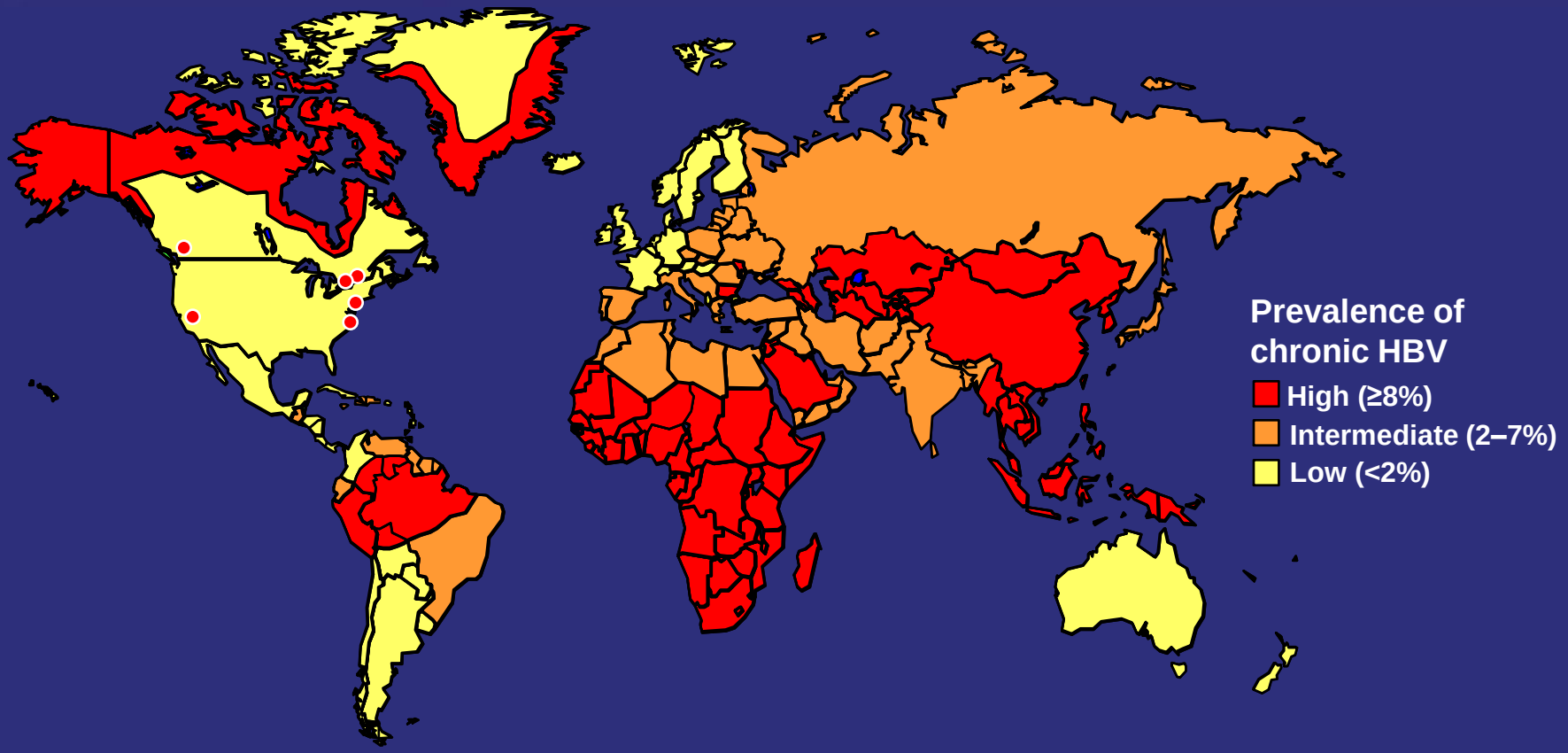
Hepatitis B

New Strategies for Diagnosis, Monitoring and Referral

Hepatitis B: Epidemiology, Screening and Referral

Peter Kwan, MD, FRCP(C)
Clinical Associate Professor
University of British Columbia
Vancouver Hospitals and Health Sciences Centre
Vancouver, BC

Global Prevalence of Chronic Hepatitis B



Canada has low overall prevalence but with high prevalence in certain groups, e.g., immigrants from endemic regions

Centres for Disease Control, 2006

The Global Burden of Chronic Hepatitis B is Significant

Worldwide

- 400 million people infected
- Endemic in Asia, Africa, Southern and Eastern Europe
- Asia accounts for 75% of cases (260–300 million)
- Causes 60–80% of world's liver cancer
- Approximately 500,000–700,000 deaths each year

Canada

- Overall prevalence unknown
- Estimates indicate 500,000 to 600,000 carriers in Canada
- Figure rising due to immigration from endemic regions
- Sub-populations with higher prevalence
  - Immigrants from endemic areas (particularly SE Asia)
  - Inuit population
  - IDUs

1. WHO Report 1996 2. Lai et al, Surgeon 2005; 3: 210–15 3. Lai et al, Lancet 2003; 362: 2089–94
4. Keeffe et al, Clin Gastroenterol Hepatol 2004; 2: 87–106

Prevalence of HBV Infection is Higher in Immigrant Populations from South-East Asia

- HBsAg seroprevalence higher in adult Asian immigrant populations in North America
  - Including Chinese, Korean and Vietnamese populations
- Large metropolitan cities in the US: 10.4%[1]
- California[2]
  - San Francisco: 12.3%
  - Los Angeles: 12.5%
  - Orange County: 9.3%
- New York City: 15%[3]

