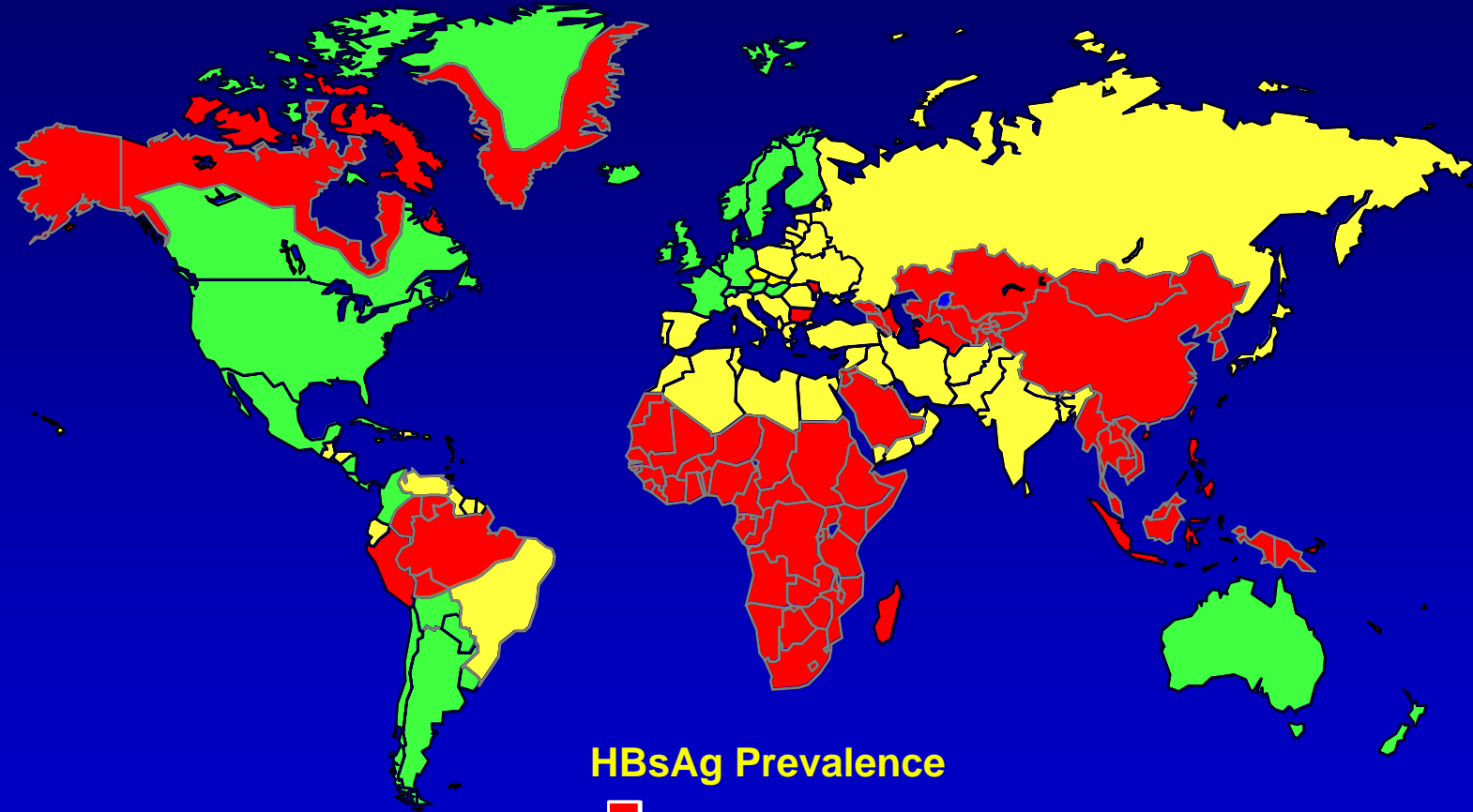
Asia

- Liver cancer is the 2nd cancer killer among Asian men and the 5th cancer killer among Asian women
- Roughly 40% of Asian men and 15% of Asian women with chronic hepatitis B will die of a liver-related illness

Estimated Number of New Cases of Chronic HBV in the US, 2000-2004

- **Acquired in the US**
 - Acute HBV infections: 74,000
 - New cases of chronic HBV: 5,000
- **From immigration**
 - No. of immigrants: 900,000
 - No. of immigrants with chronic HBV: 46,000
- **~90% new cases of chronic HBV in the US are due to immigration from endemic areas**

Geographic Distribution of Chronic HBV Infection



HBsAg Prevalence

- ≥8% - High
- 2-7% - Intermediate
- <2% - Low

Hepatitis B and Asian Americans

- **Less than 0.5% (1 in 200) Americans have chronic hepatitis B**
- **About 10-15% (1 in 8 to 10) Asian Americans have chronic hepatitis B**
- **About 50% (1 in 2) of the people in the US with chronic hepatitis B are Asian Americans**
- **A much higher percent of Asian Americans compared to Americans of other races have hepatitis B**

Why is Hepatitis B so common among Asian Americans?

- **Hepatitis B is very common in Asia**
- **Many Asian Americans were infected with hepatitis B before they came to the US**
- **Asian Americans born in the US may be infected through their mother or other family members, who are HBV carriers**

How is HBV spread?

- HBV is more easily spread than HIV and HCV
- HBV can live outside the human body for up to 7 days
- People with chronic hepatitis B can have very large amounts of virus in their blood – serum HBV DNA up to $12 \log_{10}$ copies/mL (1 trillion)

How is HBV spread?

