ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# Alaska ID ECHO

September 12, 2023

*This ECHO (Extension for Community Healthcare Outcomes) is supported by a grant from the Northwest Portland Area Indian Health Board and funding is provided by the HHS Secretary's Minority HIV/AIDS Fund.*

# AK ID ECHO

## Consultant team

- Youssef Barbour, MD Hepatologist
- Leah Besh, PA-C HIV/Hepatology Provider
- Terri Bramel, PA-C HIV/STI Provider
- Rod Gordon, R.Ph. AAHIVP Pharmacist
- Jacob Gray, MD Infectious Disease Provider
- Annette Hewitt, ANP Hepatology Provider
- Brian McMahon, MD Hepatologist
- Lisa Rea, RN HIV/STI Case Manager
- Lisa Townshend, ANP Hepatology Provider

ALASKA NATIVE
TRIBAL HEALTH
CONSORTIUM

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# Agenda

Didactic Presentation:

- Hepatitis B Virus– New Screening Recommendations and Lab Interpretation presented by Brian McMahon, MD, ANTHC Liver and Hepatitis Program

Patient Case:

- AK-ID-27, HIV/HBV patient case

# Welcome to Alaska Infectious Disease ECHO: HCV, HIV, PrEP, STIs

**Approved Provider Statements:**

JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, Alaska Native Medical Center (ANMC) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.
CPE Credit will be posted to the online CPE Monitor system within 60 days following completion of each activity when applicable.

*The ANMC Joint Accreditation CE Program Portfolio additionally supports Behavioral Health (APA), Social Work (ASWB-ACE), and Dietitians (CPEU).*

**Contact Hours:**

ANMC designates this activity for a maximum of 12 contact hours, including 3 total pharmacotherapeutics contact hours, commensurate with participation.

**Financial Disclosures:**

Youssef Barbour, MD and Lisa Townshend-Bulson, APRN / faculty for this educational event, are primary investigators in an ANTHC sponsored hepatitis C study funded in part by Gilead Sciences. All of the relevant financial relationships listed have been mitigated.

**Requirements for Successful Completion:**

To receive CE credit please make sure you have actively engaged in the entire activity, your attendance is recorded by the facilitator, and complete the course evaluation form found here: https://forms.gle/18t4EgvN2WdnM4P77

For more information contact
jlfielder@anthc.org or (907) 229-1185

ALASKA NATIVE MEDICAL CENTER

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# Hepatitis B Virus – New Screening Recommendations and Lab Interpretation

Brian J McMahon, MD

Liver Disease and Hepatitis Program

Alaska Native Tribal Health Consortium

# Objectives and Goals

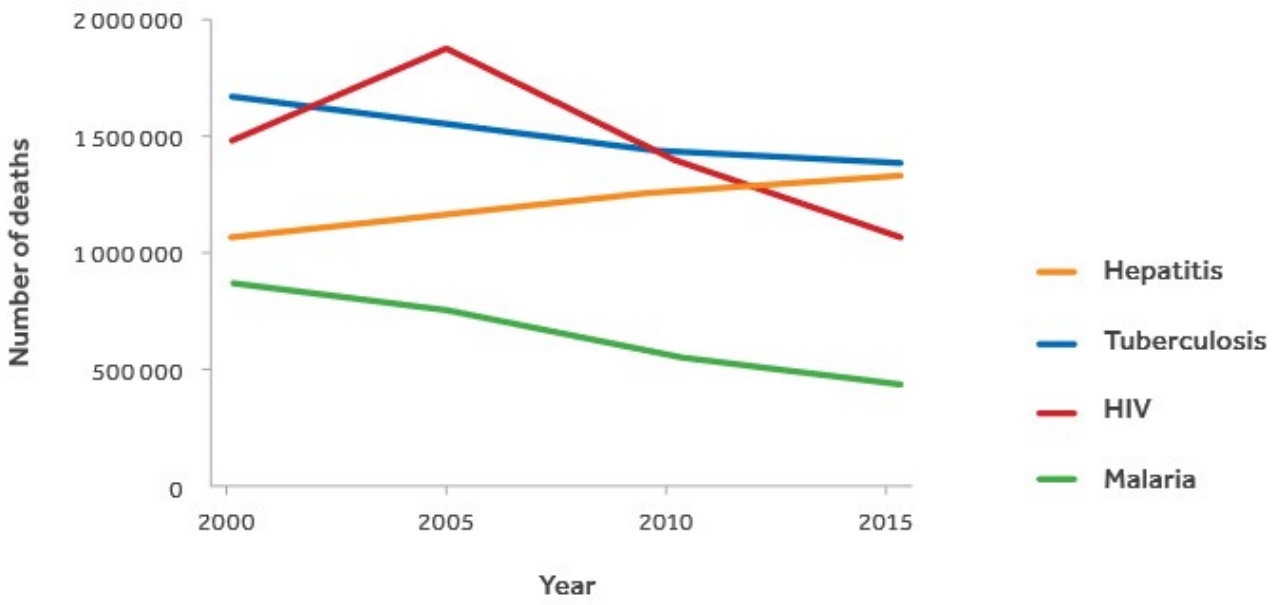
- Name the serology tests that should be ordered to screen a person for exposure to hepatitis B virus (HBV) to identify:
  - Those who are susceptible and need HBV vaccination
  - Those with chronic HBV
  - Those who previously acquired HBV but have recovered, though the virus is present but latent in their liver cells
- What other tests should be ordered if a person is found to be actively infected with HBV?
- When to order a test to measure the presence and amount of HBV virus (HBV DNA level)?
- What other tests might be useful in a person infected with HBV?

## Quiz: Which of the Following Statements are True

1. The CDC has recommended all adults should be screened for hepatitis B virus (HBV) and those negative should be vaccinated.
2. The CDC has recommended all adults should receive HBV vaccine and be screened for HBV.
3. Only people who inject drugs and persons with a history of multiple sexual partners should be screened for HBV.
4. To Screen for HBV, use HBsAg, antibody to HBsAg (anti-HBs) and antibody to HB core antigen (anti-HBc).
5. Answers 2 and 4 are true.
6. Answers 1 and 4 are true.