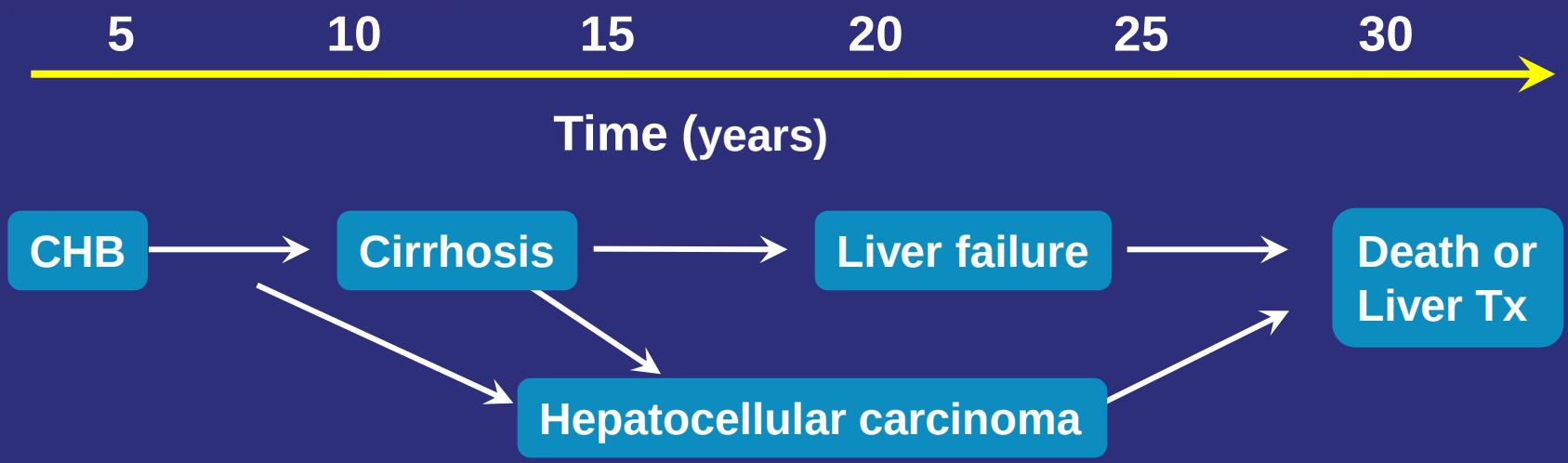
[1]Guane et al, Hepatology 2004; 40(4 Suppl. 1): 716A [2]Chao et al, Hepatology 2004; 40(4 Suppl. 1): 717A
[3]CDC, MMWR Morb Mortal Wkly Rep 2006; 55: 505–9

Transmission of Hepatitis B Virus

- Vertical
  - Mother-to-child during birth or first year of life
- Horizontal
  - Household exposure
  - Child-to-child or other close contact
  - Sexual contact
  - Blood-to-blood

Mast et al, MMWR Recomm Rep 2005; 54: 1–31

Why is it Important to Identify Patients with CHB?: Disease Progression



Cumulative incidence of cirrhosis at 5 years:[1]

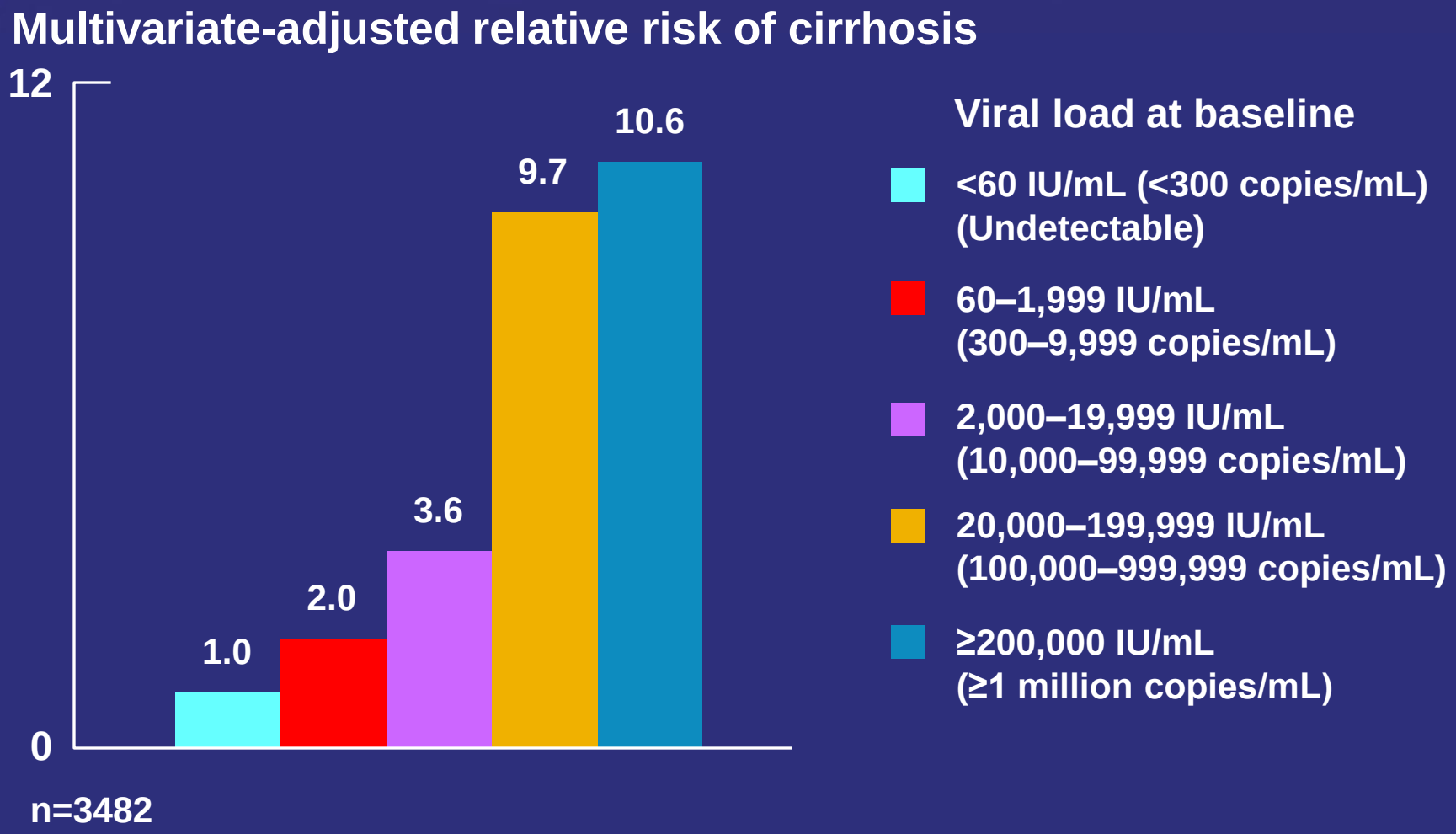
HBeAg+ 8–20%
HBeAg- 40%

Incidence of HCC (cases/100,000 person-years):[2]