Mainly through blood and bodily secretions

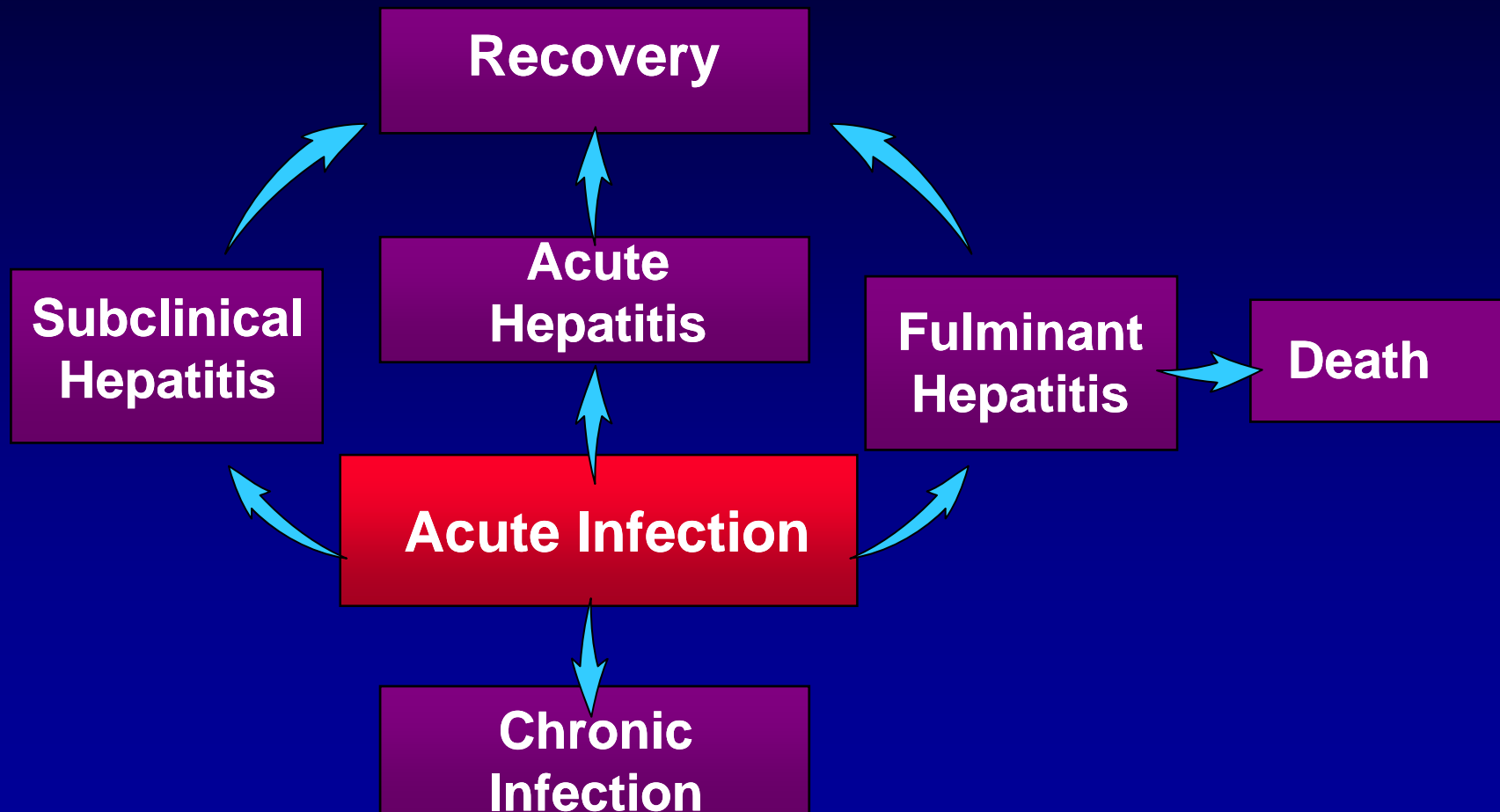
- **Infected mother to babies at birth**
- **Contact with blood from carriers through wounds, contaminated household articles such as razors, toothbrushes, or contaminated needles used for tattoos and injecting drugs**
- **Sexual contact with carriers**

How is HBV spread?

HBV is **NOT** spread by:

