Hepatitis B

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Objectives

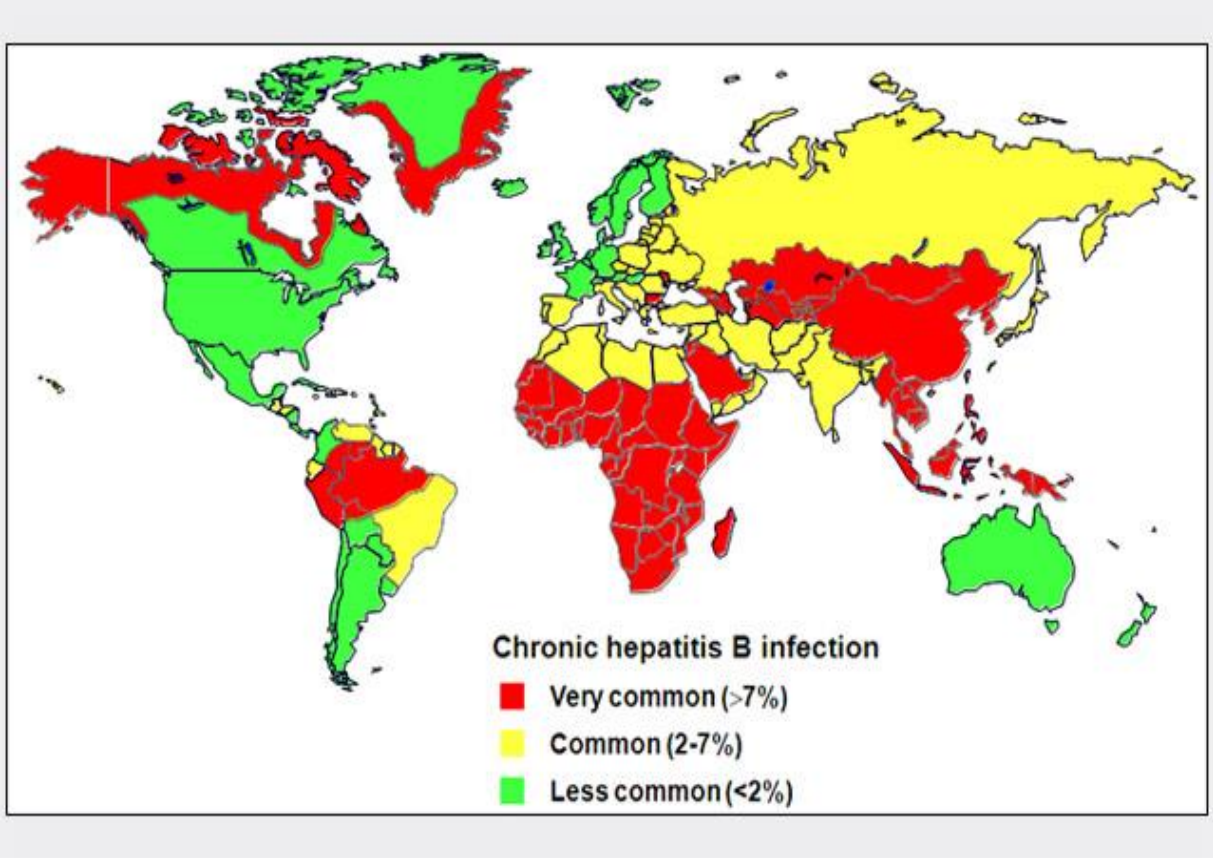
- Understand the biology of the virus
- Describe the epidemiology of hepatitis B with a focus on NC
- Describe the lab findings of stages of HBV infection
- Identify populations most appropriate for screening and vaccination