HBeAg+ 1169.4
HBeAg- 39.1–324.3

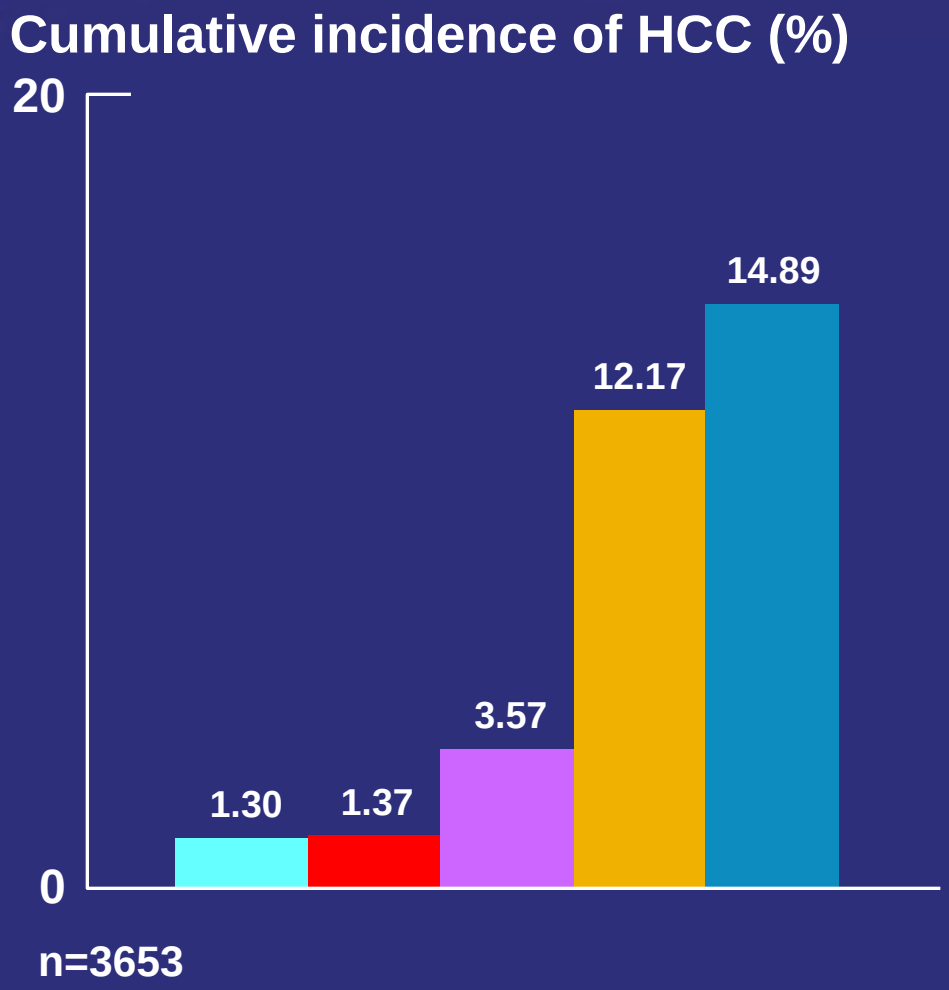
[1]*Hadziyannis et al, Semin Liv Dis 2006; 26: 130–41*
[2]*Yang et al, N Engl J Med 2002; 347: 168–74*

The REVEAL Study: Relative Risk of Cirrhosis is Higher in Adult Men with High Viral Load



Chen et al, JAMA 2006; 295: 65–73
Iloeje et al, Gastroenterology 2006; 130: 678–86

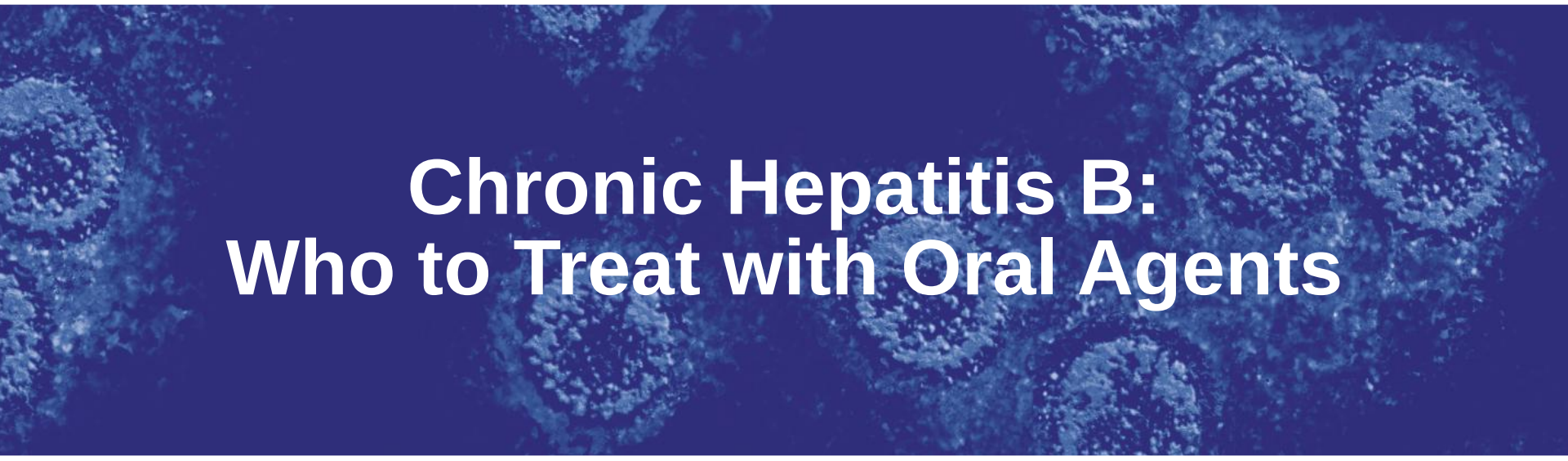
The REVEAL Study: Cumulative Incidence of HCC is Higher in Adult Men with High Viral Load



Chen et al, JAMA 2006; 295: 65–73
Iloeje et al, Gastroenterology 2006; 130: 678–86