# World Health Organization (WHO)

Global annual mortality from hepatitis, HIV, tuberculosis and malaria, 2000-2015: unlike HIV, tuberculosis and malaria, the trend in mortality from viral hepatitis is increasing




Source: WHO global health estimates (Global Health Estimates 2015: deaths by cause, age, sex, by country and by region, 2000-2015. Geneva: World Health Organization; 2016

# New data on Hepatitis B and C burden, incidence and mortality by WHO region (2021 WHO Global progress report)

**Global Burden**

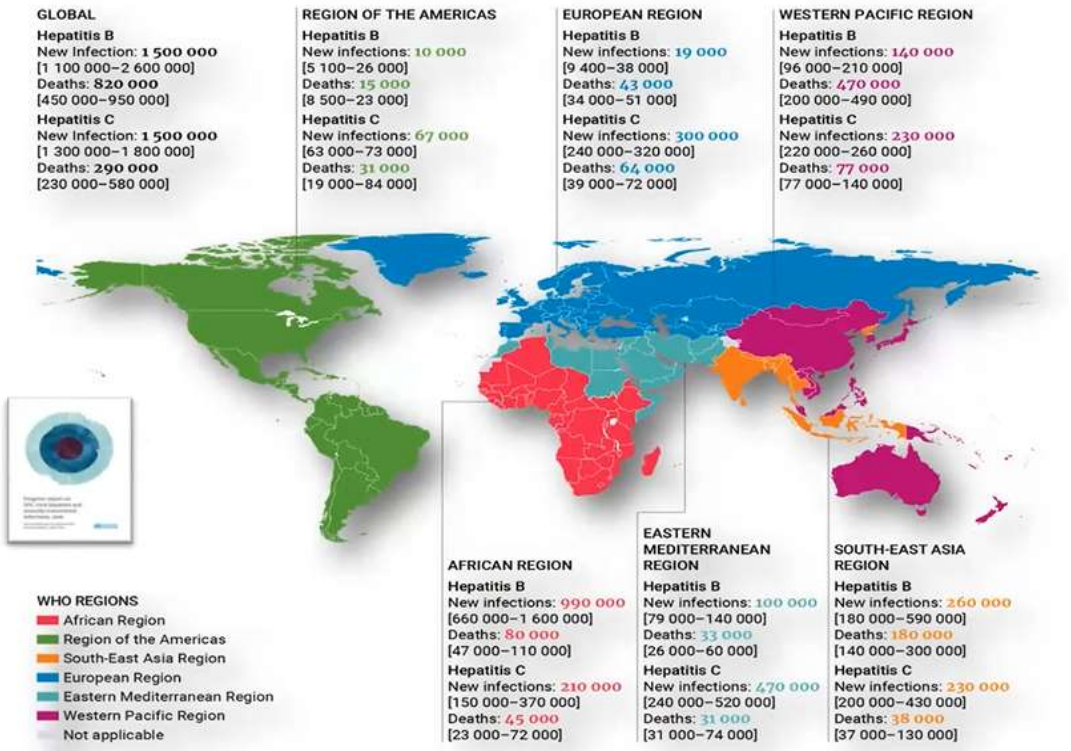
**Hepatitis B - 296 m**

**Hepatitis C - 58 m**

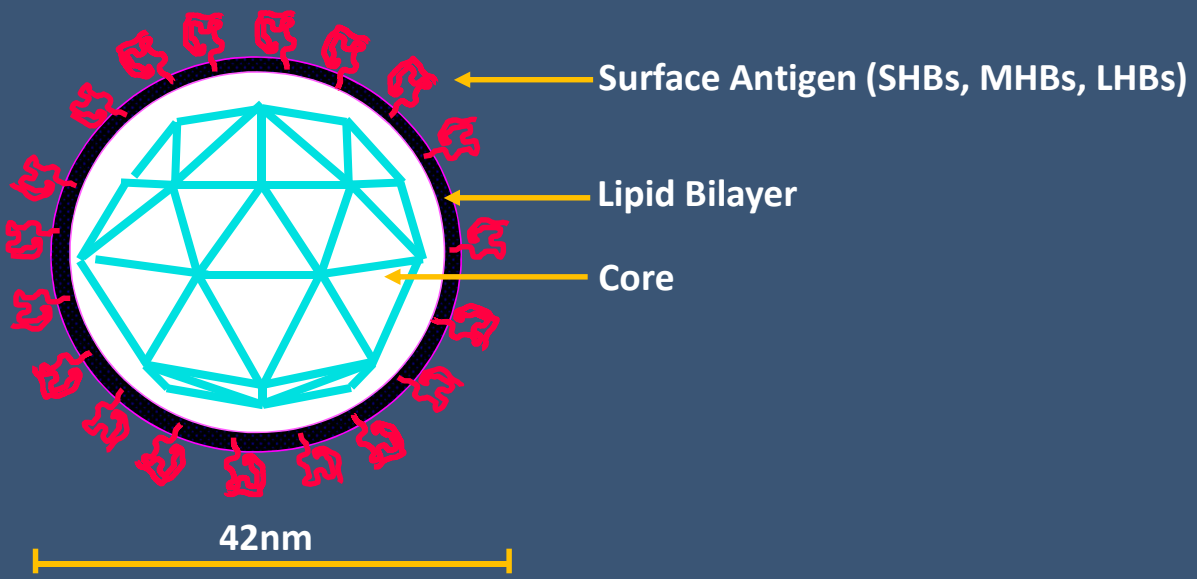
Viral Hepatitis

**New data on incidence, prevalence**

- 3.0 million new HCV & HBV infections
- 1.1 million HCV & HBV deaths with initial signs of HCV declines (290,000 deaths)
- Achieved <5 yr HepB prevalence SDG 2020 targets and GHSS goals

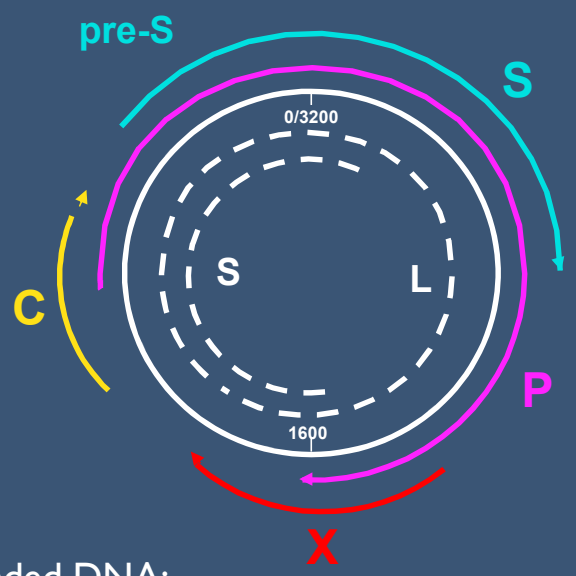


# Hepatitis B Virus




- Smallest DNA virus (3200 bp) that infects humans
- Complex genome organization – overlapping reading frames

