Hepatitis B
CATIE Webinar

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Calgary Liver Unit

Calvin, Phoebe and Joan Snyder Institute for Chronic Diseases

Faculty/Presenter Disclosure

- Faculty: Carla S. Coffin
- Financial affiliations:
  - Advisory boards: GSK, Gilead Sciences – paid to the University of Calgary
  - Consultant: GSK, Gilead Sciences – paid to the University of Calgary
  - Grants, clinical trials: Investigator Initiated, Gilead, GSK, Janssen (paid to the University of Calgary, Canadian HBV Network)
  - Participation in Clinical Trials (Local site PI): Gilead Sciences, Inc., GSK, Janssen Inc., BlueJay, Vir Pharmaceuticals

  - These slides are my own or used with permission from colleagues

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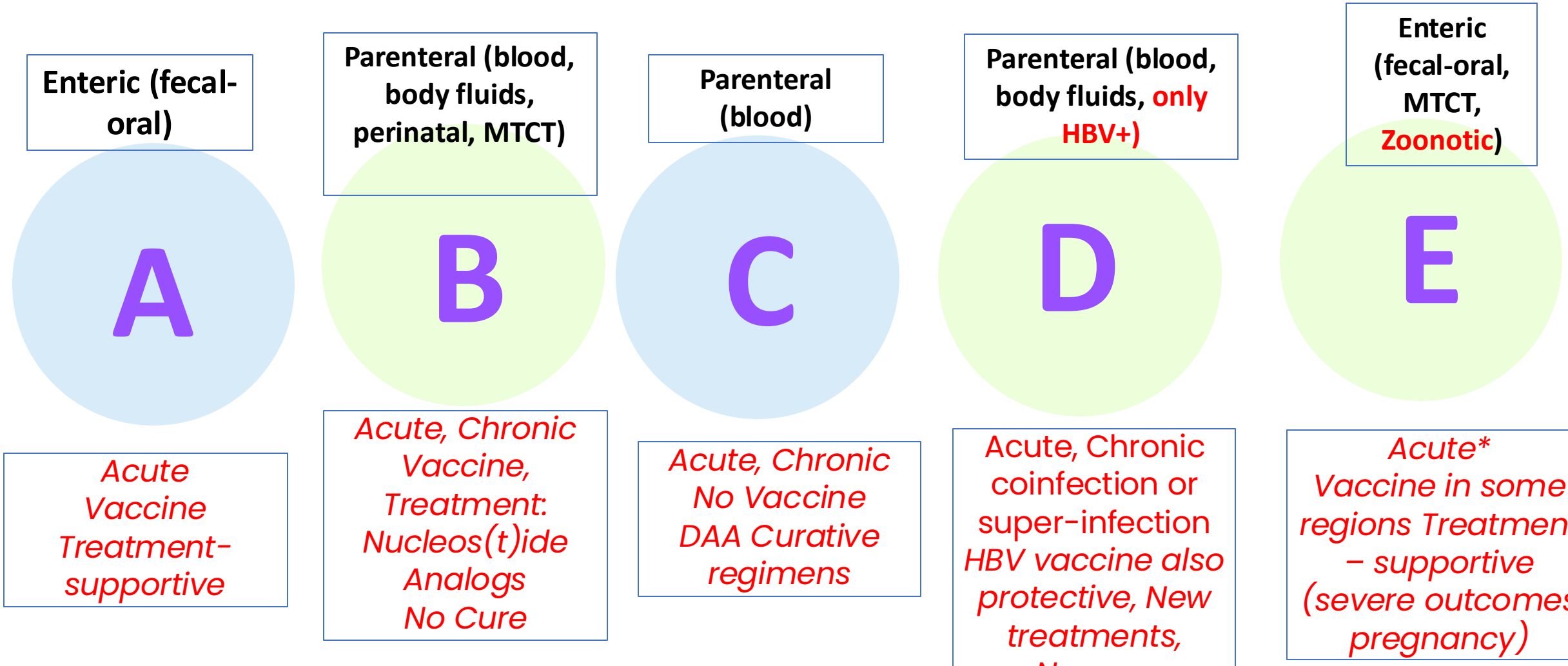
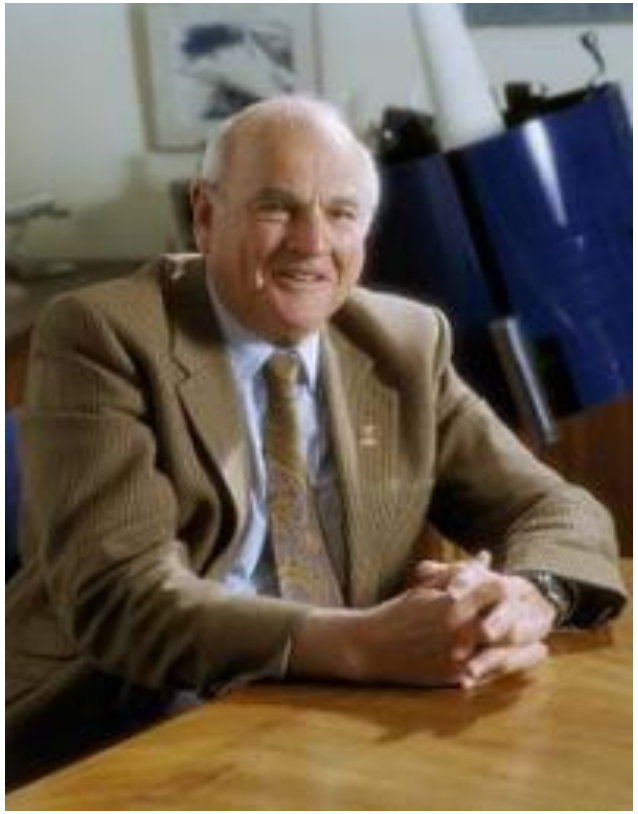
Types of Viral Hepatitis

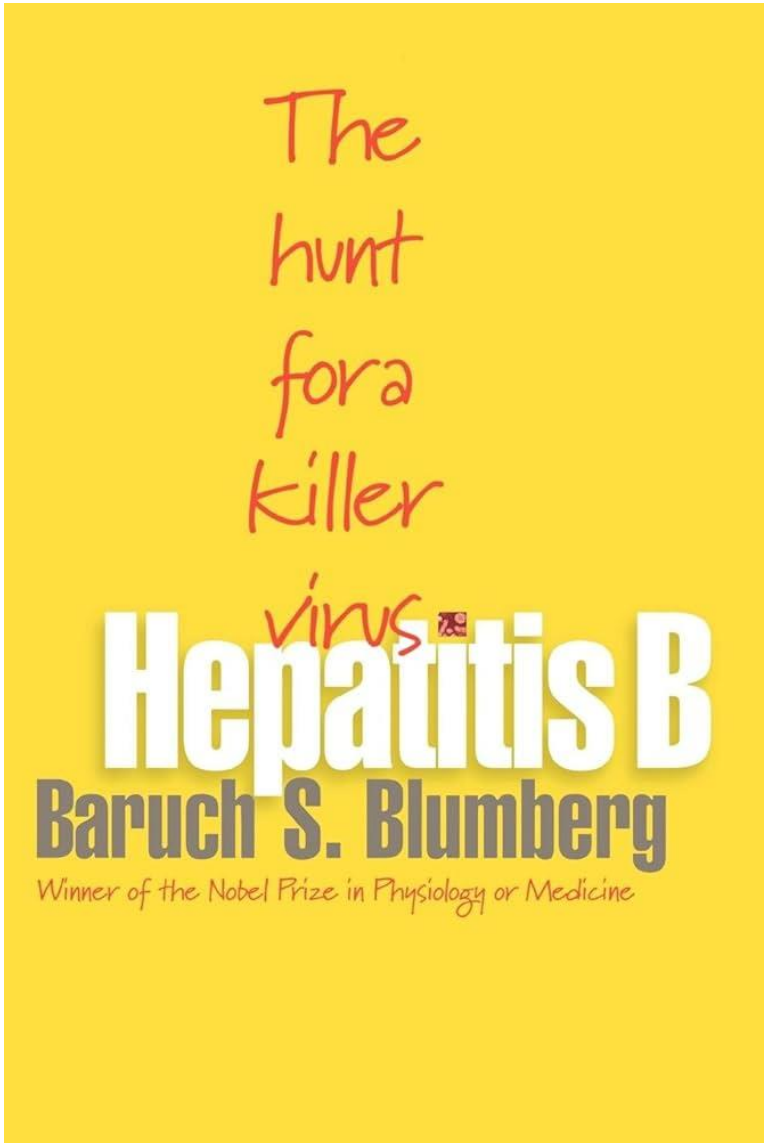


* *Immunosuppressed*

Discovery of the Hepatitis B Virus



Dr. Baruch Blumberg (1925-2011)
Discovery HBV 1965
Winner Nobel Prize in Medicine



- Collected blood samples from around the world to study genetic traits
- ”Accidently” found a “protein” in the blood of an Australian Indigenous person
- Later identified it to be the “Hepatitis B Virus Surface Antigen” (*Australian Antigen*)
- Invented the 1st Hepatitis B Vaccine in 1969
  - >70% Decreased Rates of Liver Cancer in some Countries

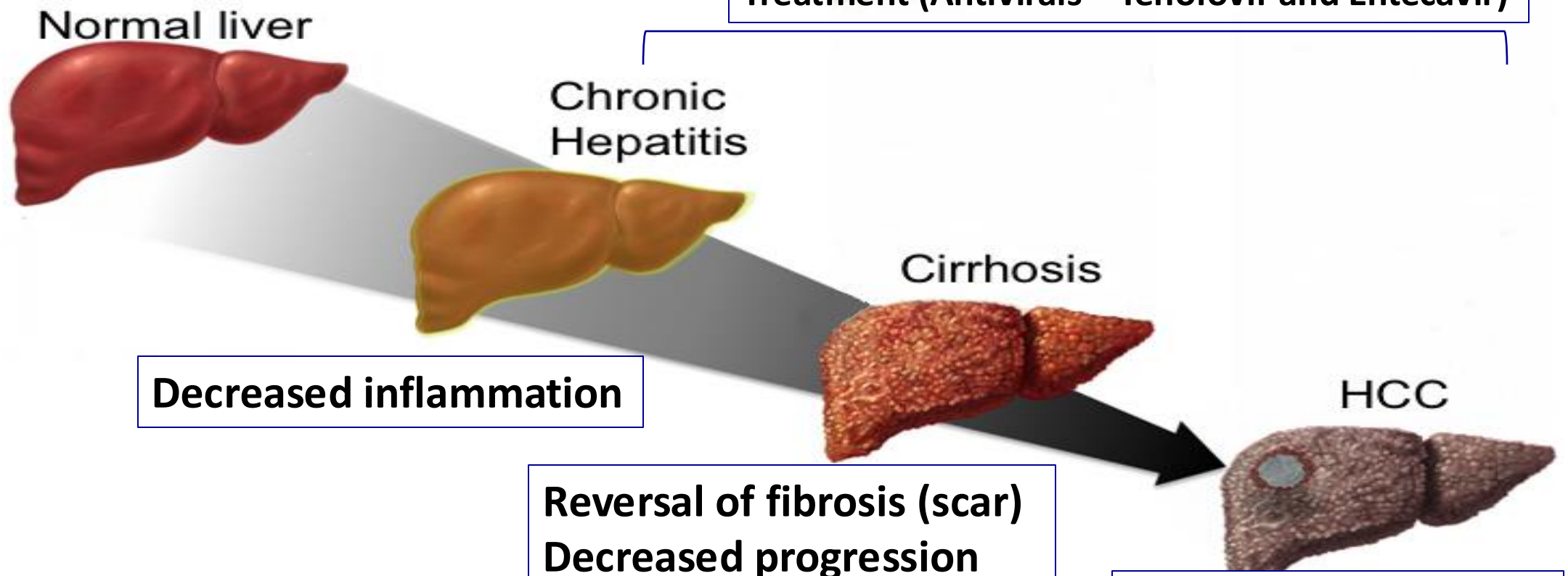
Korean Mummy Found With Hepatitis B Virus