Hepatitis B

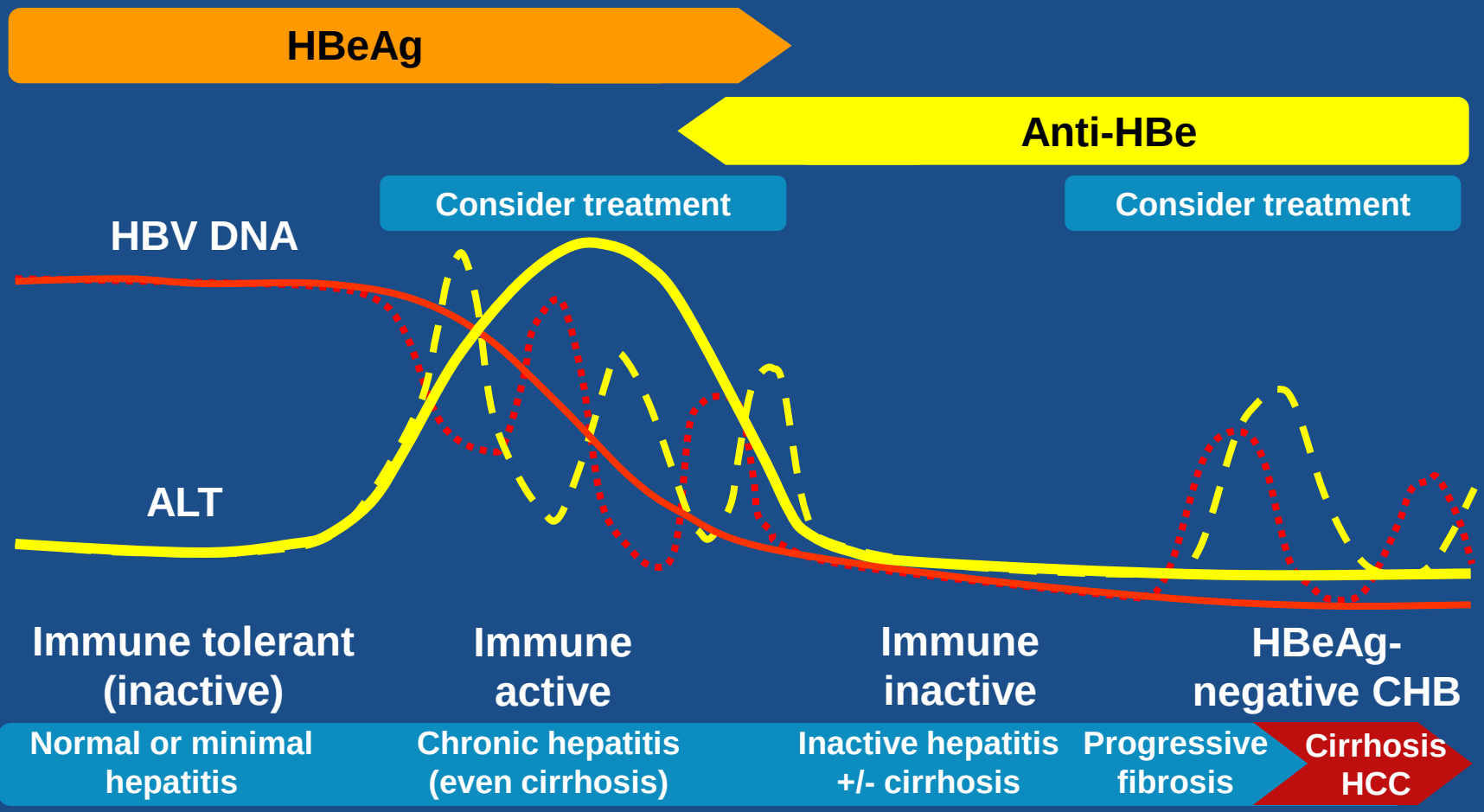
New Strategies for Diagnosis, Monitoring and Referral



Chronic Hepatitis B: Who to Treat with Oral Agents

E. Jenny Heathcote, MD, FRCP(C)
Professor of Medicine
University of Toronto
Toronto, ON

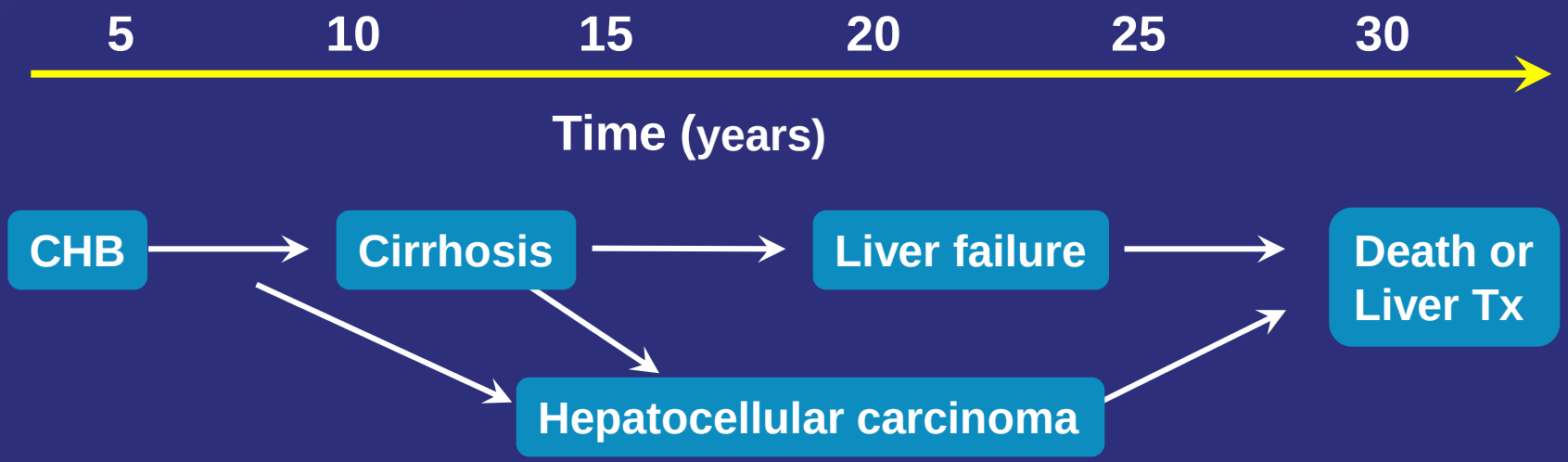
Chronic HBV Infection has a Dynamic Disease Course



CHB is a dynamic disease and patients can transition backwards and forwards between stages

Adapted from Yim & Lok, Hepatology 2006; 43: S173–81

Potential Disease Progression in Patients with Chronic Hepatitis B



Cumulative incidence of cirrhosis during disease course: 40%

Incidence of HCC (cases/100,000 person-years):[1]

HBV DNA 2 x 10^3 – 2 x 10^4 IU/mL	297
HBV DNA 2 x 10^4 – 2 x 10^5 IU/mL	982
HBV DNA ≥2 x 10^5 IU/mL	1152