# HBV Genome and Gene Products



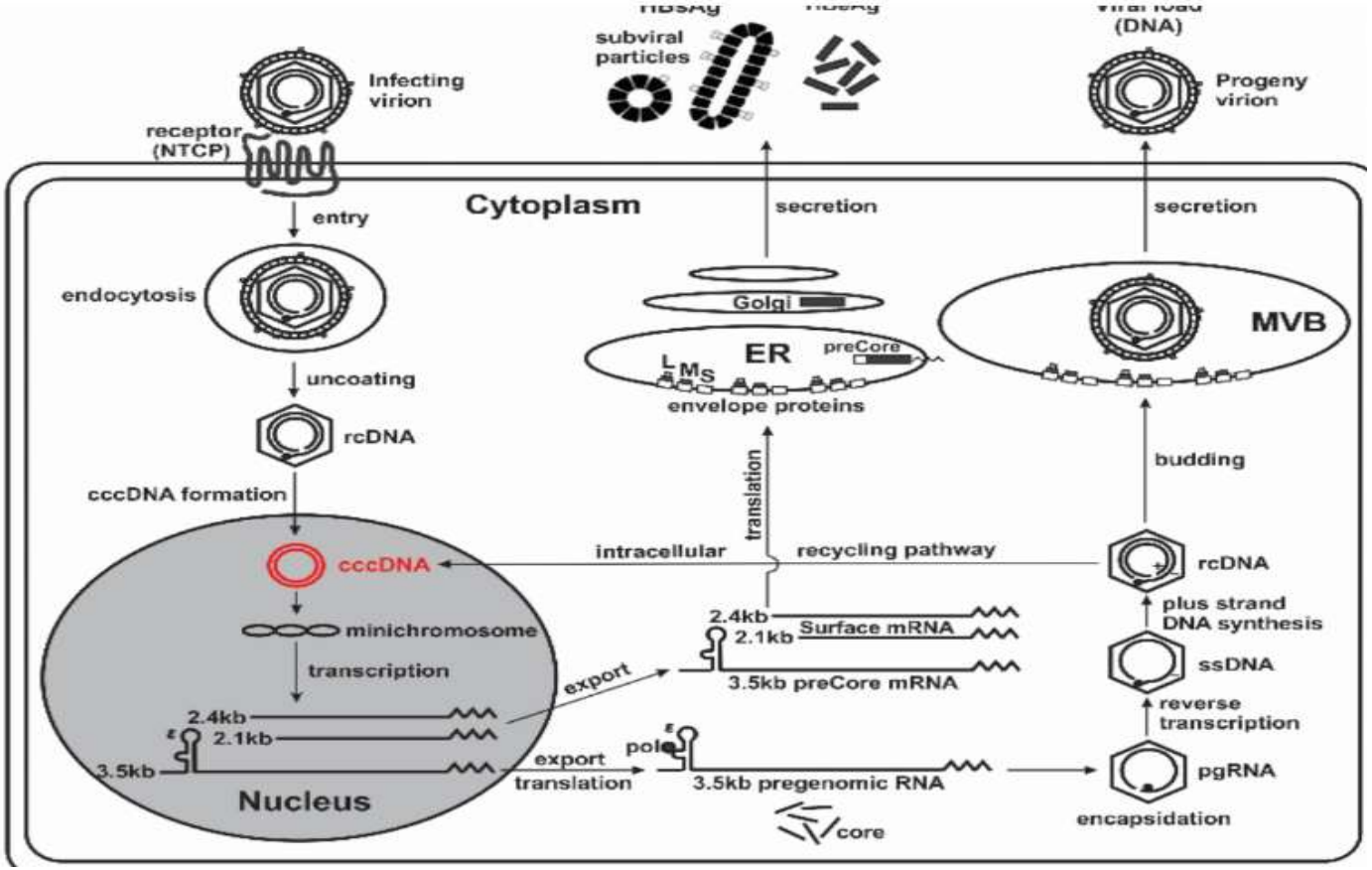

Partial double-stranded DNA:

- Long = negative
- Short = positive

Four overlapping reading frames:

- Polymerase — DNA polymerase, primase, RNAase, RT properties
- Surface antigen — Surface glycoproteins, HBSAG, preS1, preS2
- X — Transactivation - xprotein
- Core — Nucleoproteins – HBcAg, HBeAg

# HBV Replication Cycle




ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# Hepatitis B nomenclature

| | |
|---|---|
| **HBsAg** | **Hepatitis B surface antigen** (in the virus envelope): persistence beyond six months defines chronic infection |
| **Anti-HBs** | **Antibody to hepatitis B surface antigen**: defines immunity to reinfection |
| **HBcAg** | **Hepatitis B core antigen (in viral capsid)**: "particulate form" is cell-associated; no soluble form present in plasma, so don't detect like HBsAg or HBeAg |
| **Anti-HBc** | **Antibody to hepatitis B core antigen**: IgG defines any history of exposure to HBV; may be the only marker of past infection if anti-HBs declines; IgM defines acute HBV |
| **HBeAg** | **Hepatitis B E-antigen**: protein component of core; associated with increased infectivity; soluble form released into plasma from infected hepatocytes |
| **Anti-HBe** | **Antibody to hepatitis B E-antigen**: signifies lower-level of infectivity |
| **HBV DNA** | **HBV genome**: means replicating virus is present |