- **Virus discovered in the liver of a South Korean mummy**
  - **500-year-old child**
- **First time HBV ever been found in a mummified body**
- **The virus genome (*strain*) (genotype C) estimated to be 3000 - 10,000 years old**

Kahlia Bar-Gali, G et al., Hepatology 2012

Source: Seoul National University

Hepatitis B Virus Can Cause Progressive Liver Disease and Liver Cancer

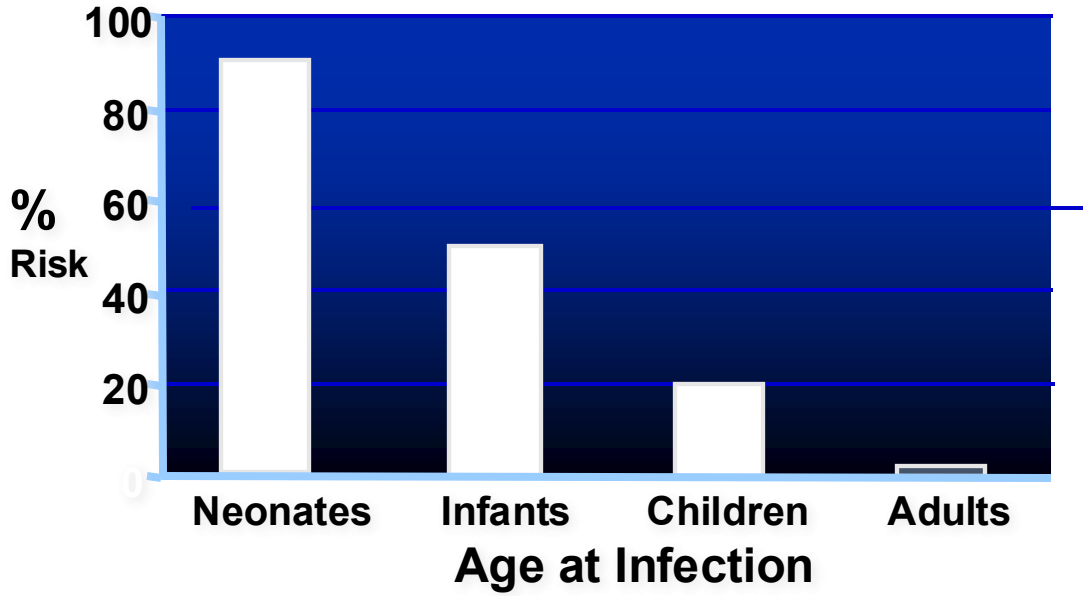


Slide Courtesy HLA Janssen

Liaw YF et al, N Engl J Med. 2004; Chang TT et al, Hepatology 2010; Marcellin P et al, Lancet 2013; Hosaka et al, Hepatology 2013; Lai CL et al., Hepatology 2013. Kim et al, Cancer 2015; Papatheodoridis et al, J Hepatol 2015

The Hepatitis B Vaccine is the 1st Cancer Vaccine and should be given as soon as possible after Birth:

HBV Vaccine Timing in Canada	Birth ✓	2 months →	Pre-Adolescence X
Province or Territory	NU, NT, NB	BC, AB, QC, PEI, YT	SK, MB, ON, NS, NL

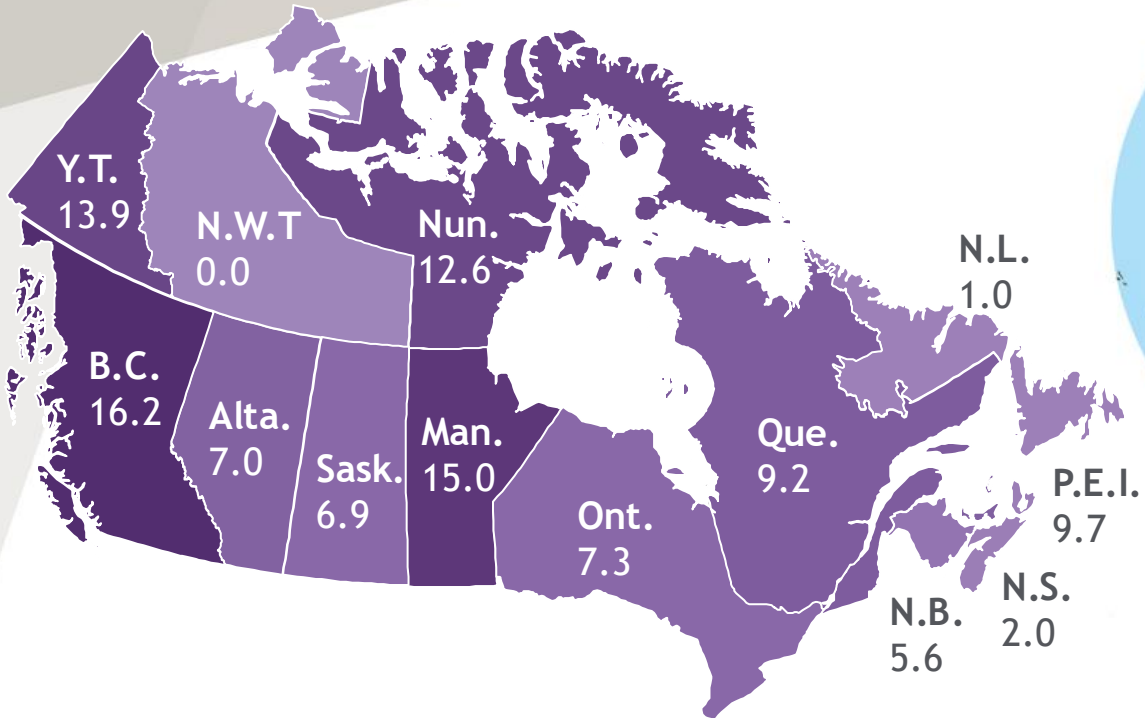


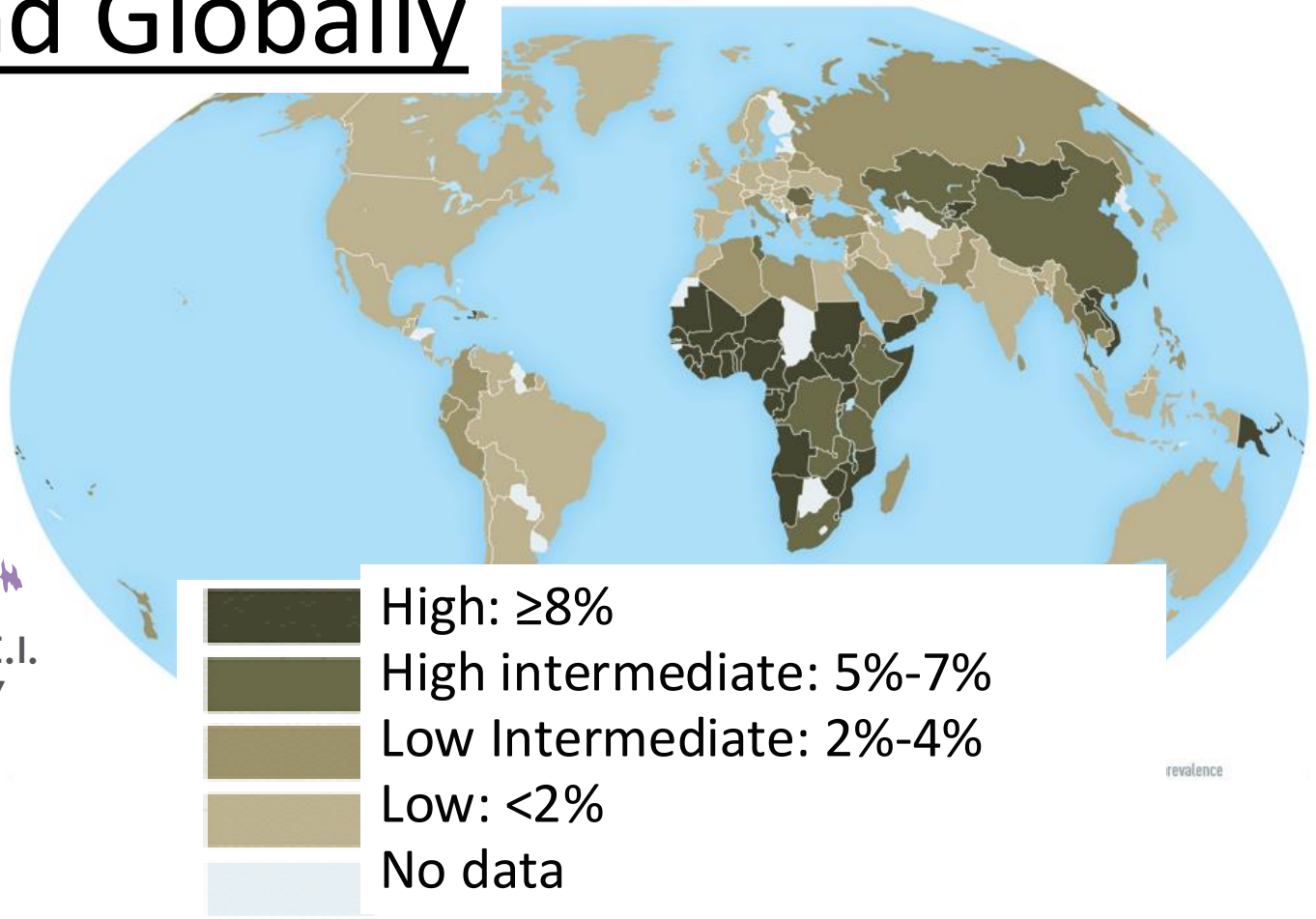
There is no cure for Hepatitis B
"An Ounce of Prevention is Worth a Pound of Cure"

- **Greatest Risk in Infants and young children**
  - 80-90% < 1 year
  - 30-50% < 6 y
  - <5% otherwise healthy teens or adults (maybe even <1%)

Coalition for Global Hepatitis Elimination. 2021. https://www.globalhep.org/country-progress/Canada. Accessed 01/2024

Hepatitis B in Canada and Globally





- **250,000 Canadians**

1.5 million new HBV infections per year
260 million people infected
2 billion people are anti-HBc positive
<10% treated

References: 1. Public Health Agency of Canada. Hepatitis B in Canada: 2021 surveillance data update. Ottawa, ON: Public Health Agency of Canada; 2023; 2. Kochaksaraei GS, et al. Ann Hepatol. 2025 Jan-Jun;30(1):101576. 3. Makuza JD, et al. Viruses. 2022 Nov 21;14(11):2579.