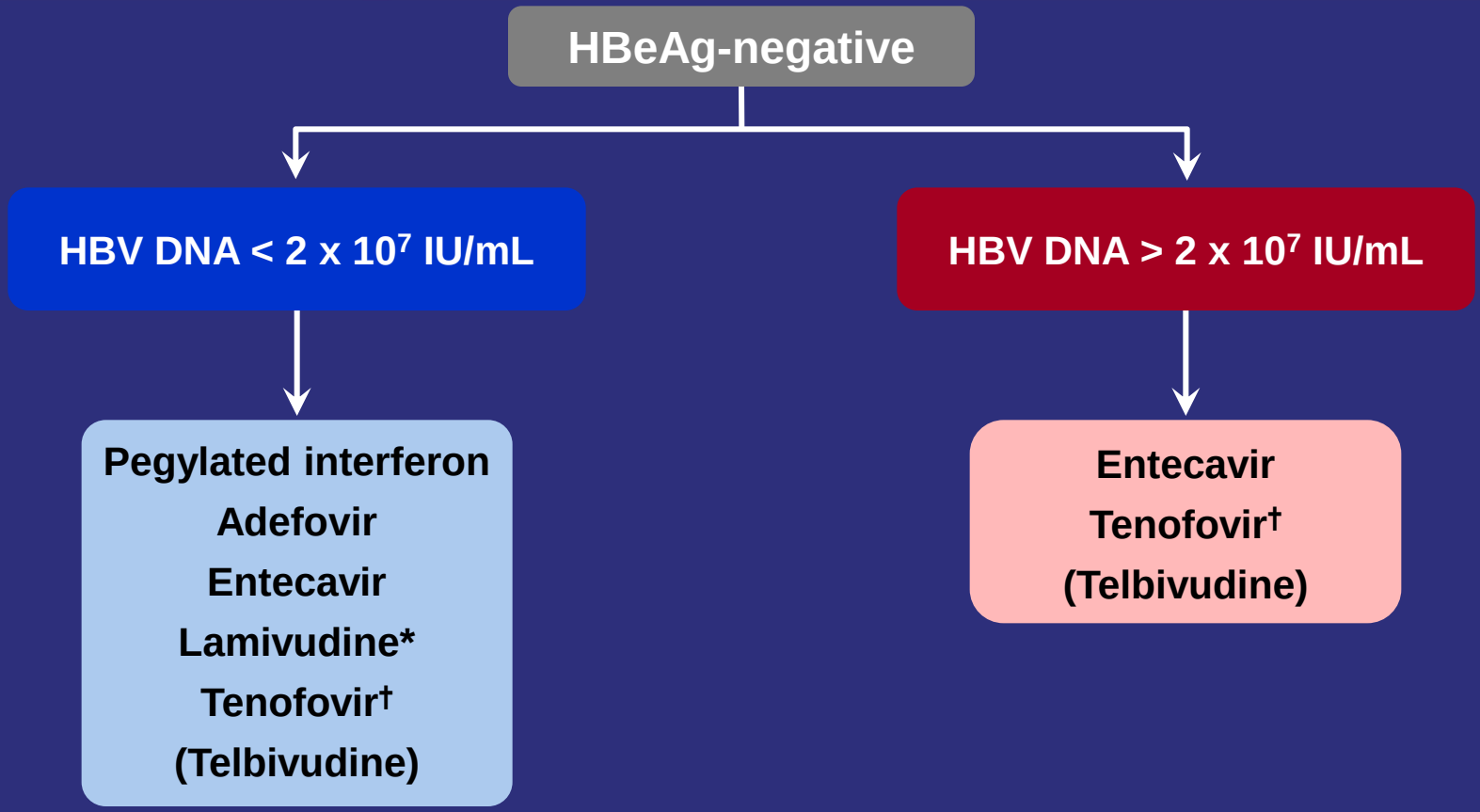
[1]Chen et al, JAMA 2006; 265: 65–73

Differentiating Immune Active (HBeAg-positive) Disease, HBeAg-negative Hepatitis B and the Inactive Carrier State

	Immune active (HBeAg-positive) disease	HBeAg-negative Hepatitis B	Inactive carrier†
HBsAg-positive	✓	✓	✓
HBeAg-positive	✓		
HBeAg-negative		✓	✓
Anti-HBe positive		✓	✓
HBV DNA	>3–8 log IU/mL	Persistently or intermittently >3 log IU/mL	Persistently <3 log IU/mL
ALT	Generally elevated	Persistently or intermittently elevated	Persistently normal

*HBV DNA levels often fluctuate; †May reactivate

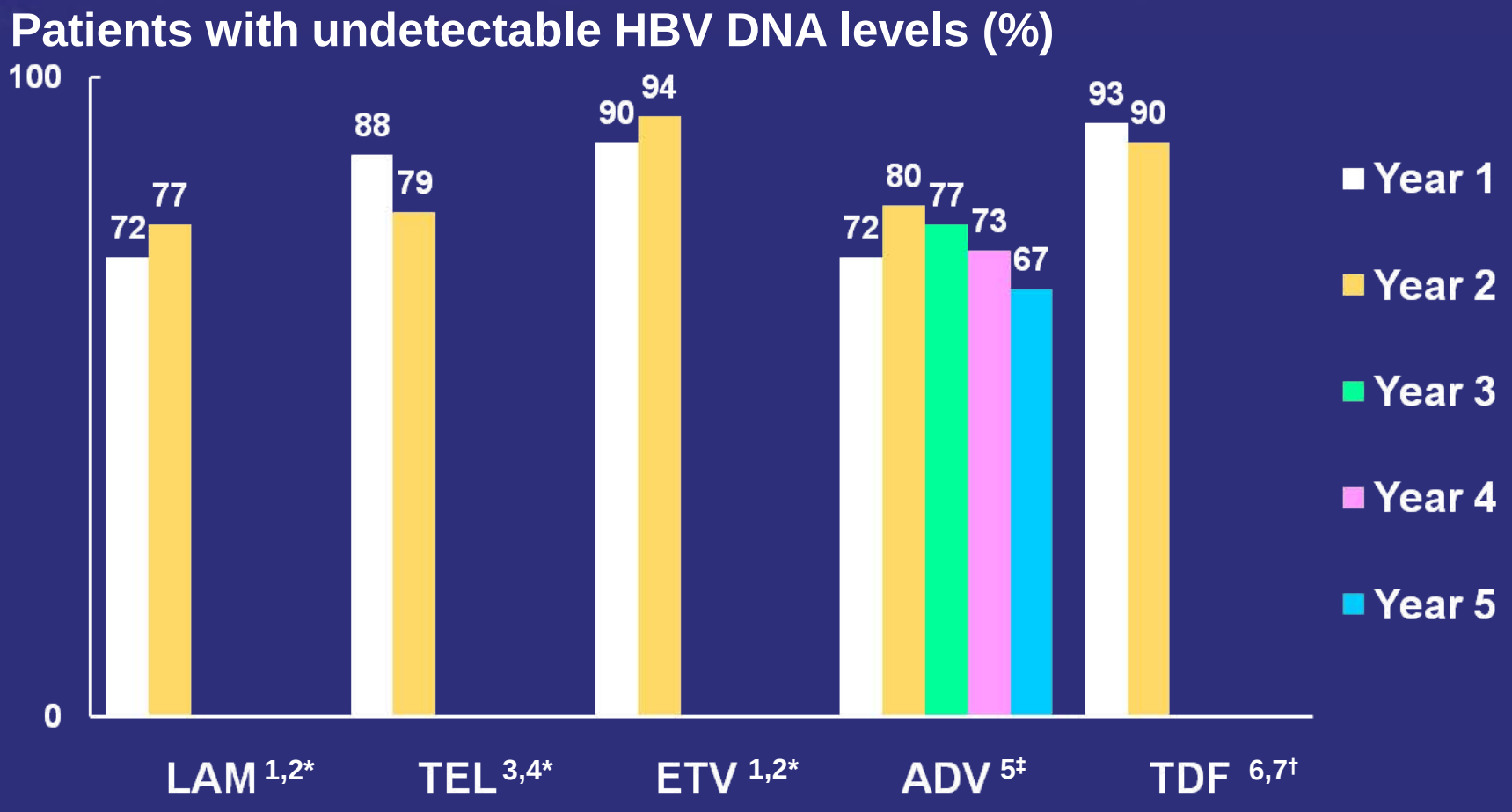
Algorithm for Selection of Specific Agents for HBeAg-negative CHB