- Hugging or kissing
- Coughing or sneezing
- Sharing eating utensils

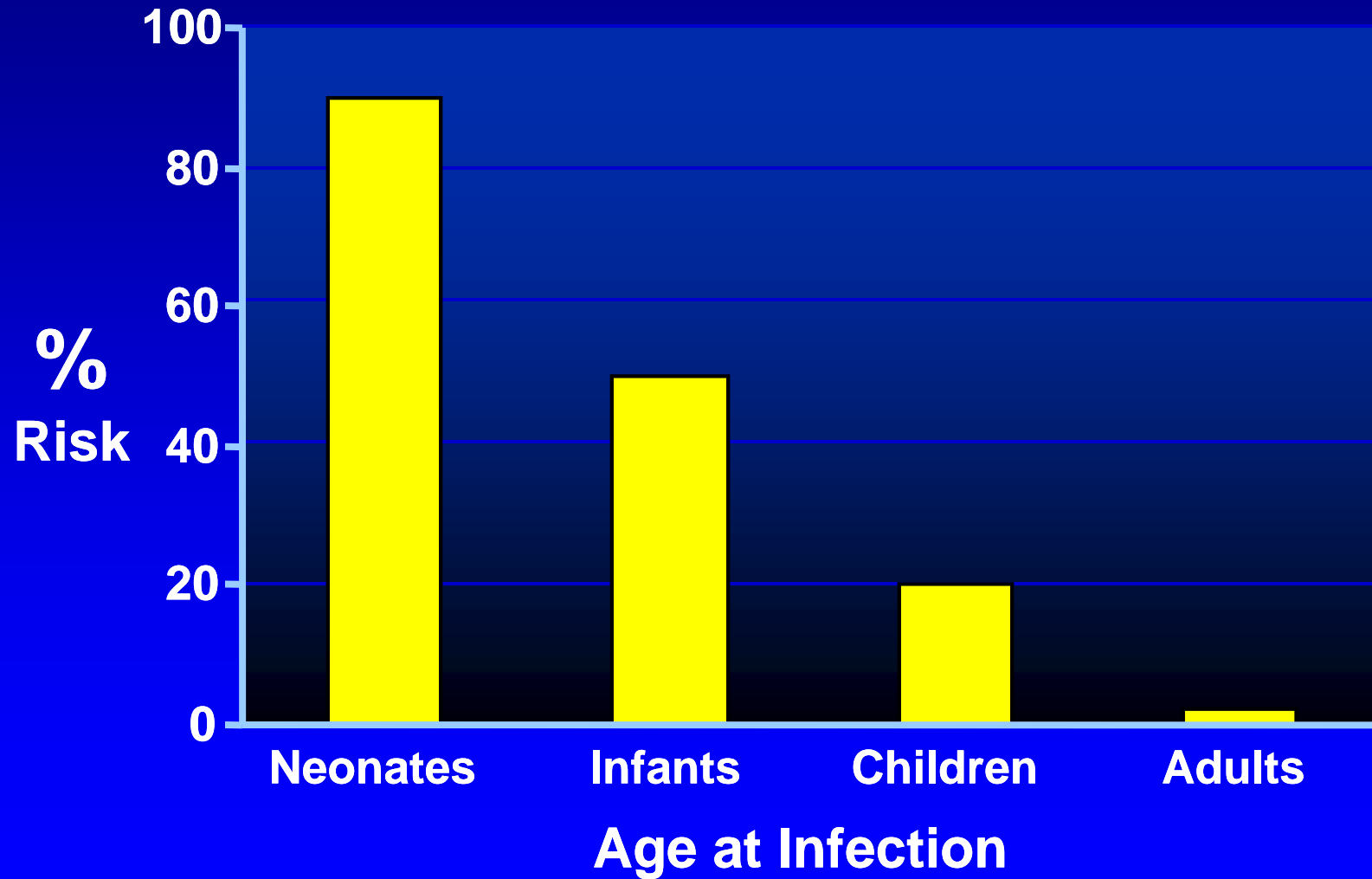
Outcome of Acute HBV Infection



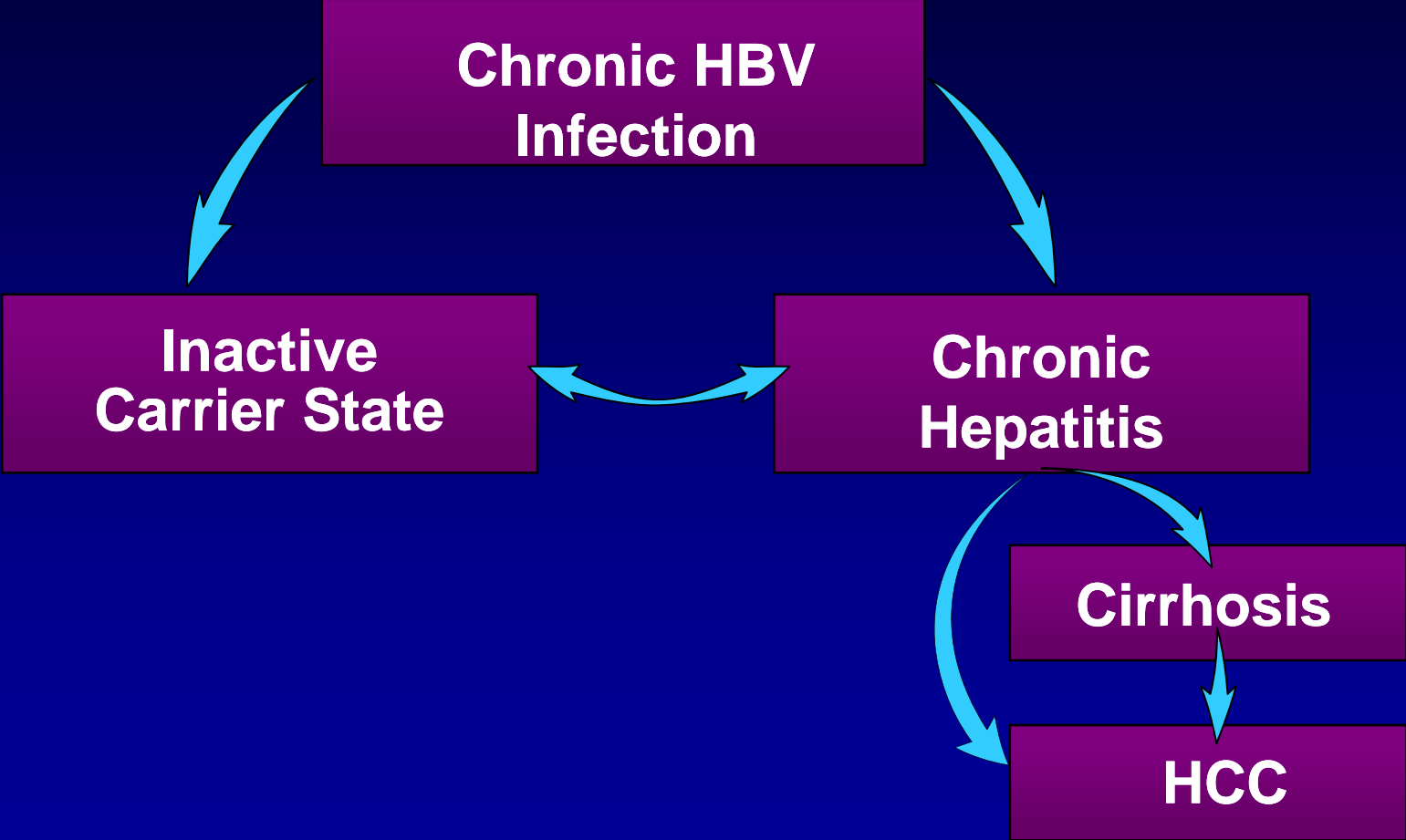
Acute Hepatitis B

- Recent infection
- May have no symptoms, especially in children
- Common symptoms: easily tired, poor appetite, nausea, abdominal discomfort, jaundice
- Roughly 95% recover, usually in 2-3 months
- About 1% severe hepatitis with acute liver failure
- About 5% go on to chronic infection, lasts longer than 6 months

Risk of Chronic HBV Infection



Outcome of Chronic HBV Infection



Chronic HBV Infection

- **Long-lasting infection, persists for more than 6 months**
- **Most people have no symptoms**
- **Common symptoms: easily tired, poor appetite, nausea, abdominal discomfort**
- **Can go on to cirrhosis, liver failure, liver cancer, and death**

How can hepatitis B be diagnosed?

- The only way to know is to have a blood test
- Most people with hepatitis B have no symptoms until late stages of liver disease
- Tests for hepatitis B or liver enzymes are not included in most routine check-ups
- Hepatitis B may be present even if liver enzymes were tested and were normal

CDC Recommendations on HBV Screening

- **Persons born in geographic regions with HBsAg prevalence of $\geq 2\%$**
 - US-born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity ($>8\%$)
- **Tissue and blood donors**