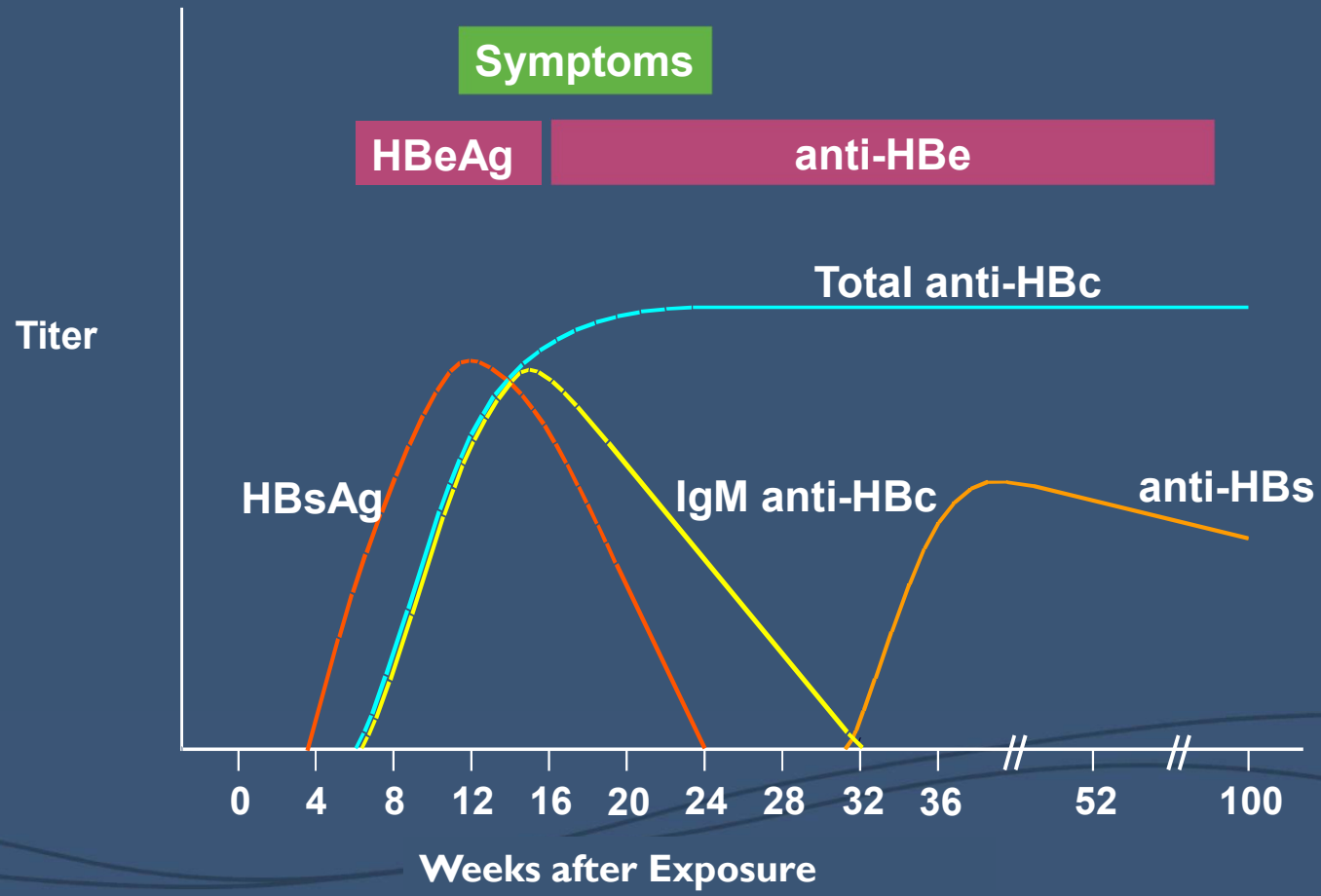
# Interpretation of Hepatitis B Labs

| Acute Hepatitis B Infection | Hepatitis B Carrier/ Chronic Infection | Previous Exposure with Immunity | Vaccination with Immunity |
|---|---|---|---|
| **Anti-HBs -** | **Anti-HBs -** | **Anti-HBs +** | **Anti-HBs +** |
| **HBsAg +** | **HBsAg +** | **HBsAg -** | **HBsAg -** |
| **IgM anti-HBc +** | **Anti-HBc Total +** | **Anti-HBc Total +** | **Anti-HBc Total -** |

| Other names for these labs/definitions | |
|---|---|
| HBsAg = Surface Antigen | Positive = Infection |
| Anti-HBs = Surface Antibody | Positive = Immunity |
| Anti-HBc Total = Core Antibody | Infection memory. Positive at onset of hepatitis B infection (acute and chronic) and persists through life. |

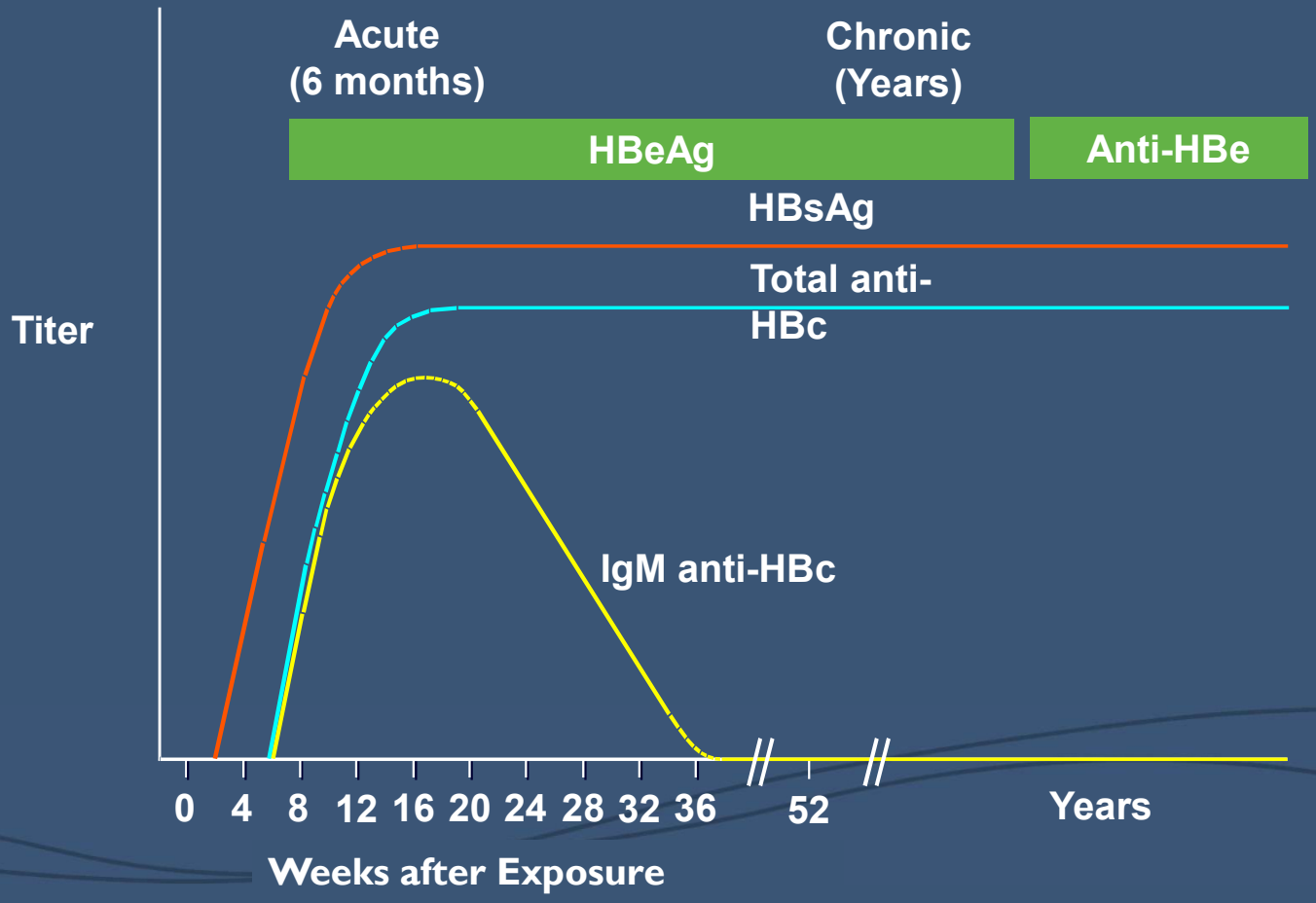
# Acute Hepatitis B Virus Infection with Recovery