*Not generally recommended for first-line use
†Approved since publication of the guidelines

Adapted from Sherman et al, Can J Gastroenterol 2007; 21(Suppl. C): 5C–24C

HBV DNA Suppression with Oral Agents in Patients with HBeAg-negative CHB

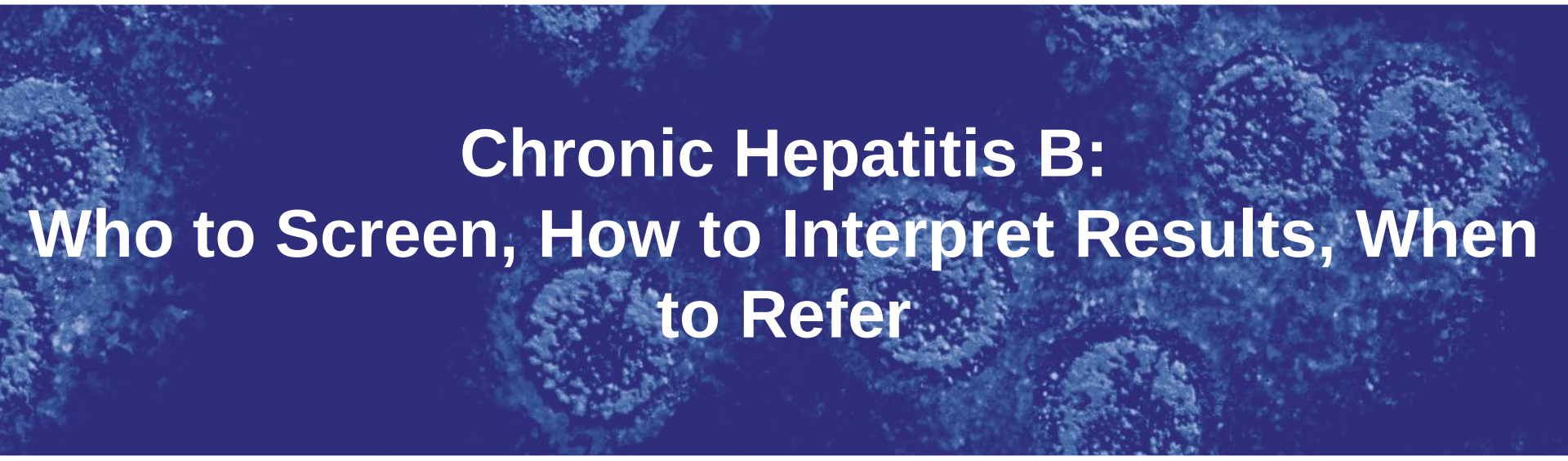


*approx. <60 IU/mL; †<80 IU/mL; ‡200 IU/mL

[1]Lai et al, N Engl J Med 2006; [2]Shouval et al, J Hepatol 2006; [3]Lai et al, Hepatology 2005; [4]Lai et al, Hepatology 2006; [5]Hadziyannis et al, Gastroenterology 2006; [6]Marcellin et al, J Hepatol 2007; [7]Marcellin et al, Hepatology 2008

Hepatitis B

New Strategies for Diagnosis, Monitoring and Referral



Chronic Hepatitis B: Who to Screen, How to Interpret Results, When to Refer

Morris Sherman, MB BCh, FRCP(C)
Associate Professor of Medicine
University of Toronto and University Health Network
Toronto, ON

Screening Tests for At-risk Patients

- **Initial screening tests**
  - **HBsAg: Indicates current infection**
  - **Anti-HBs: Indicates immunity (vaccination or past infection)**
  - **IgG anti-HBc: Indicates infection, either past or ongoing**
- **If HBsAg-positive, undertake the following investigations to better characterize stage of HBV infection**
  - **HBeAg**
  - **anti-HBe**
  - **HBV DNA**
  - **ALT / AST**
  - **Complete blood count**

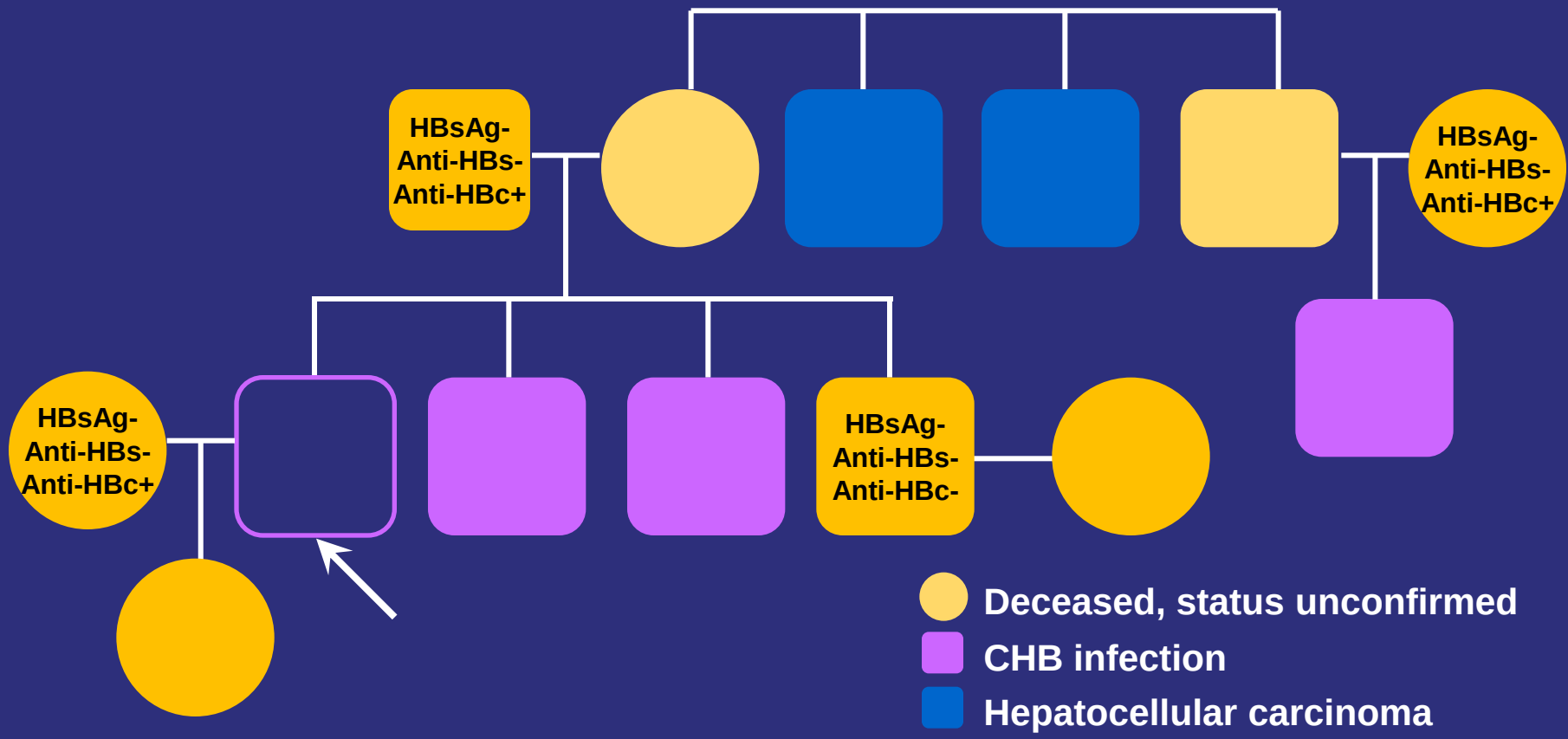
Adapted from Sherman et al, Can J Gastroenterol 2007; 21(Suppl. C): 5C–24C
Lok & McMahon, Hepatology 2007; 45: 507–39