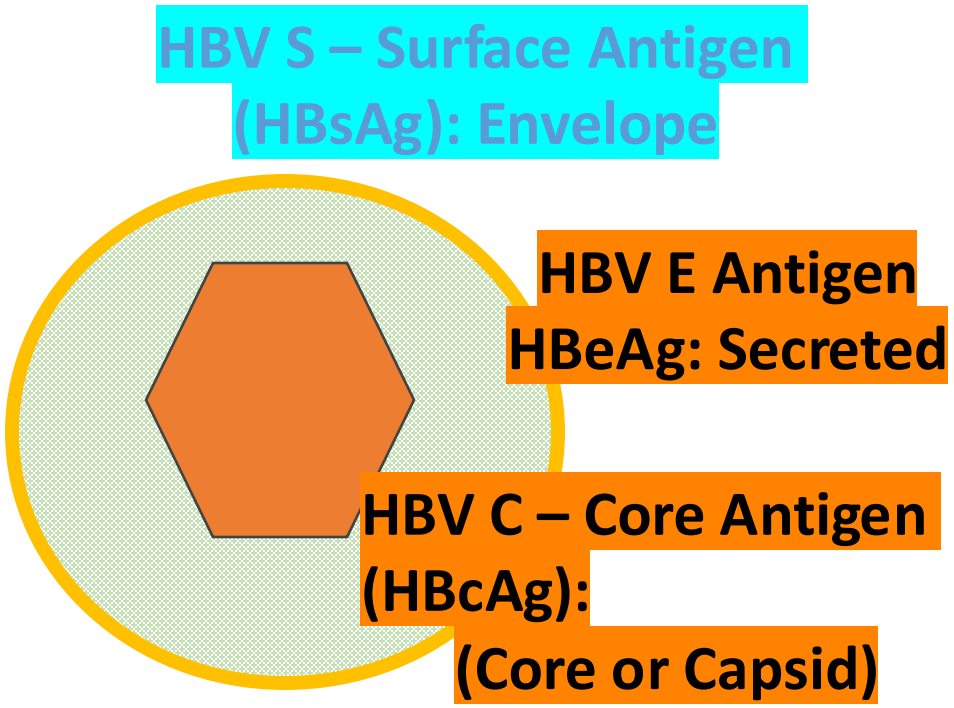
Argument for Universal HBV Screening:

- Up to 30% of people with HBV do not fall into known risk groups
- Current screening guidelines are not always followed due to complexity
- 40% of Canadians are living with HBV and don't know it

Testing is the only way to identify *all* with asymptomatic infection that might benefit from treatment to reduce liver disease and liver Cancer

Hepatitis B Serology – Triple Panel before immunosuppression

- **HBsAg: Hepatitis B surface antigen**
- **HBcAb: Hepatitis B core antibody**
- **HBsAb: Hepatitis B surface antibody**
  - **current (active)**
  - **past (resolved)**
  - **immunity**
  - **susceptible**

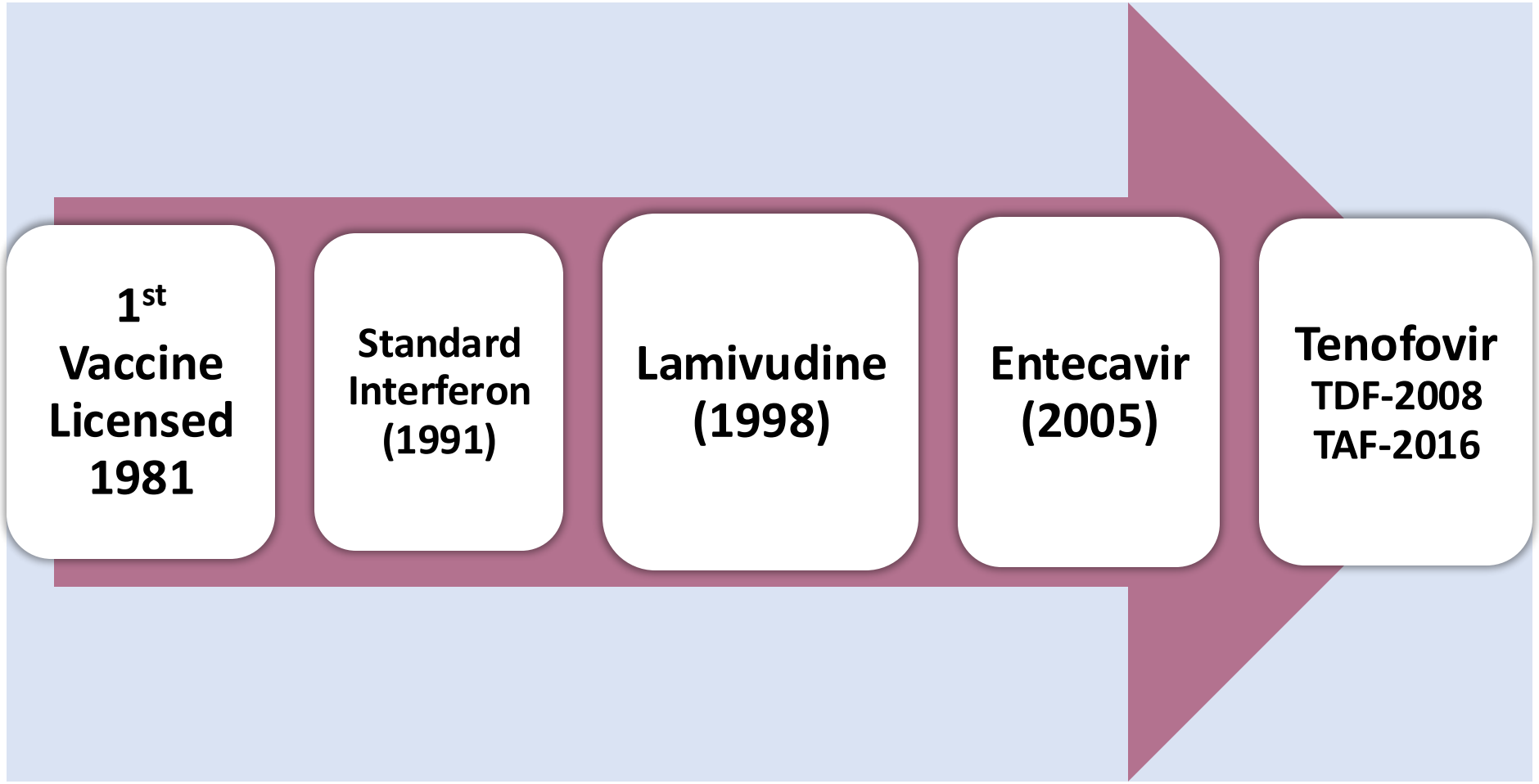


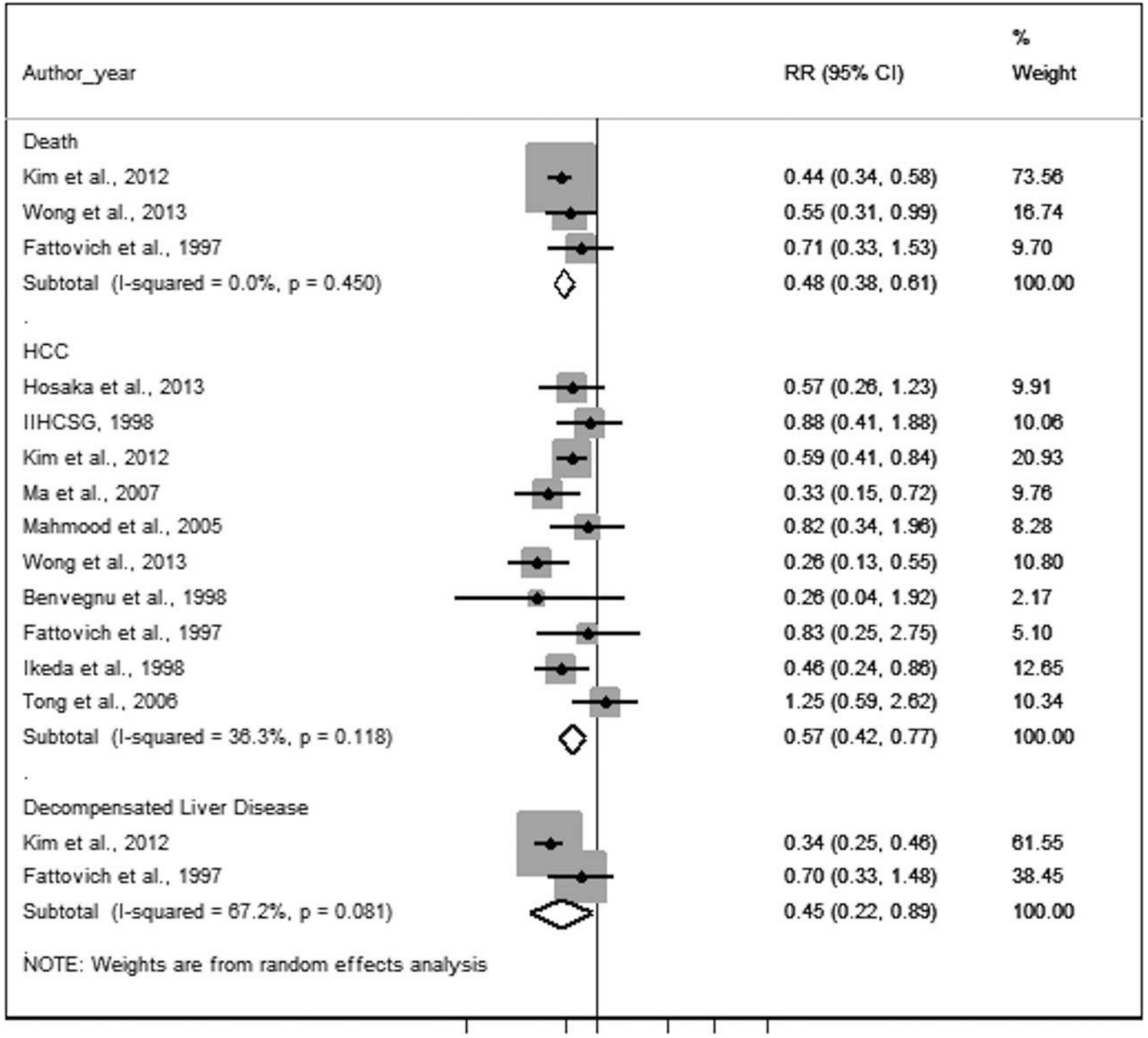
HBV	Serology Interpretation
HBsAg	Active Infection (check quantitative HBsAg if available)
HBsAb (anti-HBs)	HBV immunity from exposure or vaccination
HBeAg	"secreted" or circulating form of core protein indicates more active replication
HBeAb (anti-HBe)	lower infectivity
HBcAb (anti-HBc)	IgM – acute infection IgG – previous exposure

Mnemonics

- HBsAg, hepatitis B surface antigen (sick…have acute or chronic hepatitis B); quantitative HBsAg if available
- HBsAb, hepatitis B surface antibody (immune or anti-sick)
- *HBcAg, hepatitis B core antigen (protected in the core or capsid – not detected by serology)*
- HBcAb, hepatitis B core antibody…. "HBcAb.. come across hepatitis B", IgM = "more" recently
- HBeAg, hepatitis B E antigen…."easily transmitted"
- Anti-HBe, hepatitis B E antibody…not so easily transmitted

Timeline in Hepatitis B Care 1981-Present





Benefits of Long-Term Antiviral Therapy:

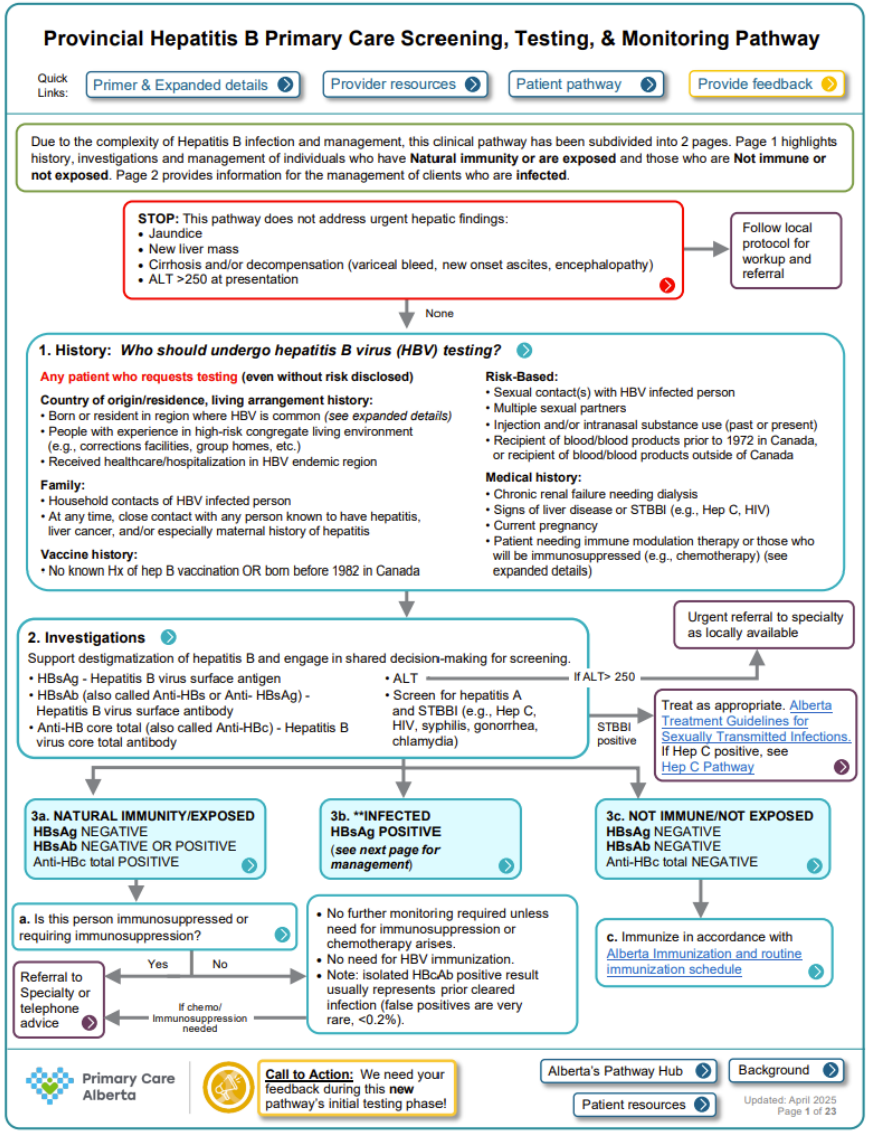
Clinical outcomes for observational studies comparing treatment vs. no treatment in 59,201 with "immune active" HBV infection:

Lower death, liver cancer and decompensated liver disease

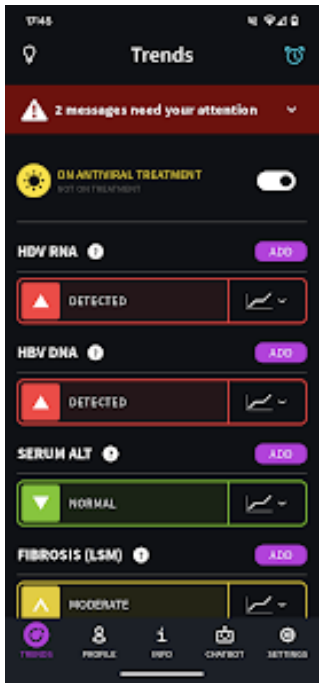
Lok et al., Hepatology, 2016; 63

Alberta Hepatitis B (HBV) Primary Care Pathway

- Published April 2025
- Available at AHS - Alberta's Pathway Hub
- **Pathway goals and scope:**
  - Raising awareness of who, in the population, may benefit from hepatitis B screening (however, screening should be offered to all individuals if requested)
  - Offering rapid differential and referral triggers for primary care
  - Promoting a consistent approach to screening, testing, monitoring, and managing hepatitis B patients in primary care
  - Improving vaccination rates
  - Reducing community transmission



HepB & Me Smartphone App (Google and iPhone)



Hepatitis B Management for the Primary Care Provider

Management of the HBsAg(+) Patient[1]

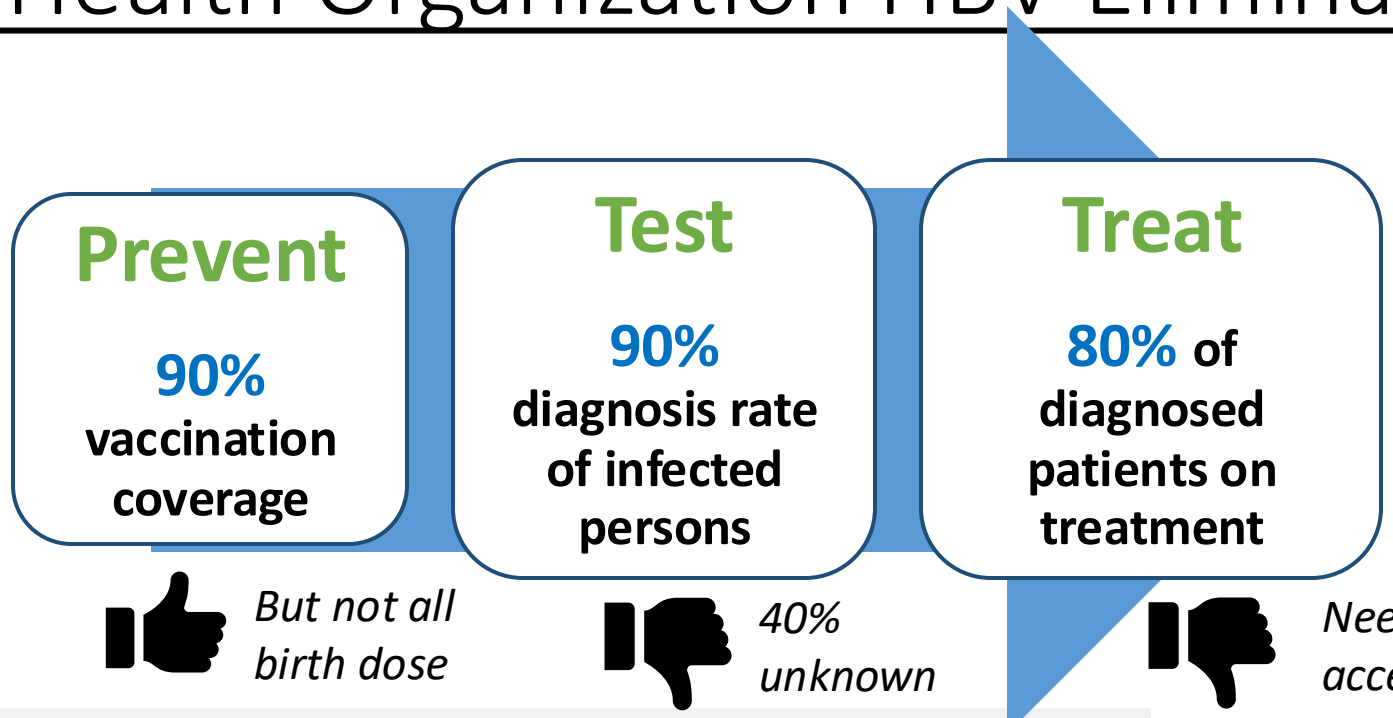
Cirrhosis	HBV DNA (IU/mL)	ALT (U/L)	Management
YES	Any	Any	> TREAT with antiviral medication (page 6) > Monitor HBV DNA and ALT every 6 months > Refer to specialist for screening endoscopy and, if needed, for other cirrhosis-related complications > HCC surveillance, including in persons who become HBsAg(-) (page 7) > All patients with decompensated cirrhosis[2] should be promptly referred to a hepatologist
NO	>2,000	Elevated[3]	> TREAT with antiviral medication (page 6) > Monitor HBV DNA and ALT every 6 months > Monitor HBeAg and anti-HBe every 6 months in patients who are HBeAg+ at time of treatment initiation to evaluate for seroconversion from HBeAg(+)/anti-HBe(-) to HBeAg(-)/anti-HBe(+) > Check HBsAg annually if/when HBeAg negative
		Normal	> Monitor HBV DNA and ALT every 6 months > Liver fibrosis assessment every 2 to 3 years
	≤2,000	Elevated[3]	> Evaluate other etiologies for elevated ALT > Monitor HBV DNA and ALT every 6 months
		Normal	> Monitor HBV DNA and ALT every 6 months and HBsAg every 1 year for seroclearance

PDF Embed API

https://www.hepatitisb.uw.edu/

www.hepB.org

World Health Organization HBV Elimination Goals



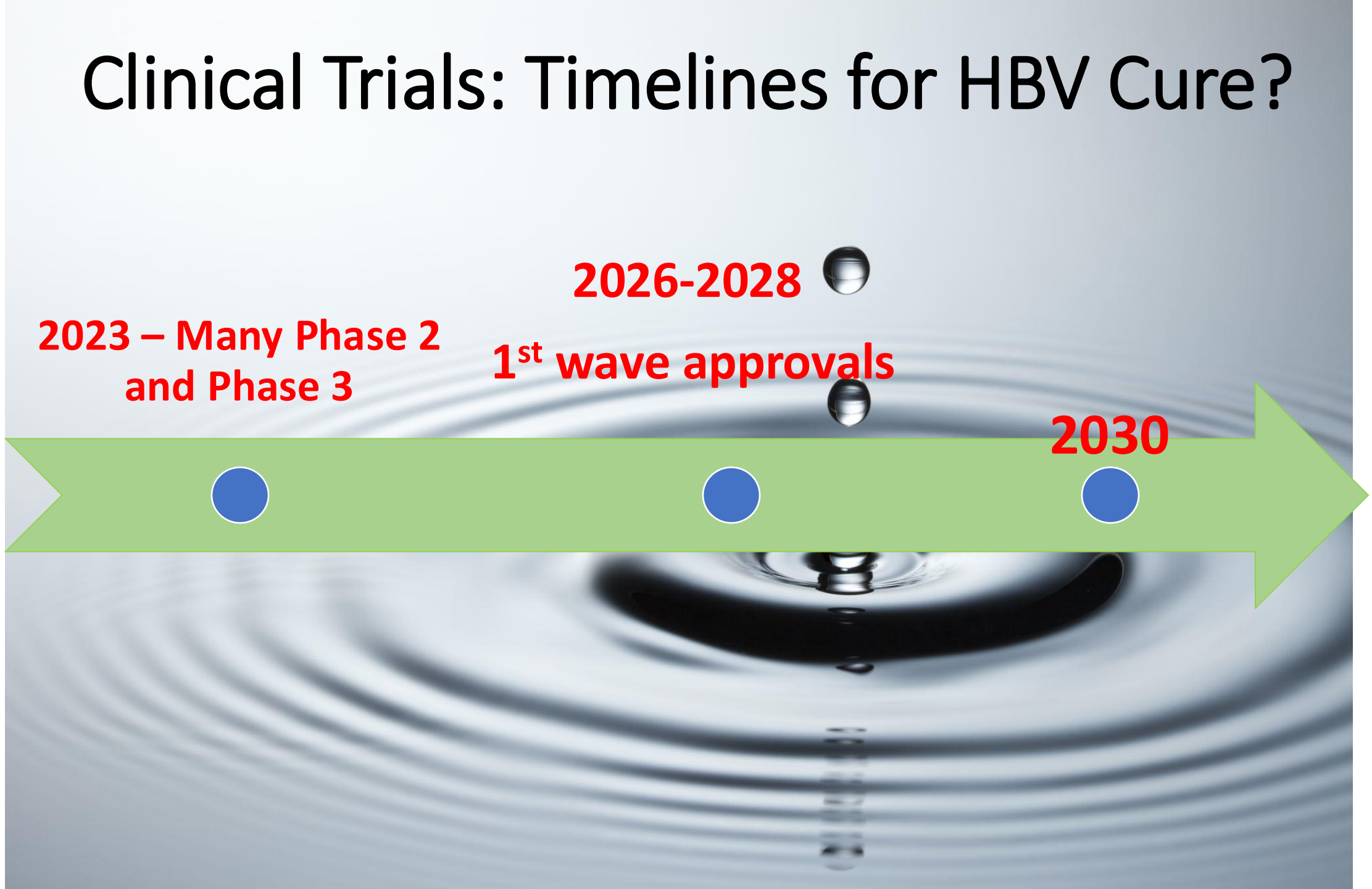
World Health Organization (WHO) Goals for HBV Elimination by 2030