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

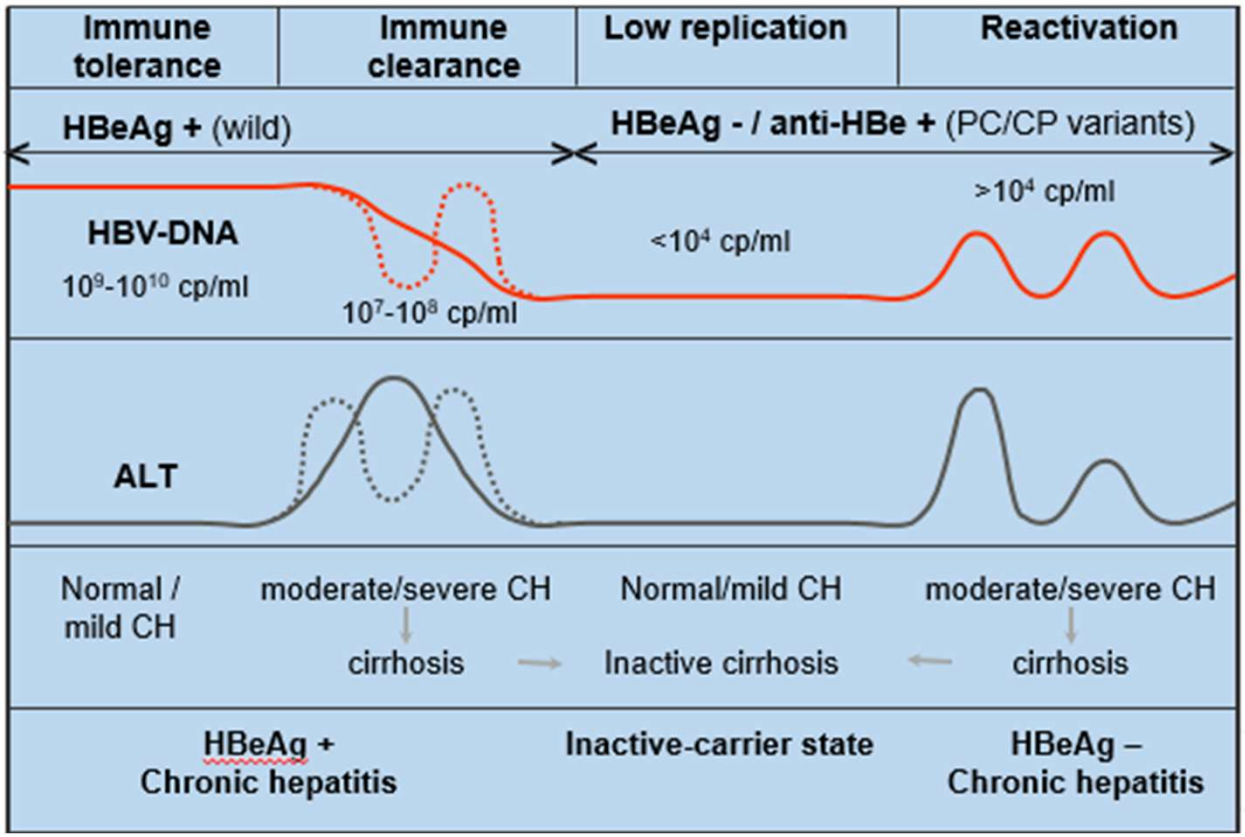


# Acute Hepatitis B Virus Infection with Progression to Chronic Infection

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM



# Fluctuating course of chronic HBV infection




ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# Association Between Age and Development of Chronic HBV Infection

- Risk of developing chronic infection is age dependent
- Occurs *more* frequently in younger age groups

| Age Group | Chronic Infection |
|---|---|
| Newborns & infants | 90 % |
| Children 1-5 years old | 25-50 % |
| Older children, adolescents, adults | 6-10 % |

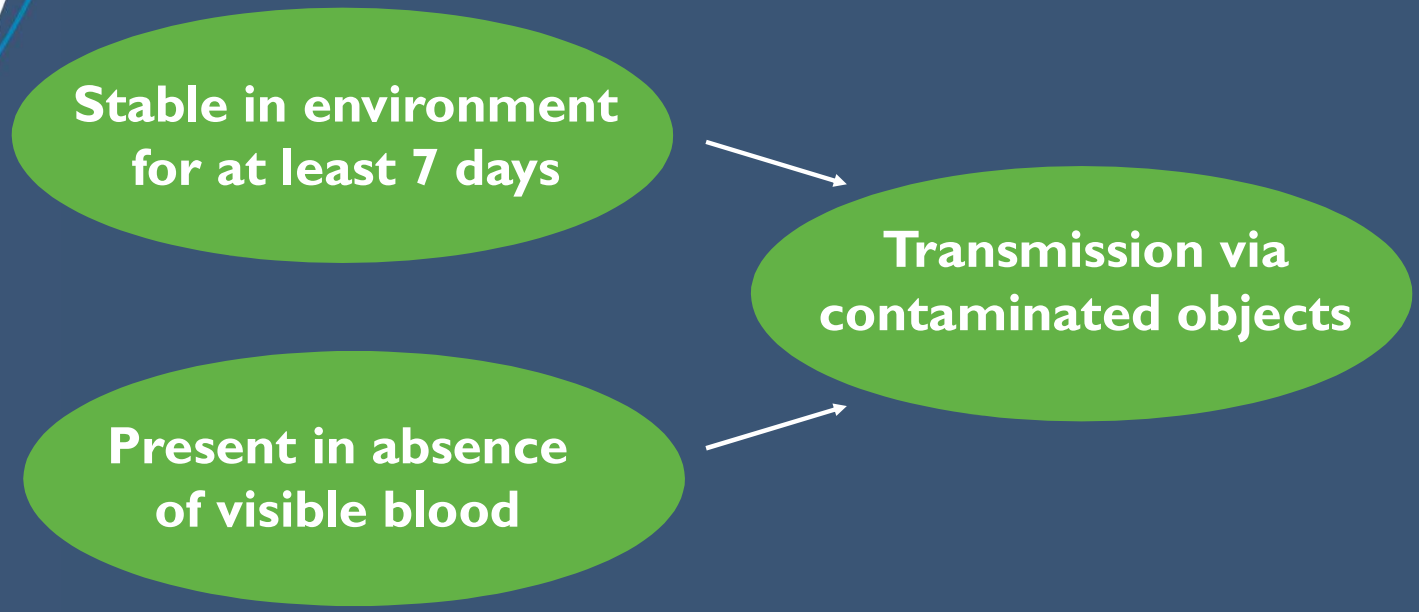
15-25% of persons with chronic HBV infection will die prematurely from HBV-related chronic liver disease

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

# Transmission of HBV

- Perinatal: HBV infected mother with high viral load to infant at birth: 90% risk of chronic HBV
- Horizontal:
  - Children ages birth to 5 years: 30% risk of chronic HBV
    - HBV survives on environmental surfaces at all temperatures for at least one week
    - Transmission occurs through open cuts or scratches
  - Children over 5 years and adults: 10% risk of chronic HBV
    - Transmission occurs via needle contamination, sexual contact, open cuts or scratches
- Adult HBV infection
  - 30% of adults with acute HBV infection will have symptomatic jaundice
  - <5% will develop chronic HBV
    - Exception is those infected with HIV who have a higher risk of chronic HBV

# HBV in the Environment




CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION


ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# Hepatitis B virus screening and testing recommendations - CDC, 2023

**Universal hepatitis B virus (HBV) screening**

- HBV screening at least once during a lifetime for adults aged ≥18 years (new recommendation)
- During screening, test for hepatitis B surface antigen (HBsAg), antibody to HBsAg, and total antibody to HBcAg (total anti-HBc) (new recommendation)

**Screening pregnant persons**

- HBV screening for all pregnant persons during each pregnancy, preferably in the first trimester, regardless of vaccination status or history of testing*
- Pregnant persons with a history of appropriately timed triple panel screening and without subsequent risk for exposure to HBV (i.e., no new HBV exposures since triple panel screening) only need HBsAg screening

**Risk-based testing: now superseded by universal testing recommendation. Not needed if person has been vaccinated but after vaccination, person at high risk test for anti-HBs to confirm immunity**

- Testing for all persons with a history of increased risk for HBV infection, regardless of age, if they might have been susceptible during the period of increased risk†
- Periodic testing for susceptible persons, regardless of age, with ongoing risk for exposures, while risk for exposures persists†

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

* **Source:** Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2018;67(No. RR-1):1–31.

† Susceptible persons include those who have never been infected with HBV (i.e., total anti-HBc negative) and either did not complete a HepB vaccine series per Advisory Committee on Immunization Practices recommendations or who are known to be vaccine nonresponders.