Tests for Hepatitis B

Test	Meaning	Comments
HBsAg	Current infection	>6 months indicates chronic infection
Anti-HBs	Past infection or vaccination	Immunity
Anti-HBc	IgM=acute infection / flare	
	IgG=past or current exposure	Vaccination not required
HBeAg	Usually high viral load	High infectivity risk
Anti-HBe	Either inactive or intermittently active disease	May not be healthy carrier
HBV DNA	Viral load	Useful for evaluating treatment response
ALT	Marker of liver cells damage on day of test	Indication of damage on biopsy

Importance of Evaluating Family History

Family history uncovers high risk for complications and detects other infected persons



Screening and Vaccination for Close Contacts

- Testing family members and close household contacts
- Routine HBV vaccination of infants and children
- Catch-up vaccination of high-risk individuals at any age
- Rapid vaccination of infants born to infected mothers
- Individuals with CHB infection should be vaccinated against HAV

HAV: Hepatitis A virus

Adapted from Sherman et al, Can J Gastroenterol 2007; 21(Suppl. C): 5C–24C

Hepatitis B
New Strategies for Diagnosis, Monitoring and Referral

Chronic Hepatitis B: Goals of Therapy

Morris Sherman, MB BCh, FRCP(C)
Associate Professor of Medicine
University of Toronto and University Health Network
Toronto, ON

Primary Goal of Hepatitis B Therapy: Preventing Cirrhosis, HCC, and Death

Monitoring Patients During Therapy with Oral Antiviral Agents

Tests	• HBV DNA, ALT, AST, Creatinine, HBeAg status
Schedule and rationale	• Months 3 and 6: – Confirm initial fall in HBV DNA level – Higher risk of treatment failure and resistance if HBV DNA remains high • Follow at 3-month intervals to: – Establish nadir, i.e., lowest on-treatment viral load – Allow for early detection of resistance
Successful outcome criteria	• Undetectable HBV DNA with the most sensitive assay available[1] • Seroconversion to anti-HBe positive (in HBeAg-positive patients)

[1]Currently the Taqman assay. Use of less sensitive assays is not recommended

Adapted from Sherman et al, Can J Gastroenterol 2007; 21(Suppl. C): 5C–24C

Hepatitis B

New Strategies for Diagnosis, Monitoring and Referral

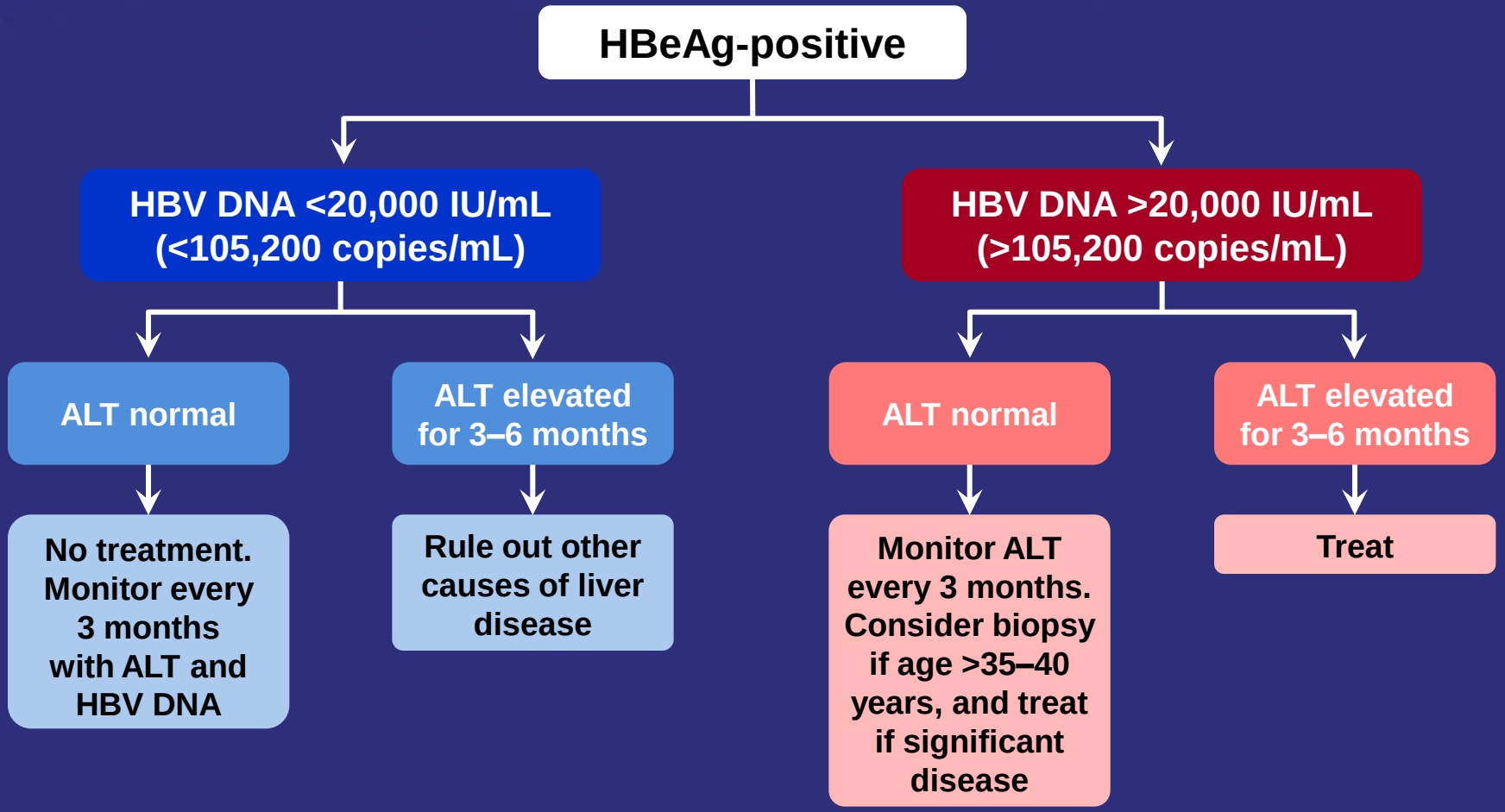
A Simplified Treatment Algorithm for Chronic Hepatitis B