- **Pregnant women, infants of HBsAg+ mothers**
- **High risk groups:**
 - Men who have sex with men, injection drug users, HIV+ persons
 - Dialysis patients
 - Household or sexual contacts of carriers
- **Persons who will be receiving cytotoxic or immunosuppressive therapy**
- **Persons with elevated ALT/AST of unknown etiology**

Serological Markers of HBV Infection

HBsAg	Acute/Chronic infection
Anti-HBc IgM	Recent infection
HBeAg	High infectivity
Anti-HBe	Low infectivity
Anti-HBs	Immunity
Anti-HBc IgG + HBsAg	Chronic infection
Anti-HBc IgG + anti-HBs	Resolved infection

Interpretation of HBV Serology

HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
-	-	-	-	
+	+	-	-	
+	+	+	-	
-	+	-	+	
-	-	-	+	

A = acute infection

B = chronic infection

C = Immunity after vaccination

D = immunity after previous infection

E = not been exposed

Interpretation of HBV Serology

HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
-	-	-	-	E - Not been exposed
+	+	-	-	B - Chronic infection
+	+	+	-	A - Acute Infection
-	+	-	+	D - Immunity from past infection
-	-	-	+	C - Immunity after vaccination

Importance of Monitoring Serum HBV DNA Levels

- Direct measurement of HBV replication
- Fluctuating levels, serial tests important for clinical assessment
- HBV DNA levels do not always correlate with ALT levels or histologic activity of liver disease
- Persistently high serum HBV DNA levels are associated with increased risk of cirrhosis and HCC