# Rationale for universal hepatitis B virus screening

- Anyone can get HBV infection
- Universal screening of adults is cost-effective.
- Universal HBV vaccination of adults can prevent HBV infection
- Widespread vaccination can prevent transmission to others and eliminate HBV
- Chronic Hepatitis B virus (HBV) infection has substantial morbidity and mortality.
- Chronic HBV infection can be detected before the development of severe liver disease using reliable and inexpensive screening tests.
- Treatment for chronic HBV infection can reduce morbidity and mortality..
- Screening enables identification and management of pregnant persons infected with HBV and their infants, which can reduce the risk for perinatal transmission.
- Screening can identify persons who are anti-HBc/anti-HBs+ and at risk for reactivation of HBV infection if immunosuppressed.

# Testing for HBV seromarkers in persons who are to receive immunosuppressive or anti-cancer medications

- In persons who had acquired an acute HBV infection previously and made a full recovery and later are scheduled to receive a drug to treat cancer or an immunologic illness, they are at risk for a reactivation of HBV that even can be fatal
- All persons who receive chemo or immunotherapy should be tested for HBsAg, anti-HBs and anti-HBc
  - If HBsAg+, they need HBV antiviral medication probably indefinitely
  - If positive for anti-HBc but negative for HBsAg, they could reactivate on above medications and consultation regarding whether to put on prophylactic antiviral therapy should be sought
  - If negative for anti-HBc and HBsAg but positive for anti-HBs, it means that they were vaccinated for HBV and need no antiviral medication

- **Postvaccine Antibody Testing**: Given the decreased response rate to hepatitis B vaccine among persons with HIV, postvaccine testing for antibody to hepatitis B surface antigen (anti-HBs) should be performed 1 to 2 months after completing the final dose of the vaccine series, with a titer of at least 10 mIU/mL considered protective; individuals who have a postvaccine anti-HB less than 10 mIU/mL are considered vaccine nonresponders.[6,31]

- **Repeat Immunization for Vaccine Nonresponders**: If a postvaccine anti-HBs concentration of at least 10 mIU/mL is not attained, the following are considered as options for these vaccine nonresponders:[2]
  - Administer a double-dose, 4-dose series with *Engerix-B* or *Recombivax-HB* given at 0, 1, 2, and 6 months (**BI**), *or*
  - Administer the *Heplisav-B* vaccine series (**CIII**).

# Long-term Protection from HBV Vaccination

- Evidence of long-term protection from vaccination
    - Studies from Alaska have found that evidence of humoral and cellular immunity in persons vaccinated >6 months of age last for at least 35 years
    - For those vaccinated as newborns, duration of protection lasts at least 18 years
        - Duration only needed 1st 5 years of life to have greatest impact on reduction of chronic HBV
    - Need for more serosurveys from MIC/LIC countries in children 5-years post infant vaccination

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

Bruce et al. Hepatology 2022
Simons-Petrusa et al. J Infect Dis 2016;214:273-80

# Natural History of Chronic HBV Infection

- Chronic HBV infection has a complicated course: HBV cannot be cured.
- Patients can go from state of high viral load and no liver disease to one of active liver disease followed by inactive disease then revert back to active liver disease again
- Progression to advanced fibrosis can be rapid, slow, or constant
- In most adults found with chronic HBV infection, their immune system will control viral replication, liver disease will not be active and antiviral therapy has no benefit
  - Integrated HBV DNA
- During the inactive periods fibrosis and even early cirrhosis can be reversed over time
- Bottom line: it's hard to predict what will happen to an individual with chronic HBV infection
- HBV reactivation occurs in 25% to 50% of persons who recovered from HBV and are only anti-HBc+ it they are put on immunosuppressive drugs or cancer chemotherapy

# Factors Associated with Progression of Chronic HBV

- Viral
  - HBV
    - Genotype
    - Pre-core mutant
    - Core Promoter mutations
  - Other: HIV, HDV, HCV
  - Demographic: Age, male sex, ethnicity
- Environmental and Social
  - Alcohol
  - Non-alcoholic fatty liver disease (NAFLD)
  - Aflatoxin

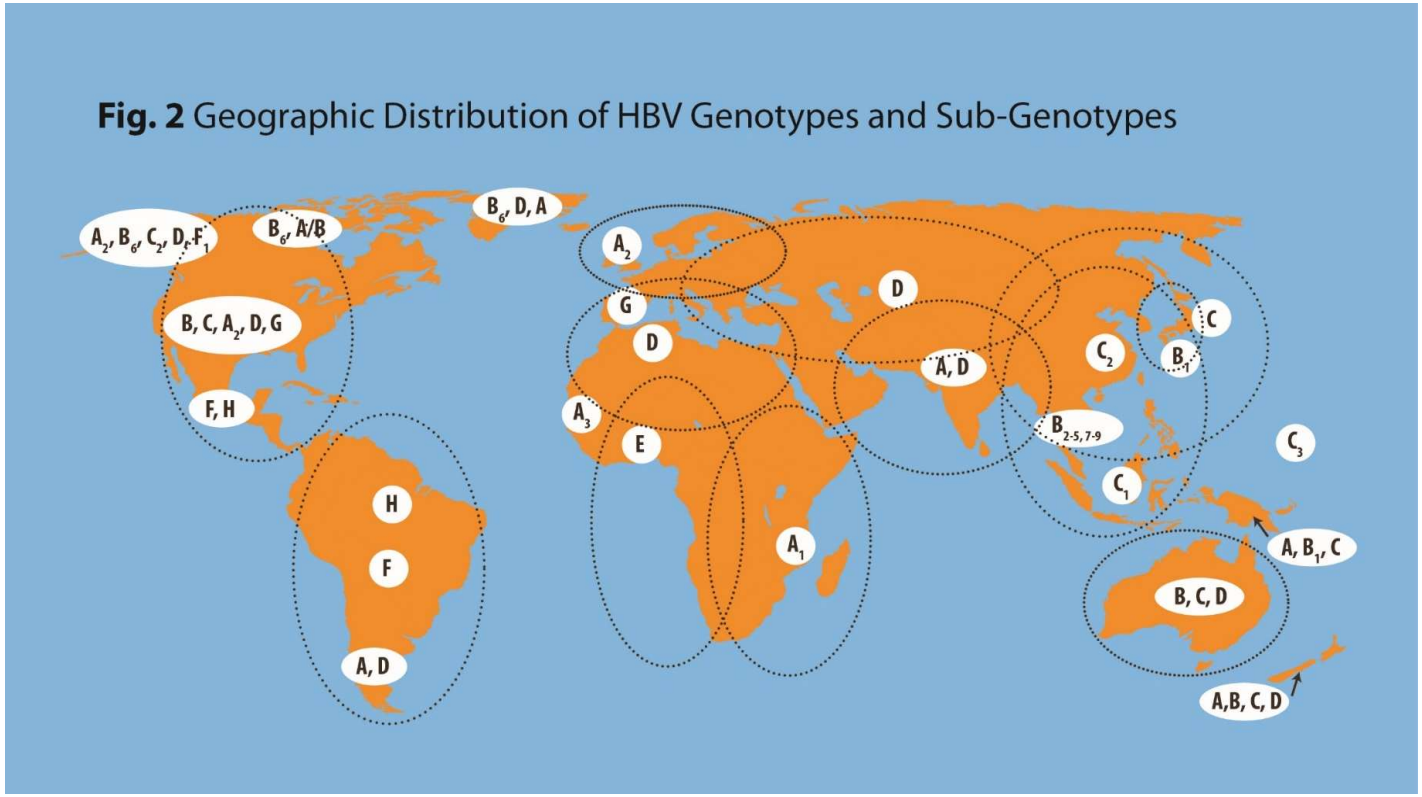
# Screening the General Population for Hepatitis B Virus Infection