- Reduce **new infections** by **90%**
- Reduce **mortality** by **65%**

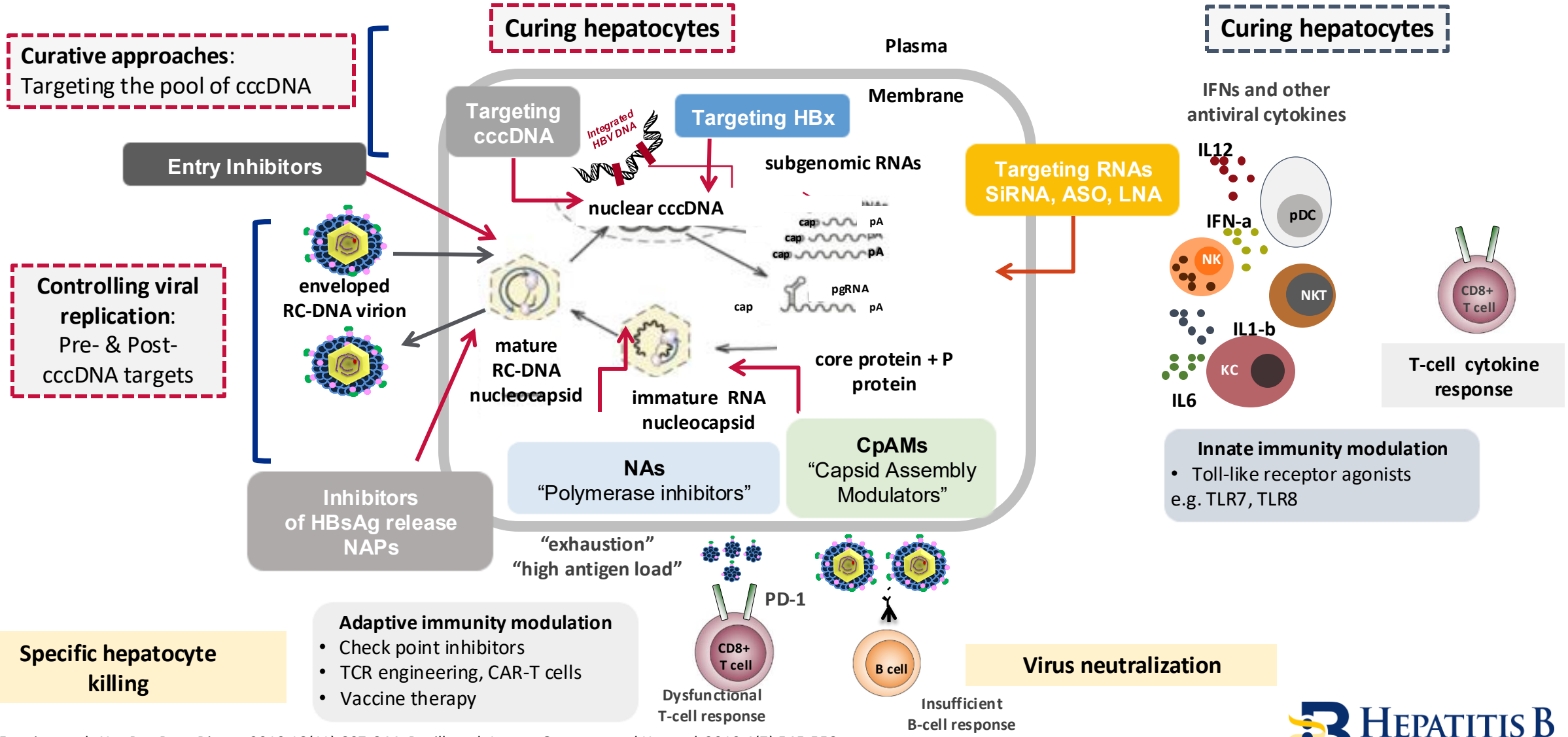
https://www.globalhep.org/country-progress/Canada; accessed Jan 2024

World Health Organization

Clinical Trials: Timelines for HBV Cure?



Emerging Treatment Targets for HBV – Stay Tuned



Fanning et al. *Nat Rev Drug Discov.* 2019;18(11):827-844; Revill et al. *Lancet Gastroenterol Hepatol*. 2019;4(7):545-558

Introduction to Updated CASL Guidelir Points

The management of chronic hepatitis B: 2025 Guidelines update from the Canadian Association for the Study of the Liver and Association of Medical Microbiology and Infectious Disease Canada

Clinical Practice Guidelines Committee Chair: Carla Osiowy PhD[1,2], Panel Members: Fernando Alvarez MD[3], Carla S. Coffin MD MSc[4,5], Curtis L. Cooper MD[6], Scott K. Fung MD[7], Hin Hin Ko[8], Sébastien Poulin MD MSc[9], Jennifer van Gennip BSc[10]

CASL/AMMI 2025 DIRECTIVES

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KEY POINTS

- Universal screening
- Universal vaccination (for those who are not immunized)
- Expanded treatment indications
- Urgent need for investment in HBV research in Canada
- Patients must be at the centre of decision-making about their own care, with their values and preferences prioritized

AMMI/CASL (Canada) 2025

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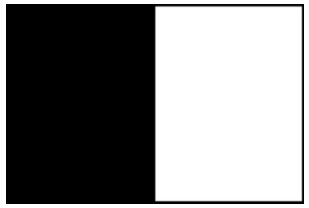
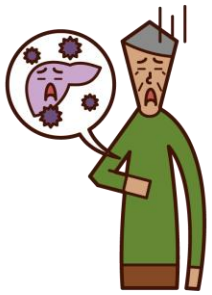
DECISION SIMPLIFICATION



It's not always **black** and **white**



Patient-Centered Approach

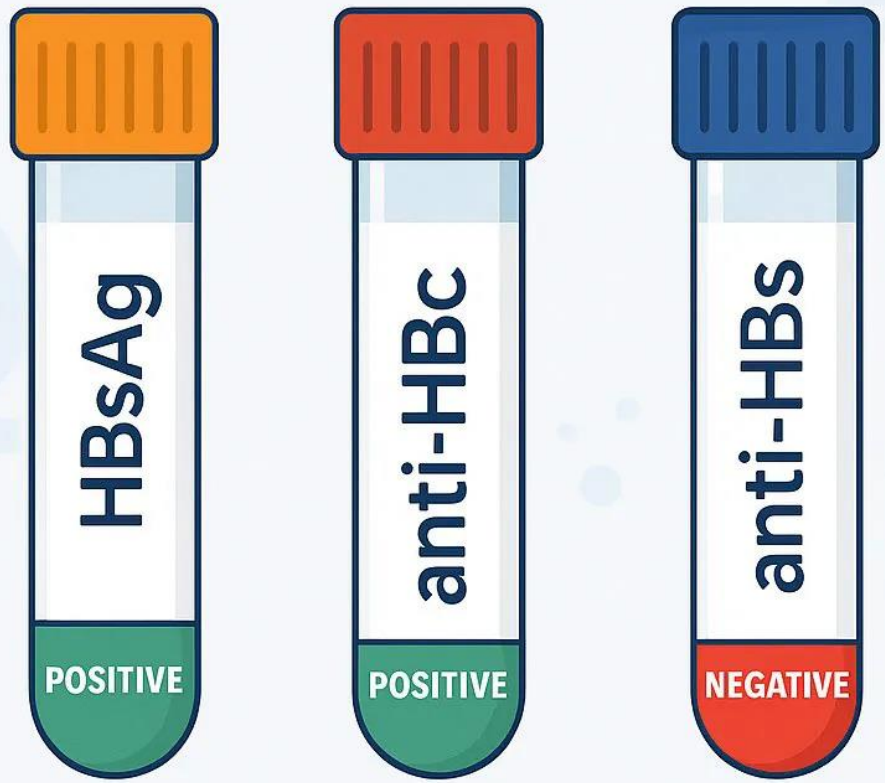
Increased trend to **TREAT MORE** patients

«INDIVIDUALISATION»

Conclusion – Hepatitis B

- Hepatitis B IS a Major Global Health Problem and in Canada
- WHO Global Targets:
  - Universal birth dose HBV vaccination – ***The 1st shot is the most timely***
  - Increase screening, linkage to care – ***You should know if you have hepatitis B***
  - Culturally appropriate public education and awareness
- Safe and effective therapies reduce liver disease risk and cancer
  - **Need to improve access to life-saving treatments**