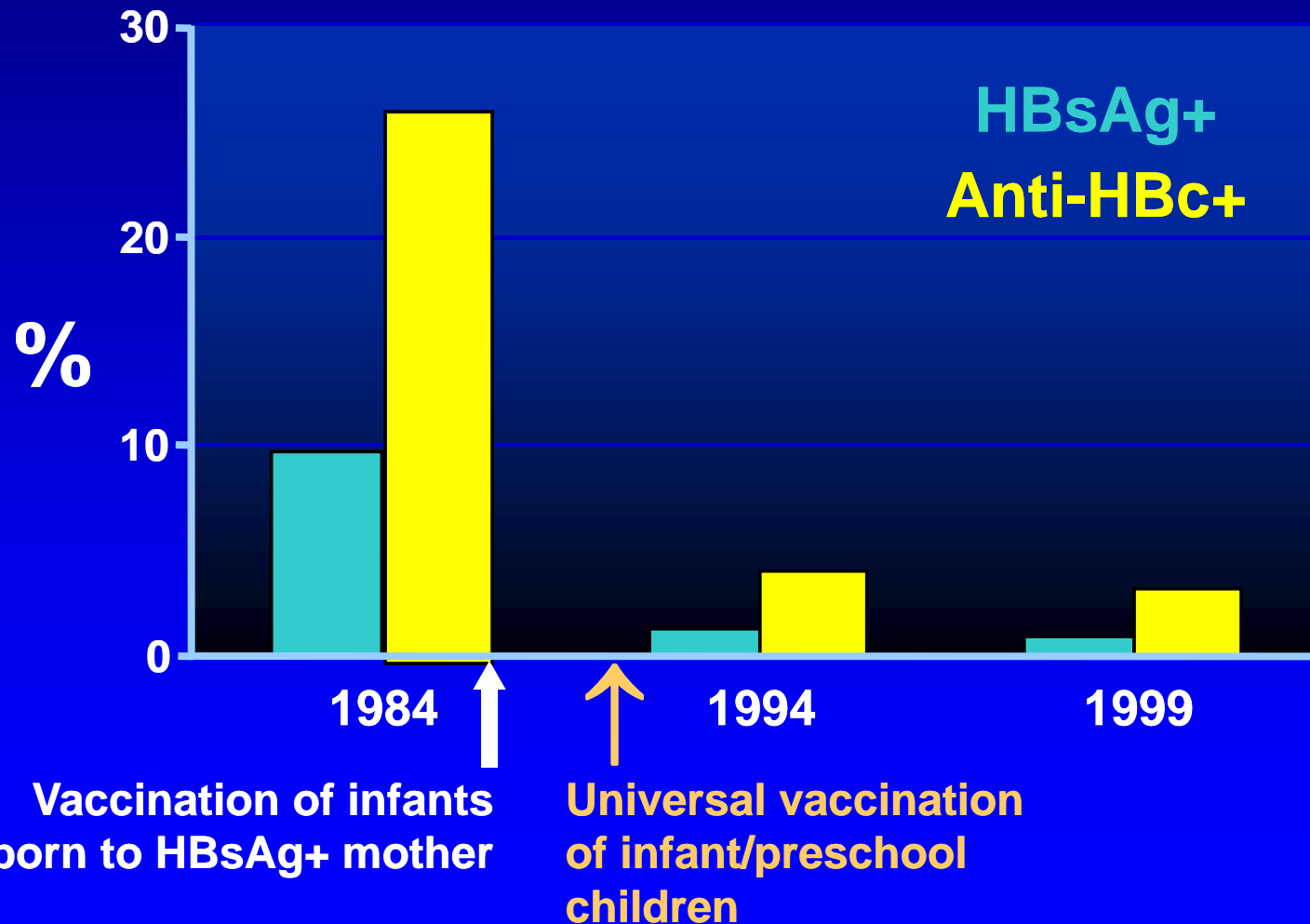
Hepatitis B Vaccines

- Genetically engineered hepatitis B surface antigen alone or in combination with hepatitis A vaccine
- 3 doses: month 0, 1, 6
- Immune response: 50% after 1 dose
95% after 3 doses
- Duration of protection: >15 years, dependent on initial antibody response
- Factors associated with poor response: older age, chronic medical illness (cirrhosis, kidney failure, diabetes), decreased immune response, smoking, obesity, genetics

Indications for HBV Vaccines

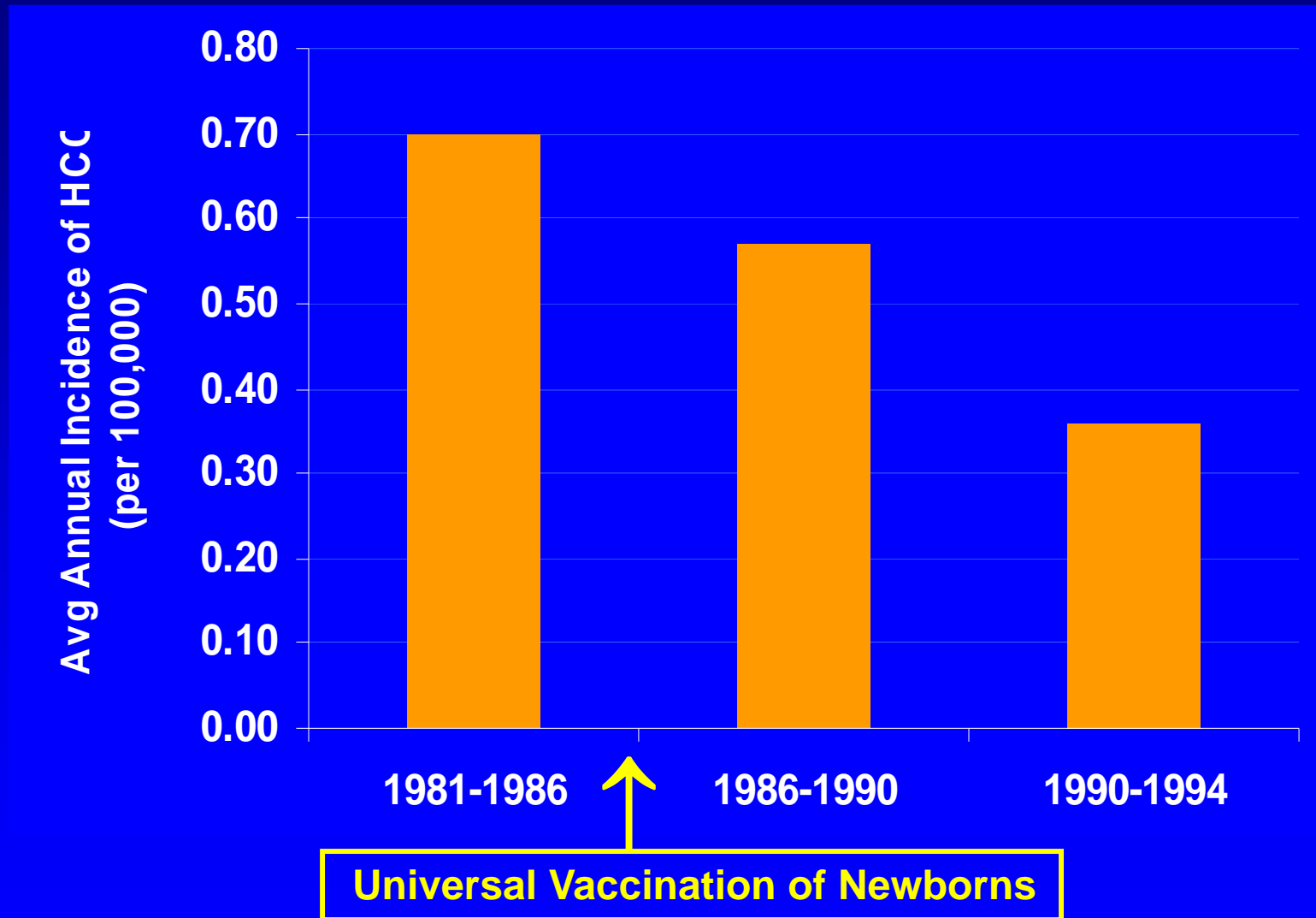
- All infants (+HBIG for infants of HBsAg+ mothers)
- All children and adolescents who were not vaccinated at birth
- Vaccination of adults at risk of infection
 - Occupational
 - Sexual / household contacts
 - Persons with high risk behaviors, e.g. injection drug users, men who have sex with men, persons with multiple sexual partners
 - Persons born in endemic areas or persons born to parents from endemic areas
 - Dialysis patients
 - Patients with chronic liver disease