Epidemiology

--350-400 million HBsAg carriers worldwide (0.1-0.5% in US vs 5-20% in Far East

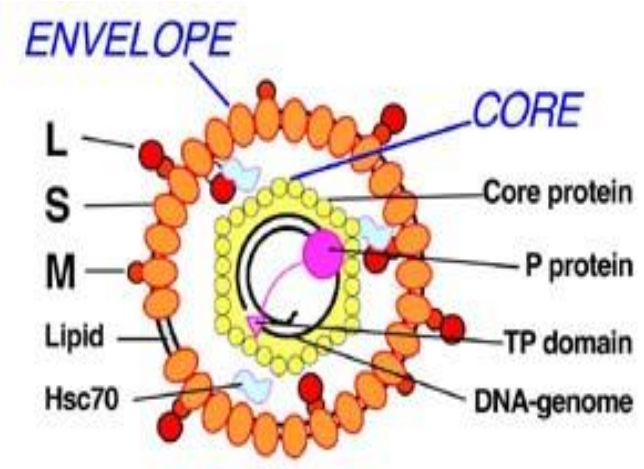
--??new infections annually

--1-10% progress to chronic infection

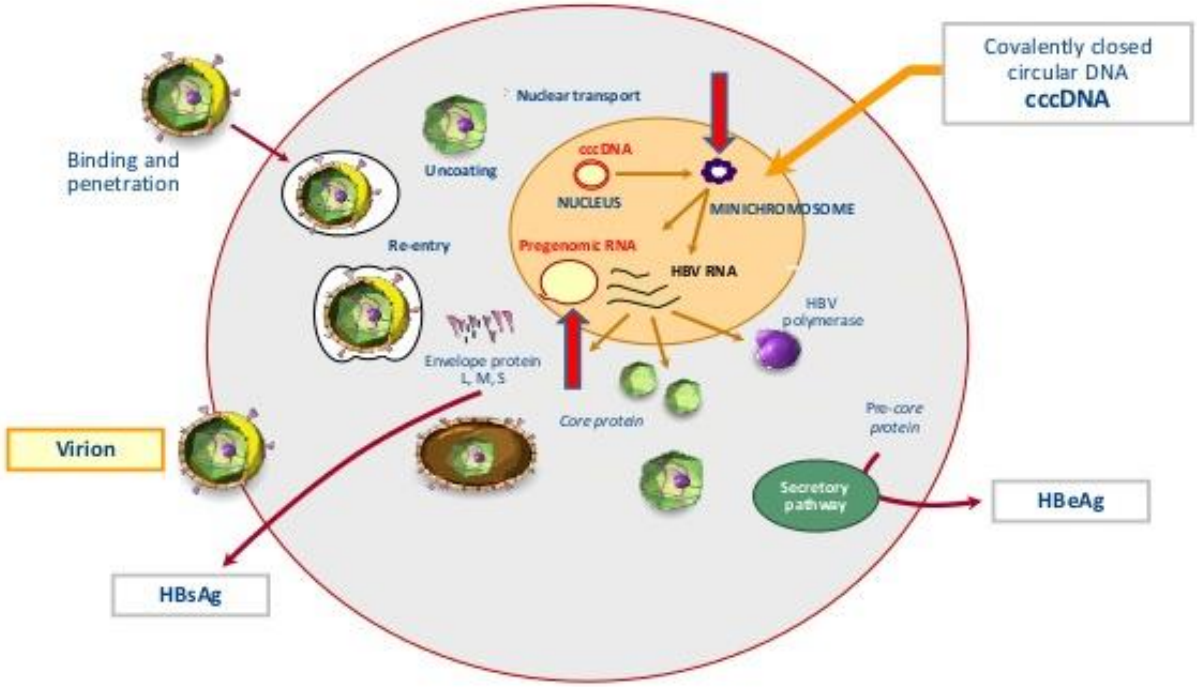


The Virus

- DNA virus; replicates in hepatocyte nucleus
- Not directly cytopathic for liver cells
- Cell mediated immunity important
- Transmission: much like HIV (blood, body fluids, perinatal)



HBV Life Cycle



Surface Antigen means current infection

	HBsAg	HBeAg	Anti-HBc	Anti-HBe	Anti-HBs	HBV DNA
Acute infection	+/-*	+	+	-	-	+
Past infection	-	-	+	+/-	+	-
Occult HBV	-	-	+	-	-	+†
Chronic hepatitis B	+	+	+	-	-	+
Pre-core mutant	+	-	+	+	-	+
Healthy carrier	+	-	+	+	-	-

*May be negative in acute infections where HBsAg is below the limit of detection.
†HBV DNA may only be detectable with sensitive PCR methods.

Envelope Ag=Infectious

	HBsAg	HBeAg	Anti-HBc	Anti-HBe	Anti-HBs	HBV DNA
Acute infection	+/-*	+	+	-	-	+
Past infection	-	-	+	+/-	+	-
Occult HBV	-	-	+	-	-	+†
Chronic hepatitis B	+	+	+	-	-	+
Pre-core mutant	+	-	+	+	-	+
Healthy carrier	+	-	+	+	-	-

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Infected, unknown timing; if concern for acute, check IgM

	HBsAg	HBeAg	Anti-HBc	Anti-HBe	Anti-HBs	HBV DNA
Acute infection	+/-*	+	+	-	-	+
Past infection	-	-	+	+/-	+	-
Occult HBV	-	-	+	-	-	+†
Chronic hepatitis B	+	+	+	-	-	+
Pre-core mutant	+	-	+	+	-	+
Healthy carrier	+	-	+	+	-	-

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Viral DNA is marker of viral activity

	HBsAg	HBeAg	Anti-HBc	Anti-HBe	Anti-HBs	HBV DNA
Acute infection	+/-*	+	+	-	-	+
Past infection	-	-	+	+/-	+	-
Occult HBV	-	-	+	-	-	+†
Chronic hepatitis B	+	+	+	-	-	+
Pre-core mutant	+	-	+	+	-	+
Healthy carrier	+	-	+	+	-	-

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†HBV DNA may only be detectable with sensitive PCR methods.