3-Test Rule



Check ALL three before any immunosuppression

THERE is HOPE for a Hepatitis B Cure

Thank you - Questions

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CIHR IRSC

ALBERTA INNOVATES

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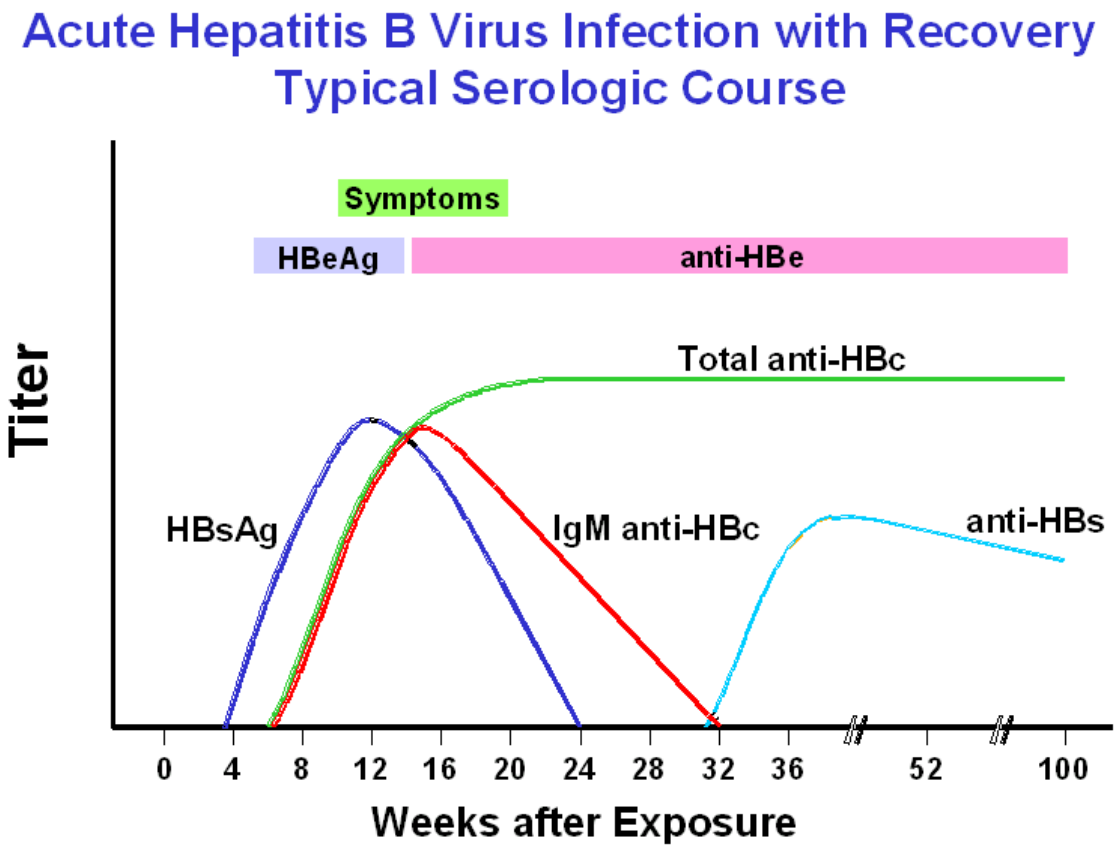
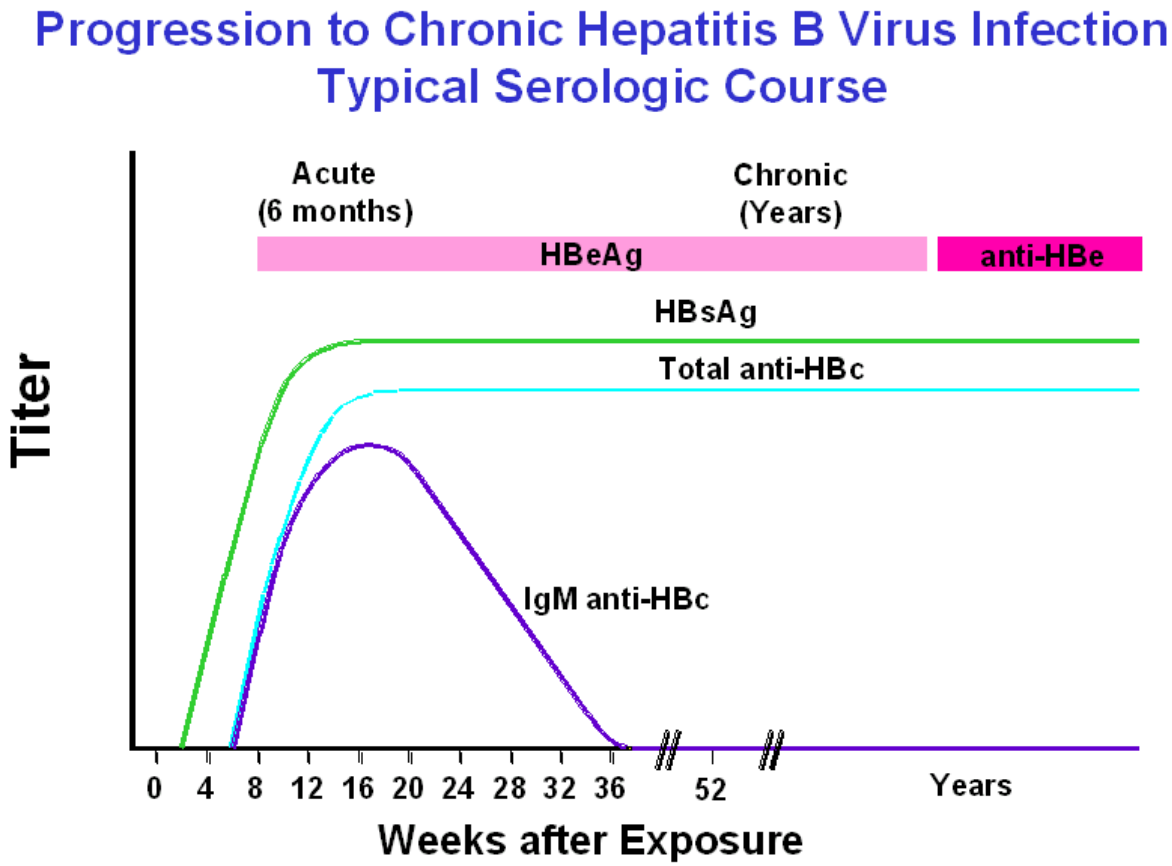
Case Presentation – suspected viral hepatitis

- 28 y F anorexia, N&V, diarrhea and RUQ pain
- Recent travel abroad with long-term partner who also had mild self-limited illness (diarrhea)
- Healthy, no regular medications, no over the counter or herbal
- works in a daycare centre
- drinks <2 glasses wine per week, non-smoker, no recreational drug use
- Exam: VSS, few cervical nodes, mild RUQ tenderness, no stigmata of chronic liver disease
- Labs: WBC 4.0, ALT 100 U/L, ALP WNL, GGT WNL, Total Bili WNL, Creatinine normal
- Pregnancy (B-HCG) - negative
- Ultrasound – mild hepatic steatosis

	Testing	Result	Interpretation
HAV	**Anti-HAV IgM** **Anti-HAV Total / IgG**	**neg** **pos**	**HAV Immune**
HBV	**Anti-HBc IgM** **HBsAg**	**neg** **pos**	**Chronic HBV infection:** **Check HBeAg, anti-HBe, HBV DNA, qHBsAg**
HCV	**Anti-HCV**	**pos**	**prior exposure susceptible; HCV RNA neg**
HDV	**Anti-HDV**	**neg**	**susceptible if HBsAg pos**
HEV	**Anti-HEV IgM** **Anti-HEV IgG**	**neg** **neg**	**susceptible**

Hepatitis B: Typical Serologic Course





www.albertahealthservices.ca/assets/info/aph/if-aph-prov-hepatitis-b-primary-care-pathway.pdf

Slide courtesy Dr. KW Burak, University of Calgary

Presenter Disclosures

- Presenter: Dr. Hin Hin Ko
- Grant/Research Support: Gilead, GSK, Intercept, Ipsen, Madrigal, Mirum, Pilant, Sanofi, Takeda
- Consultant/Speaker’s Bureau: Advanz, Gilead, GSK, Ipsen, Sanofi
- I will be discussing investigational use of medications

Management of Hepatitis B

Canadian Hepatitis B Guidelines Update 2025

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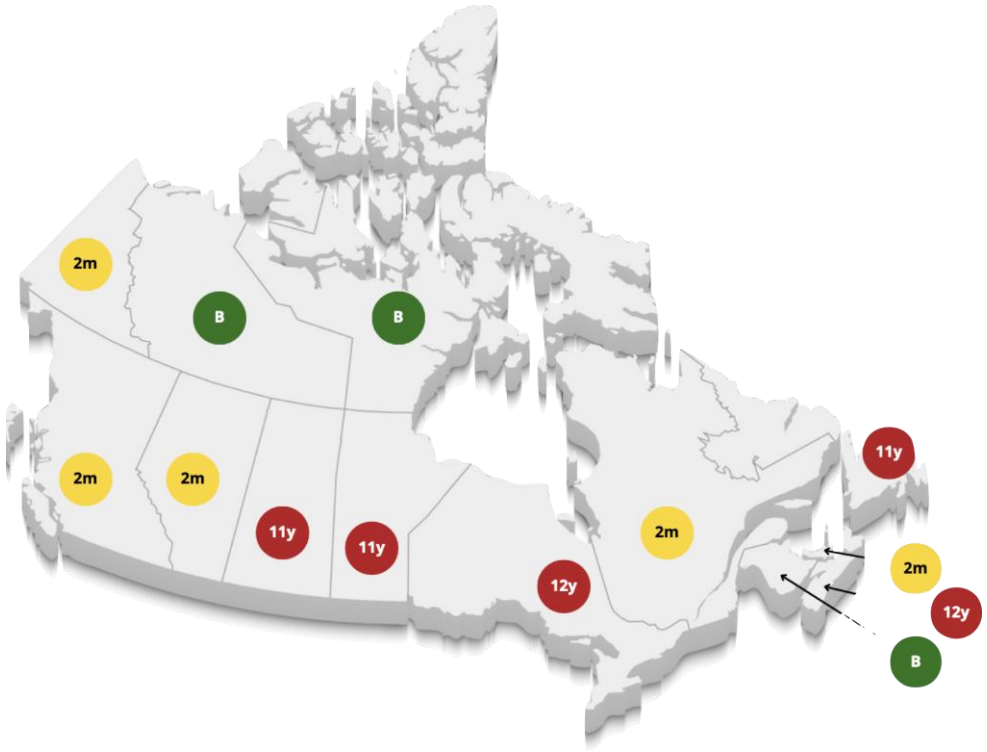
KEY POINTS

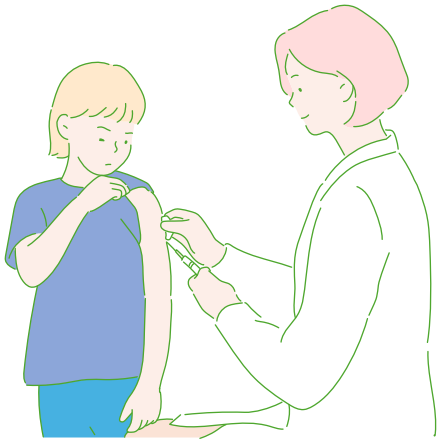
- Universal screening
- Universal vaccination (for those who are not immunized)
- Expanded treatment indications
- Patients must be at the centre of decision-making about their own care, with their values and preferences prioritized

Hepatitis B Prevention = Vaccination
Variations between different provinces



WHO recommendation
= <24h birth

Routine implementation of infant immunization across Canada is the best way to bring the number of new infections among children to near zero.



https://www.actionhepatitiscanada.ca/hepb.html

Recommendations for Hepatitis B vaccinations

1. **UNIVERSAL INFANT IMMUNIZATION (ideally at BIRTH)** is recommended in **ALL** Canadian provinces and territories. (Strong recommendation; Level 1)

2. **UNIVERSAL Catch-up Vaccination (for ADULTS)** is recommended for **ALL** individuals who have not received a complete series of HBV vaccine doses or are unsure of their vaccination history. (Strong recommendation; Level 3)

Infant Vaccination and Follow-up

1. All infants born to HBsAg-positive pregnant persons should receive HBIG (hep B immunoglobulins) and HBV vaccine as soon as possible after birth, and completion of 2nd and 3rd HBV vaccine doses before 6 months. (Strong recommendation; Level 1)

2. Infants should be tested for HBsAg and anti-HBs between 1 and 4 months after the last dose of vaccine (by age 1 year) to confirm that they are uninfected and immune to HBV. (Strong recommendation; Level 1)
    - Test *no earlier* than 1-2 months after the last HBV vaccine dose due to residual anti-HBs from HBIG (see Letter to the Editor, Can. Liv Journal in press)
    - Testing up to 15 months may lead to delayed diagnosis of vaccine failure