Impact of HBV vaccination on HBV infection rates in Taiwanese children



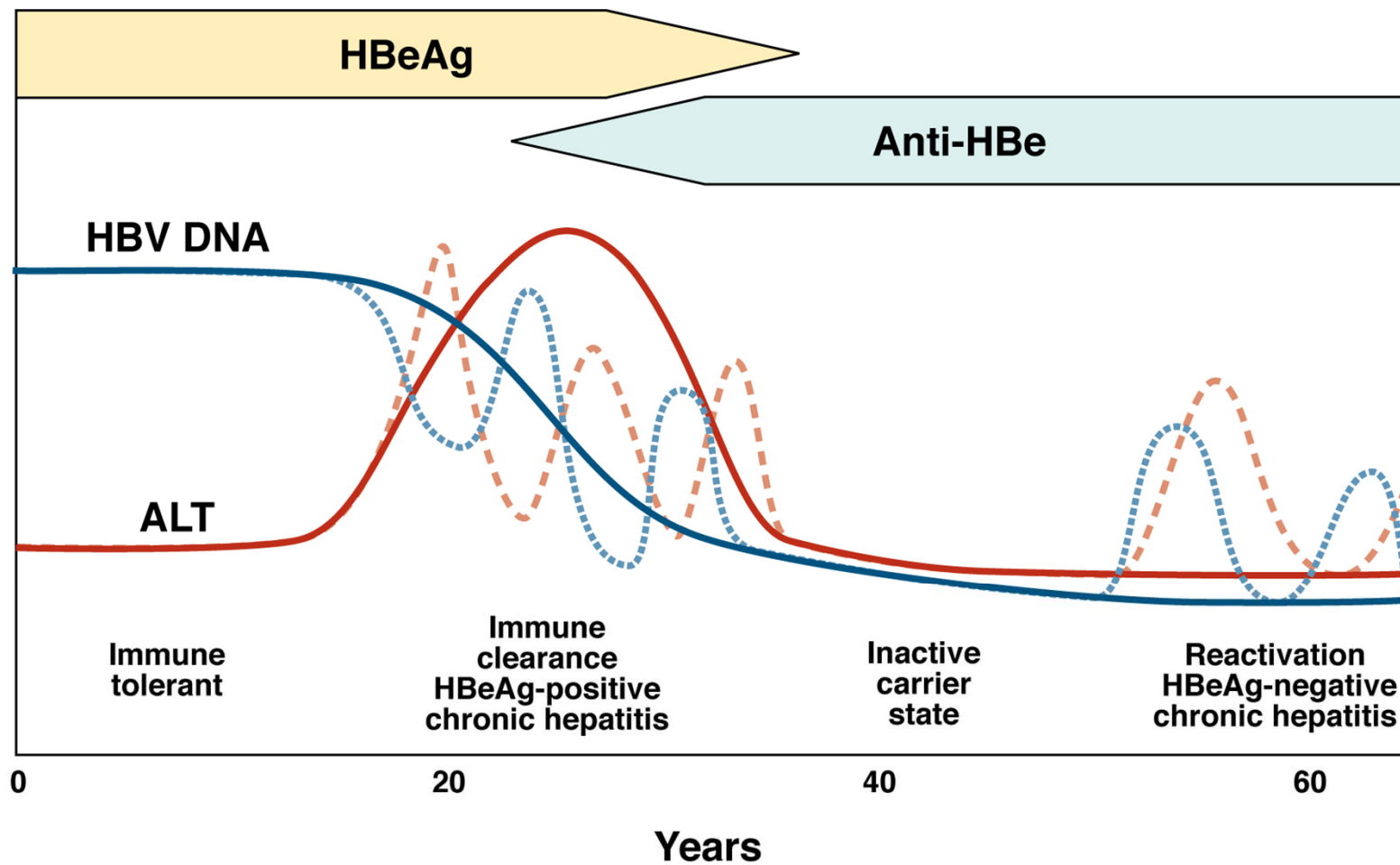
Ni YH, *Ann Intern Med* 2001;135:796

Impact of HBV Vaccination on Incidence of HCC in Taiwanese Children



Chang MH, NEJM 1997;336:1855

Phases of Chronic HBV Infection

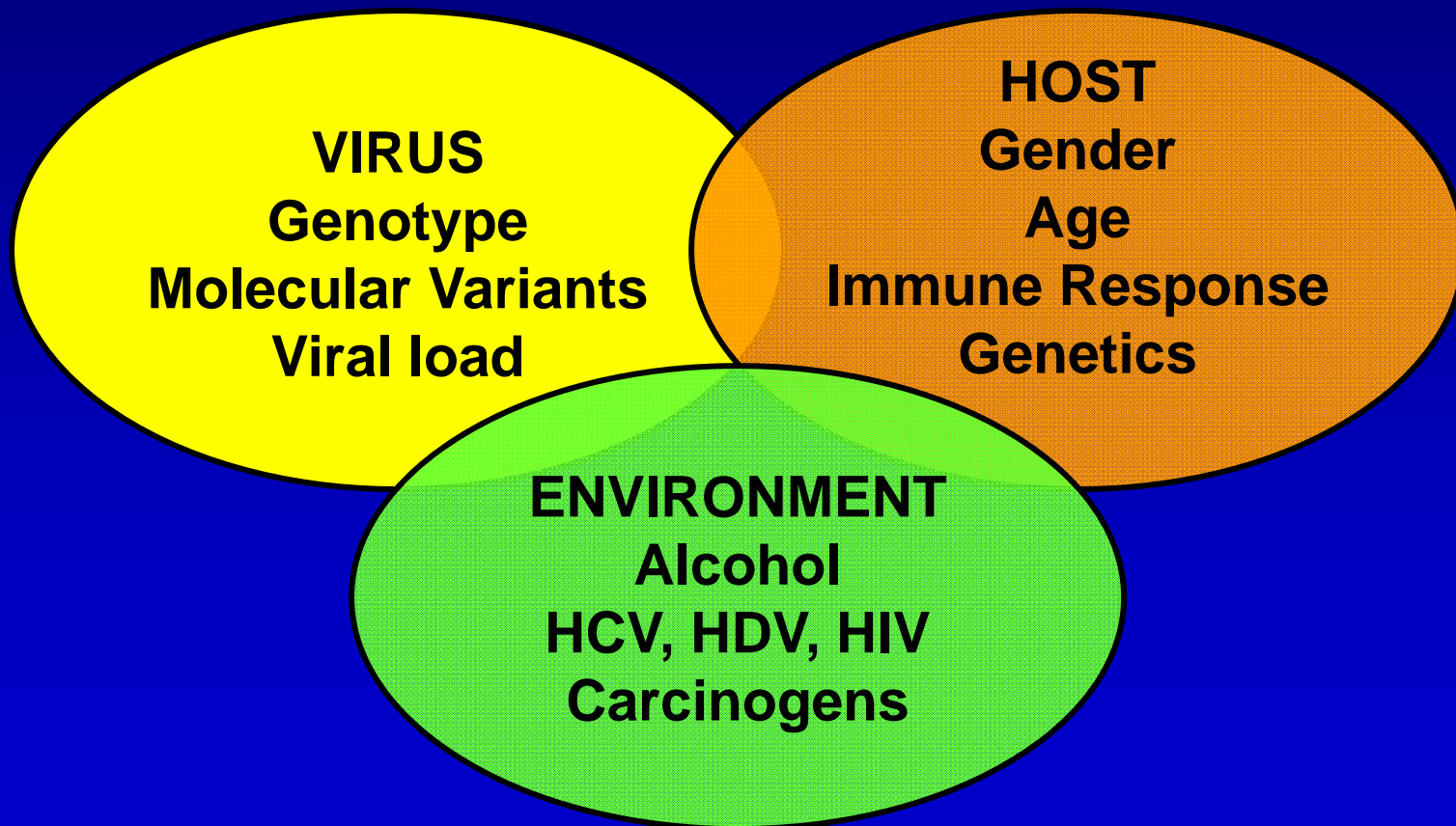


Initial Evaluation of Patients with Hepatitis B

- **Clinical evaluation**
- **Lab tests**
 - **HBeAg, anti-HBe, HBV DNA**
 - **Tests to r/o HCV, HDV, HIV, other causes of liver disease if indicated**
 - **Tests to assess liver disease severity – liver chemistry, CBC+P, PT**
- **+/- Abdominal ultrasound – assess cirrhosis, surveillance for liver cancer**
- **+/- Liver biopsy**
- **Vaccination against hepatitis A**
- **Counseling on precautions to prevent transmission of infection, alcohol use, and healthy lifestyle**

Hepatitis B

Factors affecting disease activity and progression



Unique Aspects of Natural History of Chronic HBV Infection in Asians

- **Immune tolerance phase – long, low rate of spontaneous or treatment related HBeAg seroconversion**
- **Higher incidence of HCC compared to Caucasians**
- **Predominant HBV genotypes B and C, genotype C associated with lower rates of spontaneous HBeAg seroconversion, more rapid progression to cirrhosis and HCC**

What can patients do to protect their liver?

- Do not drink alcohol
- Do not take any herbal medicine that might hurt the liver
- Eat a balanced diet, exercise regularly, avoid getting overweight

Hepatitis B is a chronic health problem, HBV levels and severity of liver damage can change with time, see their doctor and get tested at least once a year even if they have no symptoms

Treatment of Chronic Hepatitis B

Goals

- **Suppression of HBV replication**
- **Decrease hepatic necroinflammation and fibrosis**
- **Prevent progression to cirrhosis, liver failure and HCC**

Responses to HBV Treatment

- **Virologic Response**

- Decrease in serum HBV DNA: preferably to undetectable by PCR
- HBeAg loss / seroconversion: applicable to HBeAg+ patients only
- HBsAg loss: Ultimate goal