- CDC recommends that providers test for HBsAg, anti-HBs and anti-HBc
  - HBsAg = Surface Antigen. Positive = Infection: acute or chronic
  - Anti-HBs = Surface Antibody. Positive = Immunity
  - Anti-HBc Total = Core Antibody. Infection memory. Positive at onset of hepatitis B infection (acute and chronic) and persists through life
- For persons who are jaundice of symptomatic, test for anti-HBc IgM and HBsAg
  - IgM anti-HBc = IgM Antibody.  Only present during acute hepatitis B infection

# What Tests to Order in Persons Newly Found to be HBsAg+

- HBV DNA
- Full panel LFTs
- AFP
- Hepatitis B "e" antigen (HBeAg) and it's antibody (anti-HBe)
- Consider HBV genotype
- For persons who are not Alaska Native, consider hepatitis Delta antibody

# HBV Genotype Distribution Throughout The World




ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# HBV Genotype and it's Influence on Natural History of Chronic HBV Infection

- Globally 8 HBV Genotypes
  - 5 HBV genotypes found in AN population
- Genotype testing is commercially available
- HBV Genotype HBV genotypes associated with
  - Clearance of HBeAg
  - Incidence of HCC
  - Likely risk of developing cirrhosis over lifetime
- Genotypes C and Ba have high rates of HCC

# Median Age of HBeAg Seroconversion by Genotype: Median 21 Years Follow-up*

| Genotype | No. HBeAg+ | Age 50% lost HBeAg | Age 75% lost HBeAg |
|---|---|---|---|
| $A_2$ | 34 | 19.8 | 32.1 |
| $B_6$ | 6 | 19.5 | 27.5 |
| $C_2$ | 36 | 47.8 | 58.1 |
| $D_{2,3}$ | 305 | 18.0 | 27.3 |
| $F_{1b}$ | 126 | 16.1 | 24.5 |

Livingston et al. Gastroenterology 2007;133:1452-57

# HBV genotype and HCC in Alaska

- Incidence of HCC is strongly associated with HBV Genotype
- Family history of HCC
- After adjustment for geographical distribution, gender, age at diagnosis, presence of cirrhosis and family history of HCC, genotype F significantly associated with HCC ($p<0.001$) at all ages and genotype C only after age 40 years ($p = 0.012$) compared to controls
- Replicons of Genotype F derived from persons who developed HCC when placed in immune modulated mice with humanized livers produce multi-oncogenic genes compared with replicons from Genotype F patients without HCC

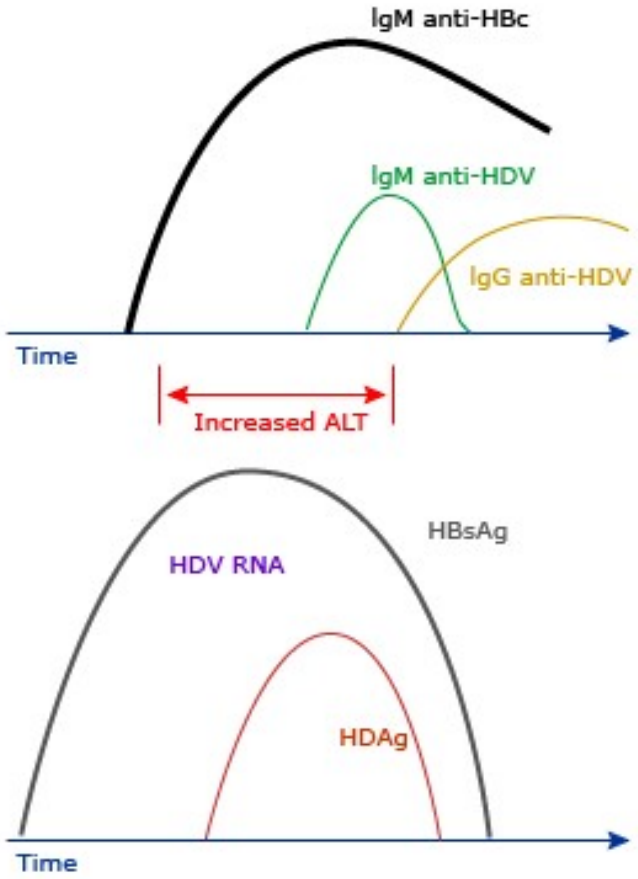
ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

Livingston et al. Gastroenterology 2007;133:1452-57
Ching et al. Liver International 2016;10:16-22
McMahon et al. Hepatology 2021;74:2965-73
Hayashi D. L. et al. Hepatology 2019;69:19-33

# Hepatitis Delta Virus (HDV)

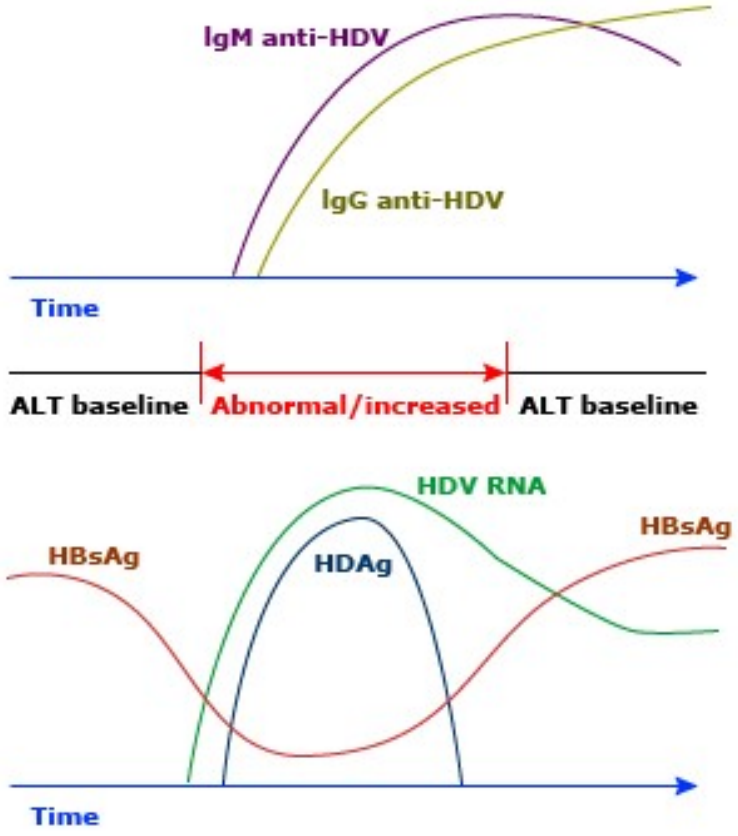
- RNA Virus that infects with HBV
- Requires HBsAg as it's coat and delta antigen as a protein which surrounds the nucleus of the virus
- Two outcomes after exposure to HDV
  - In person never infected with HBV, high risk of severe acute hepatitis but high probability of recovery from both viruses
  - In a person who already has chronic HBV, high risk of acute fulminant hepatitis and high risk of developing chronic HBV and HDV in those who recover with more rapid risk of developing liver failure
- Does not respond well to nucleoside or nucleotide analogues used to treat HBV
  - Usual treatment interferon plus nucleoside analogue
- Much more aggressive chronic hepatitis course with much higher risk of cirrhosis
- Is not found in the Alaska Native Population but other persons positive for HBsAg should be considered for testing for delta antibody