Hepatitis B treatment and Breastfeeding

1. Breastfeeding during Hep B treatment (i.e. tenofovir) is NOT contraindicated. (Strong recommendation; Level 1)

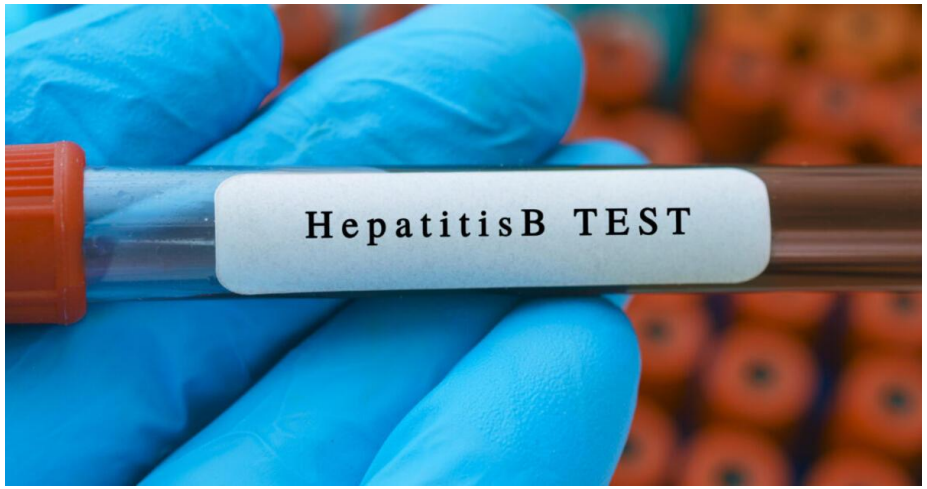
All HBsAg+ mothers on treatment should be educated about value and safety of breastfeeding. Practice nipple care if cracked/bleeding but reassure HBIG and vaccine will protect against transmission

Recommendations for HBV screening

- A single **UNIVERSAL SCREENING** of all adults (> 18 years of age) in Canada should be implemented.

- Screening should be performed using triple serology including tests for **HBsAg, anti-HBs, and anti-HBc***.

- In consultation with the patient, the presence of new activity or a persistent risk of hepatitis B infection should warrant periodic screening if the patient is not immune (i.e., anti-HBs negative).



Recommendations for screening for Hepatitis D

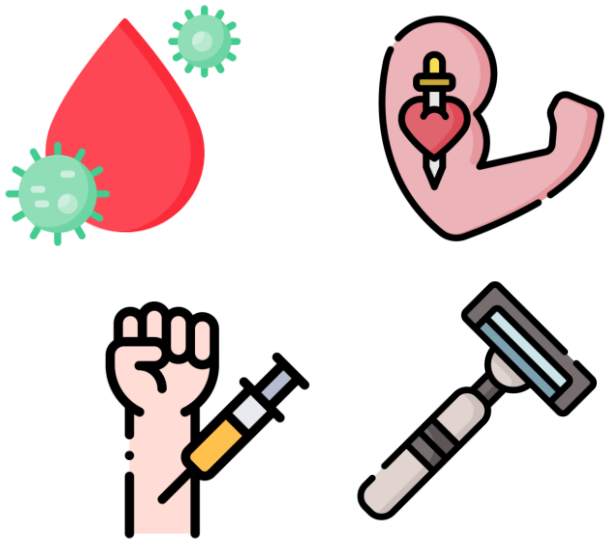
1. **REFLEX UNIVERSAL SCREENING* of HBsAg-positive individuals for anti-HDV antibodies** should be performed.

2. Retesting for HDV antibodies is warranted if there is a **new activity or persistent risk** for HDV, or **elevation in liver enzymes** without increased activity of Hep B .

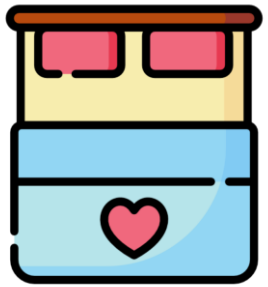
   (Strong recommendation; Level 3)

HDV Routes of Transmission

HDV can be prevented by immunization against Hep B!



Contact with infected blood

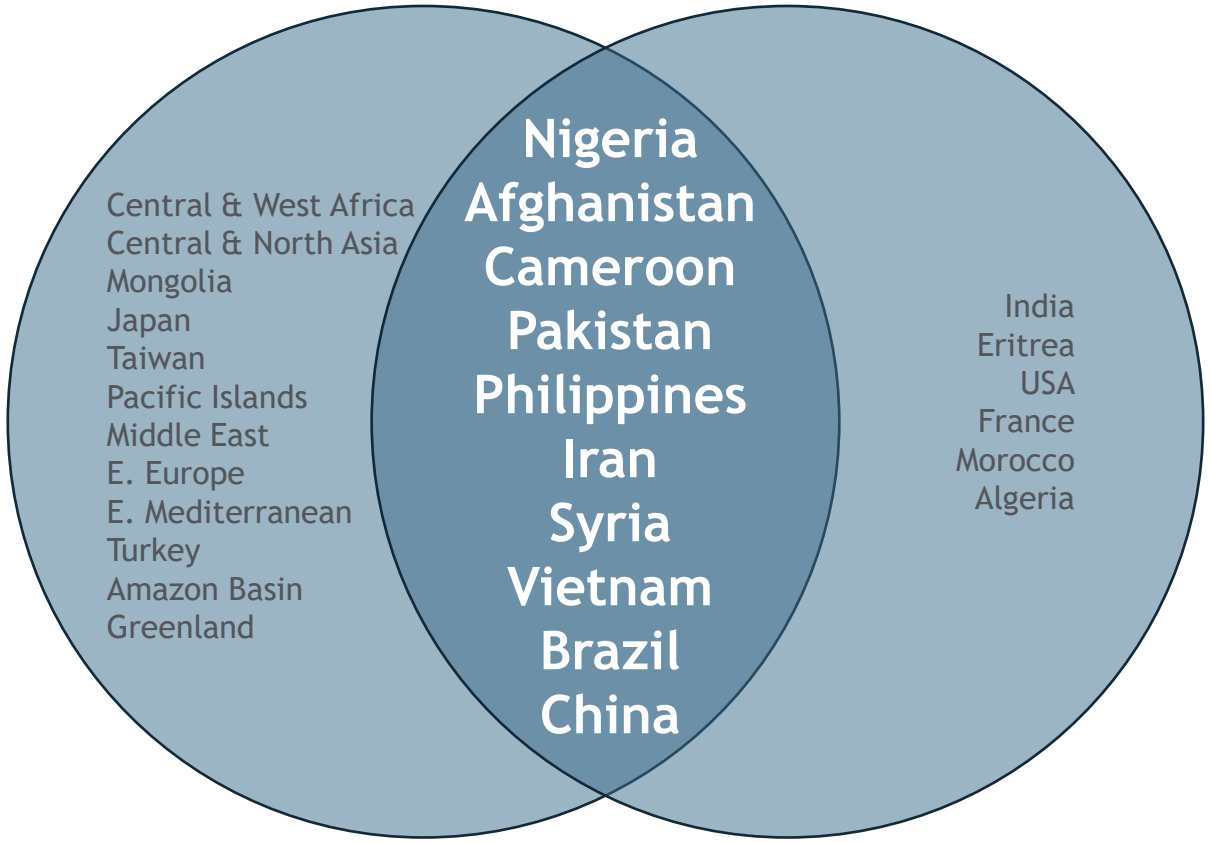


Sexual contact with infected individual

Mother-to-child transmission

Significant overlap between HDV-endemic regions and sources of Canadian immigration

WHO-Declared HDV Endemic Regions[1]



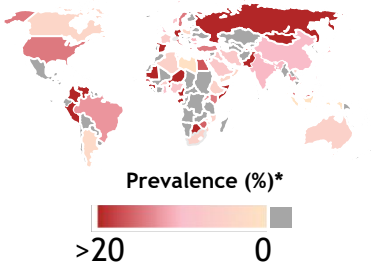
Permanent Residents Admitted to Canada

2023 Report by Top 30 Source Countries[2]

Over 31% of total Permanent Residents who immigrated in 2023 are from HDV Endemic Regions

1. Sagnelli C, et al. World J Gastroenterol. 2021 Nov 14;27(42):7271-7284.
2. IRCC (Government of Canada). 2023 Annual Report to Parliament on Immigration.

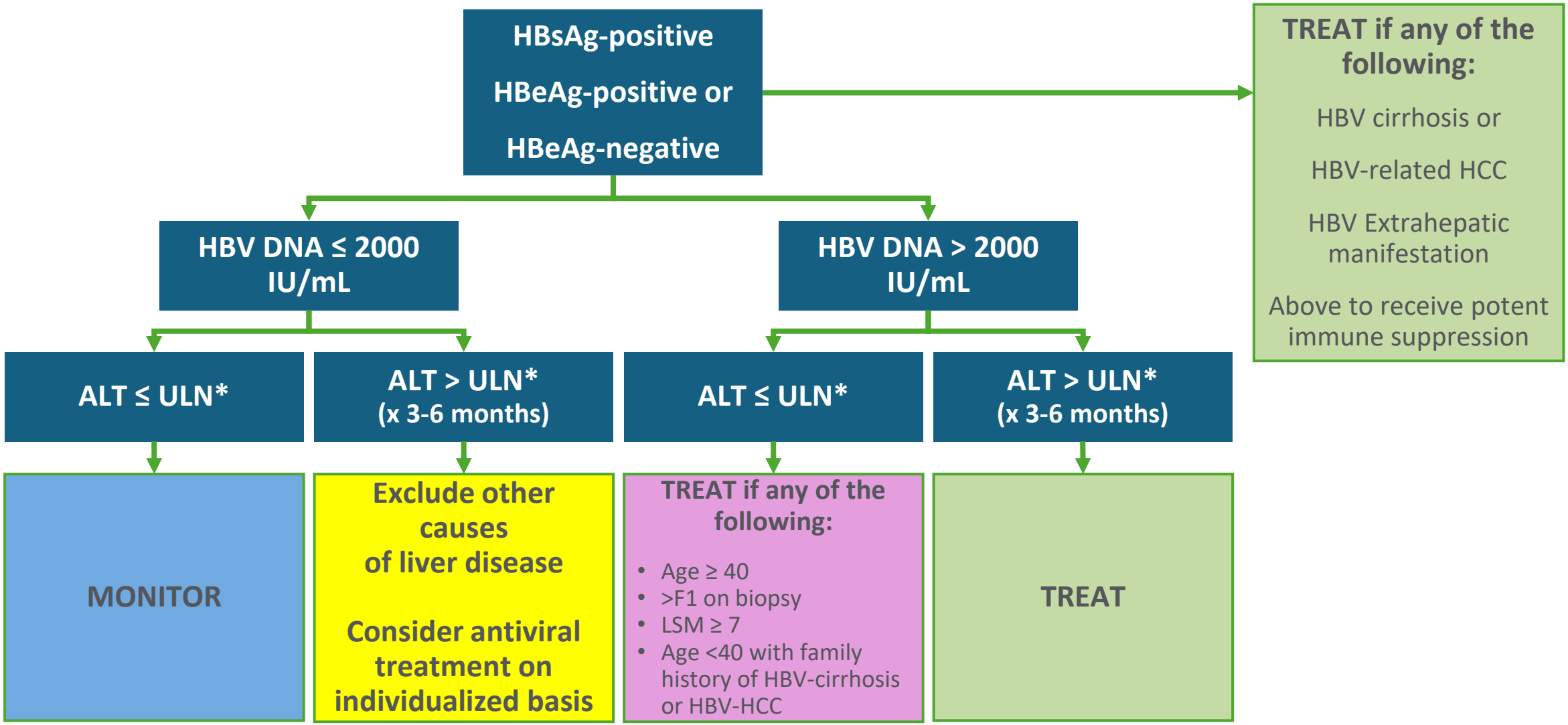
Overview of HDV prevalence studies in Canada



	HBV+ population studied	% anti-VHD+	Case Anti-VHD+	Prevalence ARN VHD+	RNA+ Cases
Polaris Observatory (J. Hepatology, 2023)	214,000 (estimate)	3.0% (adjusted)	6,400	64.8% (adjusted)	4,100 (adjusted)
Wong and all (J. Vir. Hep., 2024)	550,000 (estimate)	6.37%	35,059	64.8%	22,750
Osiowy and all (J. Hepatology, 2022)	7,080 (referred samples)	4.8%	338	64.8%	
Lee, Osiowy, Murphy (AASLD, 2024)	8,401 (referred samples)	3.2%		35.9%	

HDV+ patients were more likely diagnosed with cirrhosis or liver cancer.