Morris Sherman, MB BCh, FRCP(C)
Associate Professor of Medicine
University of Toronto and University Health Network
Toronto, ON

Treatment Goals Differ in Patients with HBeAg-positive and HBeAg-negative Disease

HBeAg-positive disease	HBeAg-negative disease
HBeAg loss ± seroconversion Durable suppression of HBV DNA to low or undetectable levels Normalization of ALT HBsAg loss (rare)	Durable suppression of HBV DNA to low or undetectable levels Normalization of ALT HBsAg loss (rare) Off-therapy relapse is usual • Long-term therapy frequently indicated with oral agents

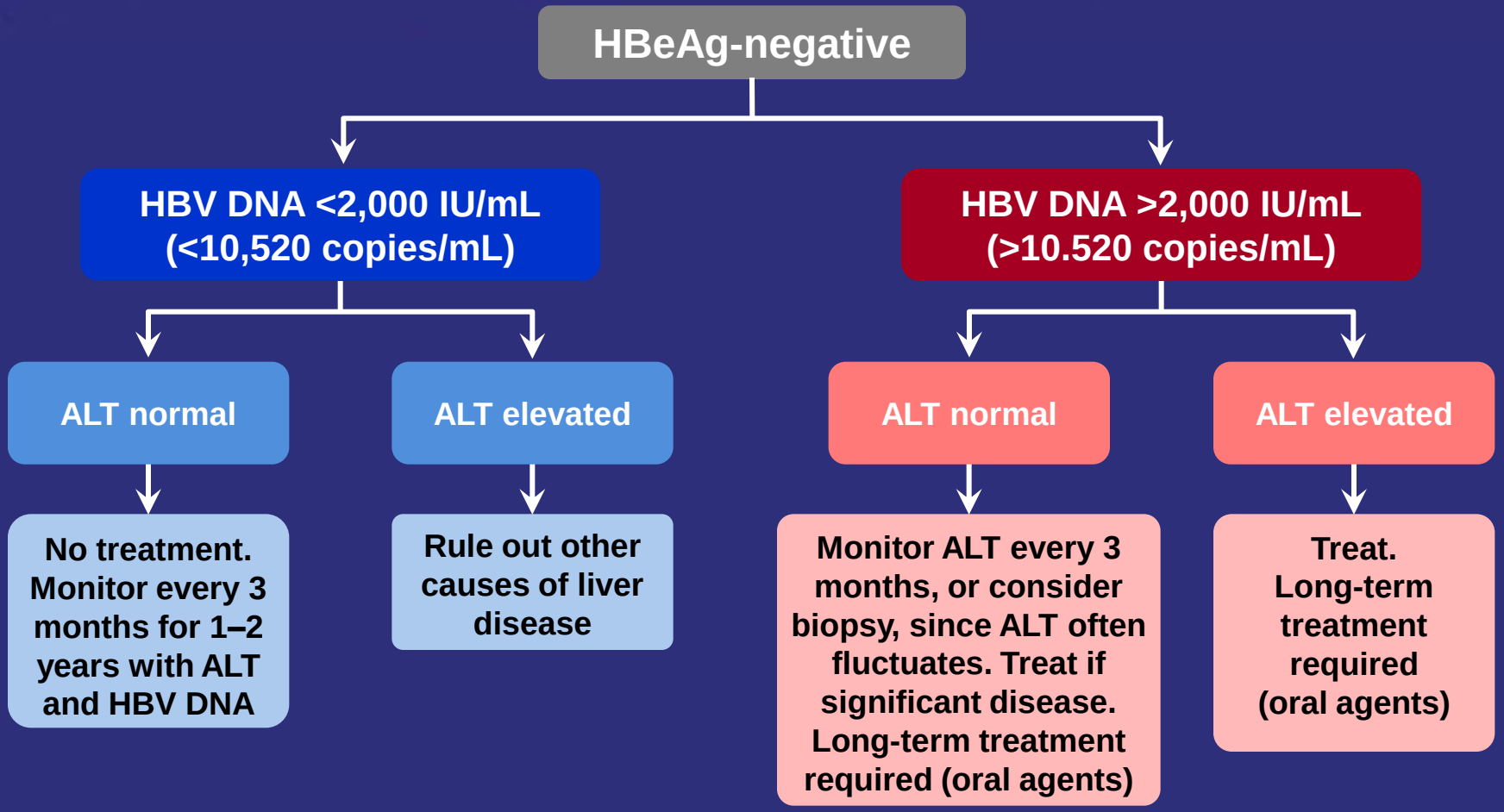
Algorithm for Selecting HBeAg-positive Patients for Treatment



Based on a conversion factor of 1 IU/mL = 5.26 copies/mL

Sherman et al, Can J Gastroenterol 2007; 21(Suppl. C): 5C–24C

Algorithm for Selecting HBeAg-negative Patients for Treatment



Based on a conversion factor of 1 IU/mL = 5.26 copies/mL

Sherman et al, Can J Gastroenterol 2007; 21(Suppl. C): 5C–24C

Antiviral Treatment Options for Specific Drug Resistance

Resistance pattern	LAM-R	ADV-R (ADV monotherapy)	LAM + ADV-R (combination therapy)	ETV-R	TBV-R
Treatment options	Add on ADV *Preferred option* TDF LAM	Add on LAM or, TDF or, ETV or, TBV	TDF LAM	ADV TDF	ADV or TDF

LAM: lamivudine; ADV: adefovir; ETV: entecavir; TBV: telbivudine; TDF: tenofovir; -R: -resistant

Adapted from Sherman et al, Can J Gastroenterol 2007; 21(Suppl. C): 5C–24C