# Serum markers of acute, self-limiting HBV/HDV coinfection




From Up To Date

# Serum markers of an HDV superinfection of a chronic HBV carrier




ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# In Conclusion: Test persons for HBsAg, anti-HBs and anti-HBc

- All adults who have never been tested and have never received HBV vaccine and vaccinate those negative for all three markers
  - Persons may need more frequent testing based on their risk factors
- All persons to be prescribed any immunosuppressive and chemotherapy
- All persons with acute hepatitis or who are found to have elevated LFTs on routine lab screening need testing for HBV seromarkers
- At every pregnancy
- Persons with elevated liver enzymes

# Quiz: Which of the Following Statements are True

1. The CDC has recommended all adults should be screened for hepatitis B virus (HBV) and those negative should be vaccinated.
2. The CDC has recommended all adults should receive HBV vaccine and be screened for HBV.
3. Only people who inject drugs and persons with a history of multiple sexual partners should be screened for HBV.
4. To Screen for HBV, use HBsAg, antibody to HBsAg (anti-HBs) and antibody to HB core antigen (anti-HBc)
5. Answers 2 and 4 are true.
6. Answers 1 and 4 are true

ALASKA NATIVE
TRIBAL HEALTH
CONSORTIUM

# Questions

You're welcome to unmute yourself or add your question in the chat box.

## AK ID ECHO

Alaska Infectious Disease ECHO:
HCV, HIV, PrEP and common STIs

- Second Tuesday of every month from noon-1:00 PM AKDT
- Upcoming sessions
  - October 10: DoxyPEP
- www.anthc.org/ak-id-echo
- akidecho@anthc.org

## AK LD ECHO

Alaska Liver Disease ECHO

- Third Thursday of every month from noon-1:00 PM AKDT
- Upcoming sessions
  - September 21: Recognizing Common Autoimmune Liver Diseases Seen in Alaska Native and American Indian Peoples
- www.anthc.org/ak-ld-echo
- akldecho@anthc.org

## Indian Country ECHOs

- www.IndianCountryECHO.org
  - Multiple ECHOs hosted by the Northwest Portland Area Indian Health Board

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM

# Evaluation and Continuing Education Credit

JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

**Approved Provider Statements:**

In support of improving patient care, Alaska Native Medical Center (ANMC) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

The ANMC Joint Accreditation CE Program Portfolio additionally supports Behavioral Health (APA), Social Work (ASWB-ACE), and Dietitians (CPEU).

**To claim Continuing Education credit:**

- The QR code will connect to the electronic evaluation to claim the CE credit certificate for today's AK ID ECHO.
- A PDF certificate of credit will be automatically emailed to the address provided in the electronic evaluation form.
- The evaluation link will be sent out via email to all registered participants.
- https://forms.gle/18t4EgvN2WdnM4P77

# AK ID ECHO Contacts

ANTHC Staff

- Leah Besh PA-C, Program Director: labesh@anthc.org
- Lisa Rea RN, Case Manager: ldrea@anthc.org
- Jennifer Williamson, Program Coordinator: jjwilliamson@anthc.org

ANTHC Early Intervention Services/HIV Program: 907-729-2907

ANTHC Liver Disease and Hepatitis Program: 907-729-1560

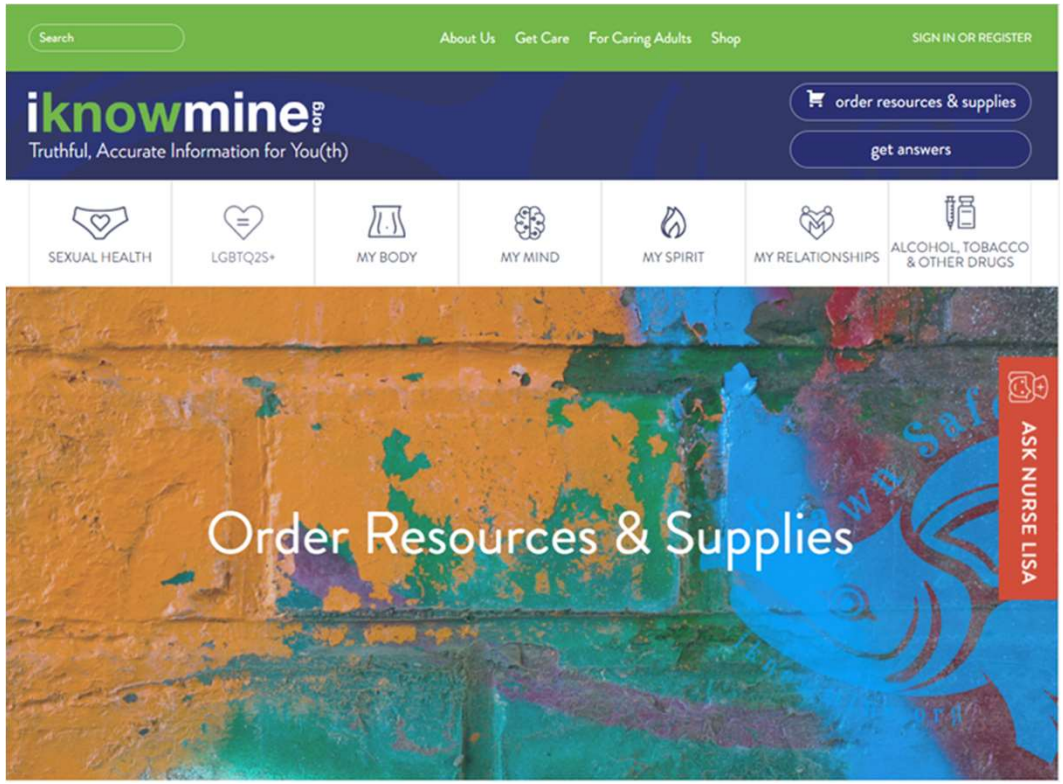
Northwest Portland Area Indian Health Board // www.indiancountryecho.org

- David Stephens, Director Indian Country ECHO: dstephens@npaihb.org
- Jessica Leston, Clinical Programs Director: jleston@npaihb.org

# ANTHC's iknowmine.org program

Free prevention resources are available at iknowmine.org/shop.

ALASKA NATIVE TRIBAL HEALTH CONSORTIUM




HARM REDUCTION KIT


CONDOMS FOR ORGANIZATIONS

HIV SELF-TEST KIT

ALASKA NATIVE
TRIBAL HEALTH
CONSORTIUM

# Thank you!

*AK ID ECHO is supported by a grant from the Northwest Portland Area Indian Health Board and funding is provided from the HHS Secretary's Minority HIV/AIDS Fund.*