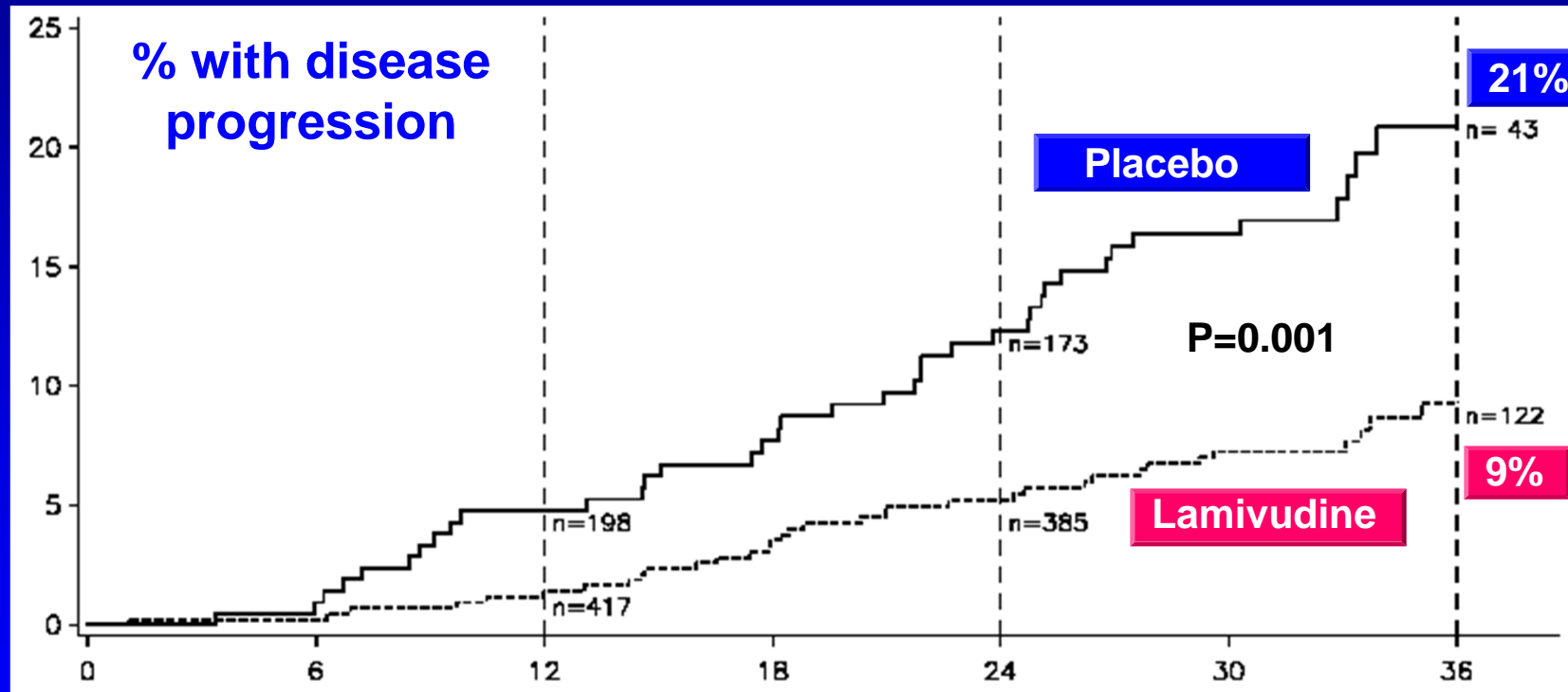
- **Biochemical Response**

- ALT normalization

- **Histological Response**

- **Clinical Response**

Antiviral Therapy is Effective in Slowing Disease Progression in patients with Cirrhosis HBeAg+ and/or serum HBV DNA >700,000 gEq/mL



Time to disease progression (months)

—	Placebo (n=215)	ITT population
.....	Lamivudine (n=436)	p=0.001

When to start treatment?

Benefits

Likelihood of
sustained response
cirrhosis and HCC

Risks

Side effects
Drug resistance

Patient's age
Co-morbid illness
Costs

High likelihood of cirrhosis / HCC in the next 10-20 yrs

High likelihood of sustained viral suppression after a defined
course of treatment

High HBV DNA, high ALT, older age

Approved HBV Treatments

- Interferon alpha 2b – 1992
- Pegylated interferon alpha 2a – 2005
- Lamivudine (Epivir) – 1998
- Adefovir (Hepsera) – 2002
- Entecavir (Baraclude) – 2005
- Telbivudine (Tyzeka) – 2006
- Tenofovir (Viread) - 2008

Treatment

Interferon

Nucleos/tide Analogues

Route

Parenteral

Oral

Duration of treatment

Finite duration ~ 12 mos

Long duration, yrs to life long

Antiviral activity

Modest, additional immunomodulatory effects

Stronger antiviral activity

HBsAg loss

1-3% after 1 yr

Rare, 0-1% after 1 yr

Resistant mutants

None

0-25% after 1 yr

Side effects

Frequent

Rare, Adefovir / tenofovir nephrotoxicity

Safety and Efficacy of Oral Antiviral Therapies

	LAM	ADV	ETV	LdT	TDF
Antiviral activity	++	+	+++	+++	+++
Safety	+++	++	+++	++	++
Rate of antiviral resistance	high	intermediate	low	high	low

LAM = lamivudine, ADV = adefovir, ETV = entecavir, LdT = telbivudine, TDF = tenofovir

* Rate of resistance higher in patients who have prior lamivudine resistance

When can treatment be stopped?

- **IFN: finite duration, 12 mos**
- **Nucleoside/tide analogues**
 - HBeAg+ patients: 12 mos after HBeAg seroconversion (~50% after 5 yr Rx)
 - HBeAg- patients: endpoint not defined, ?until HBsAg loss (~5% after 5 yr)
 - Cirrhosis patients: endpoint not defined, ?life-long

**Hepatitis B can be a deadly
disease**

BUT

**It can be prevented,
and it can be treated**

GET TESTED