Recommendations for the Treatment of HBV

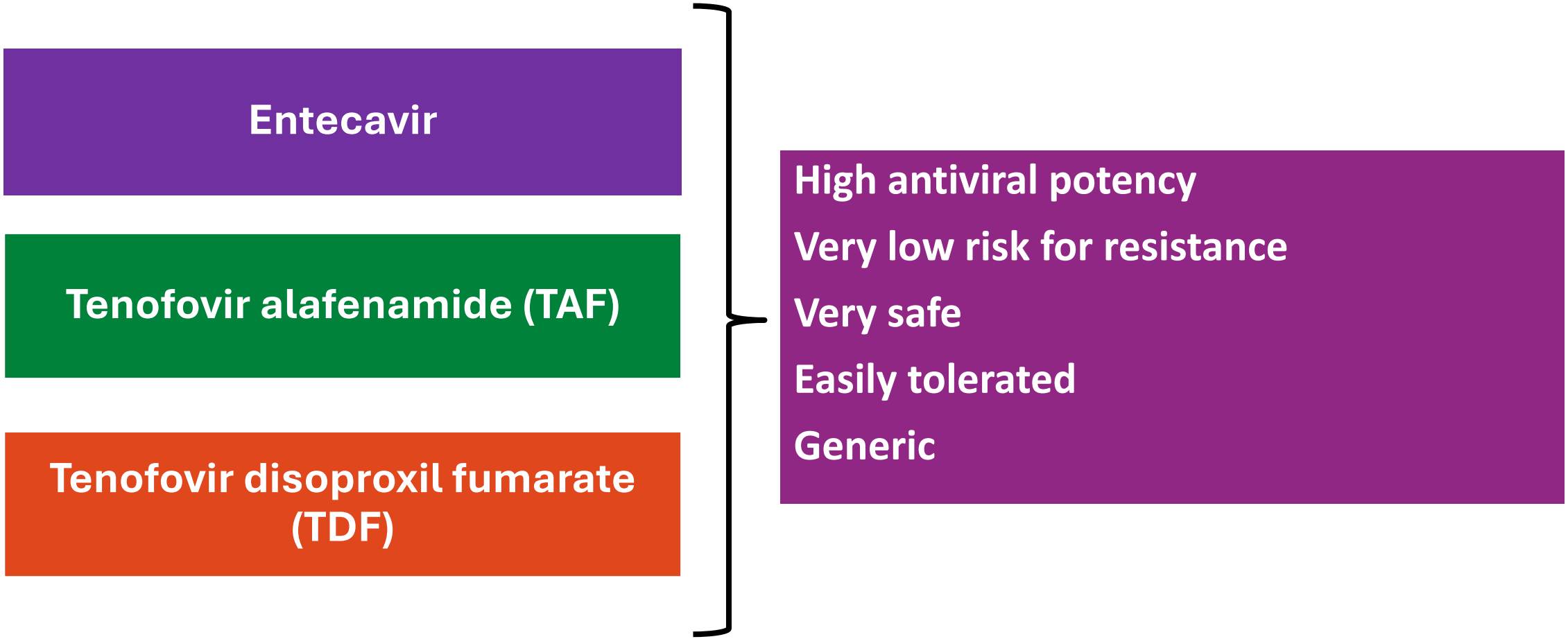


All HBsAg-positive patients may be considered for antiviral treatment on an individualized basis

*ALT ULN = 25 IU/L (F) and 35 U/L (M). ALT = Alanine transaminase; HBeAg = Hepatitis B e antigen; HBsAg = Hepatitis B surface antigen; HBV = Hepatitis B virus; HCC = Hepatocellular carcinoma

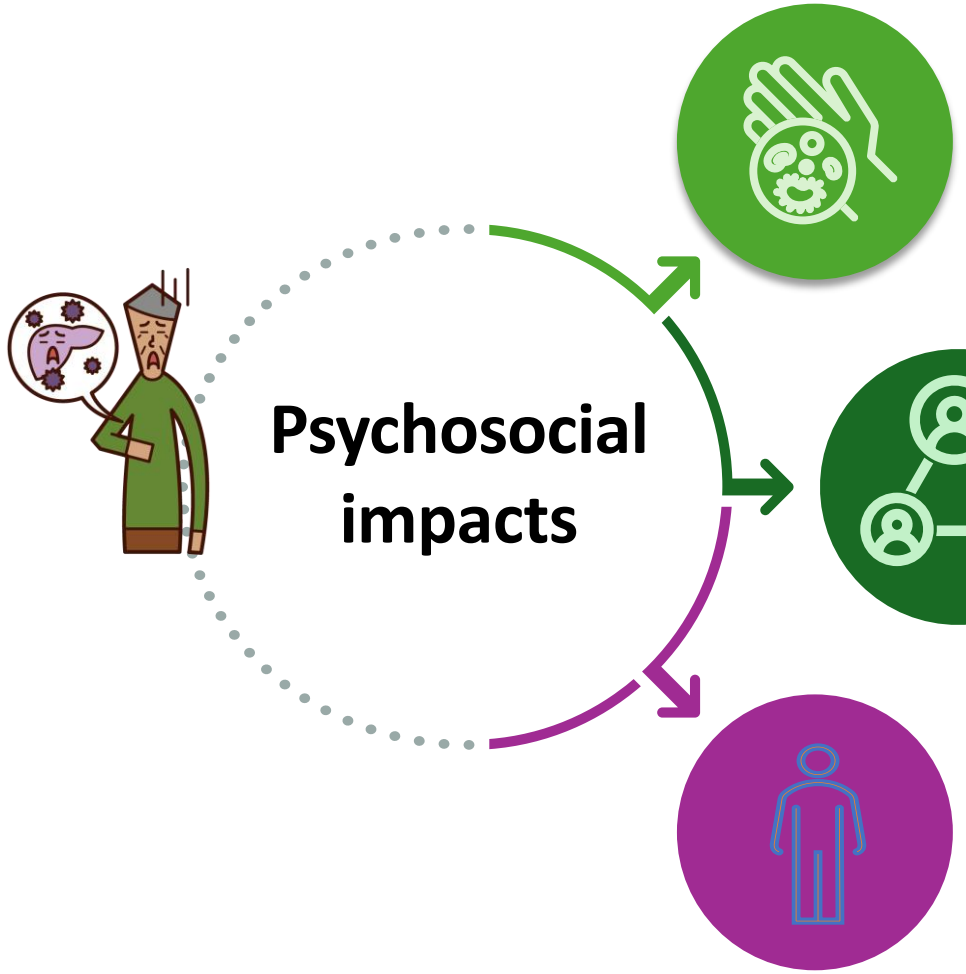
Osiowy et al. *Can Liv J*. 2025;8(2). https://doi.org/10.3138/canlivj-2025-0012-e

Hepatitis B Treatment: Oral Nucleos(t)ide Analogue Therapy



Terrault. Hepatology 2018; 67:1560 Slide credit : CCO

Beyond DNA and ALT: Psychosocial impacts of HBV



Primary:

- Fear of disease progression
- Financial loss
- Fear of transmission to others

Secondary:

Stigma and discrimination of:

- Community
- Health care workers
- Institutions(e.g. companies, educators, governments)

Tertiary:

- Silence and solitude
- Withdrawal from the company
- Self-stigma and guilt
- Passivity

Tu. Viruses. 2020;12:515. Slide credit : CCO

Perinatal HBV Management

Screen for HBV during each pregnancy

Pre-conception counselling*

HBsAg(+)[2]

HBsAg(–)

Screen all household and sexual contacts for HBV

Vaccinate If HBV susceptible

Indications for Treatment for Active Hepatitis – > Start TDF or TAF and continue until meet stopping criteria

All infants should receive birth dose HBV vaccine and HBIG as soon as possible after birth, complete HBV vaccine series on schedule and post vaccination serology at 1-2 months after completion last HBV vaccine dose to confirm HBV negative and immune

Perinatal HBV Management cont.

Repeat HBV DNA before 28 weeks pregnancy

HBV DNA <200,000 IU/mL

Low risk for MTCT
No antiviral needed

HBV DNA >200,000 IU/mL

High risk MTCT, start TDF or TAF before 28 weeks *or earlier*

Case by case continue until all family planning completed*

Stop TDF or TAF at 3 months after birth and monitor for ALT flares at monthly x 3 then q 6 months

HBV and Breastfeeding
All HBsAg pos mothers including those on TDF or TAF should be educated about *value* and safety of breastfeeding. Practice nipple care if cracked/bleeding but reassure HBIG and vaccine will protect against transmission

MTCT: maternal to child transmission

Recommendations for HCC (liver cancer) Screening in HBV

Monitoring for HCC is recommended as liver cancer risk is increased in individuals with Hep B.
Abdominal ultrasound and alpha fetoprotein (AFP) screening every 6 months are recommended: (Strong recommendation; level 3)

- All patients with **cirrhosis**, regardless of age (even those who have lost HBsAg)
- **Men aged 40 years or older**
- **Women aged 50 years** or more
- Individuals of **African (Black) descent aged 30 years or older** (due to the risk associated with certain African genotypes of HBV and environmental factors, including exposure to aflatoxin)
- **Family history of first-degree HCC** (from age 40 or 10 years before the affected first-degree family member, whichever occurs first)
- All patients co-infected with HIV (from 40 years of age)
- All **HBV/HDV** co-infected individuals (from 40 years of age, or earlier if > F3

Canadian Hepatitis B Peer Support Group

Mission

- Provide a platform for patients with hepatitis B and their families across the country to connect and find support
- Enrich patients and families' understanding of their hepatitis B through education programs/events
- Empower patients to manage their disease well through shared knowledge
- Create opportunity for patients to participate in advisory and advocacy activities

Contact Information

Canadian HBV NETWORK
Réseau canadien du VHB

Websites:

Canadian Hepatitis B Network
https://canadianhbvnetwork.ca/for-patients

Canadian Association for the Study of the Liver (CASL)
https://hepatology.ca/partners/patient-information/

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Thank You
Спасибо
Gracias
Grazie
Merci
Danke
Tak
Kiitos
Obrigado
Dankie
Dankjewel
Sagolun
Xièxie
Takk
Köszönöm
Mahalo
Rahmat
Faleminderit
Matondo
Misaotra
Hvala
Mercé
Toda
Terima Kasih
Mauruuru
Efharisto
ありがとう
תודה
شكرا

CATIE