Surface Antibody=immunity

	HBsAg	HBeAg	Anti-HBc	Anti-HBe	Anti-HBs	HBV DNA
Acute infection	+/-*	+	+	-	-	+
Past infection	-	-	+	+/-	+	-
Occult HBV	-	-	+	-	-	+†
Chronic hepatitis B	+	+	+	-	-	+
Pre-core mutant	+	-	+	+	-	+
Healthy carrier	+	-	+	+	-	-

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Envelope Antibody=recovery from acute infection

	HBsAg	HBeAg	Anti-HBc	Anti-HBe	Anti-HBs	HBV DNA
Acute infection	+/-*	+	+	-	-	+
Past infection	-	-	+	+/-	+	-
Occult HBV	-	-	+	-	-	+†
Chronic hepatitis B	+	+	+	-	-	+
Pre-core mutant	+	-	+	+	-	+
Healthy carrier	+	-	+	+	-	-

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†HBV DNA may only be detectable with sensitive PCR methods.

What is a pre-core mutant?

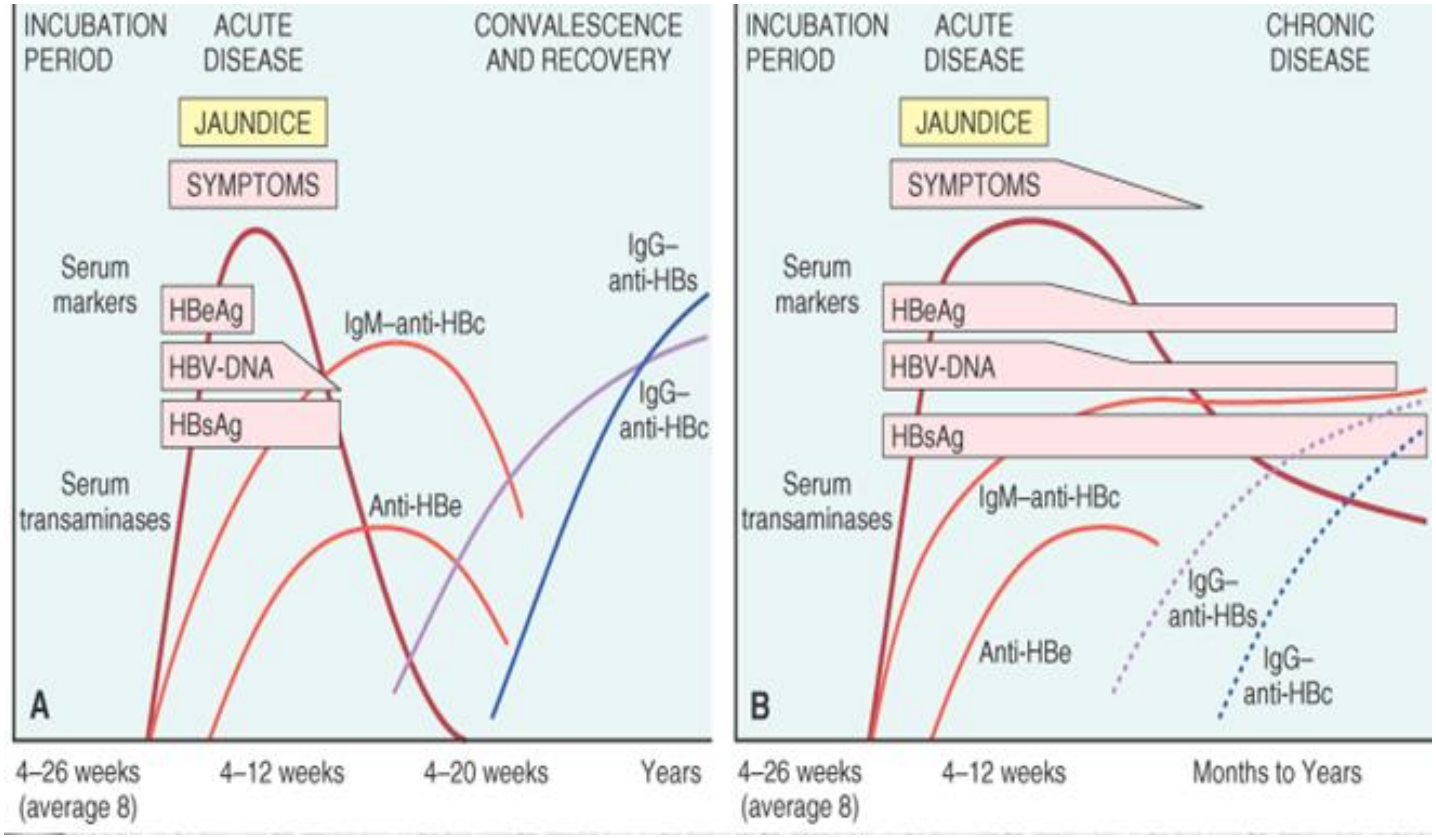
- No envelope antigen but otherwise infectious
- Can be difficult to treat
- Can be prolonged infection and has a higher risk of liver cirrhosis

Modes of transmission

- Semen and vaginal fluids
- Blood
  - Sharing needles, syringes, or other drug-injection equipment
  - Sharing items such as razors or toothbrushes with an infected person
  - Direct contact with the blood or open sores of an infected person
  - Exposure to blood from needlesticks or other sharp instruments

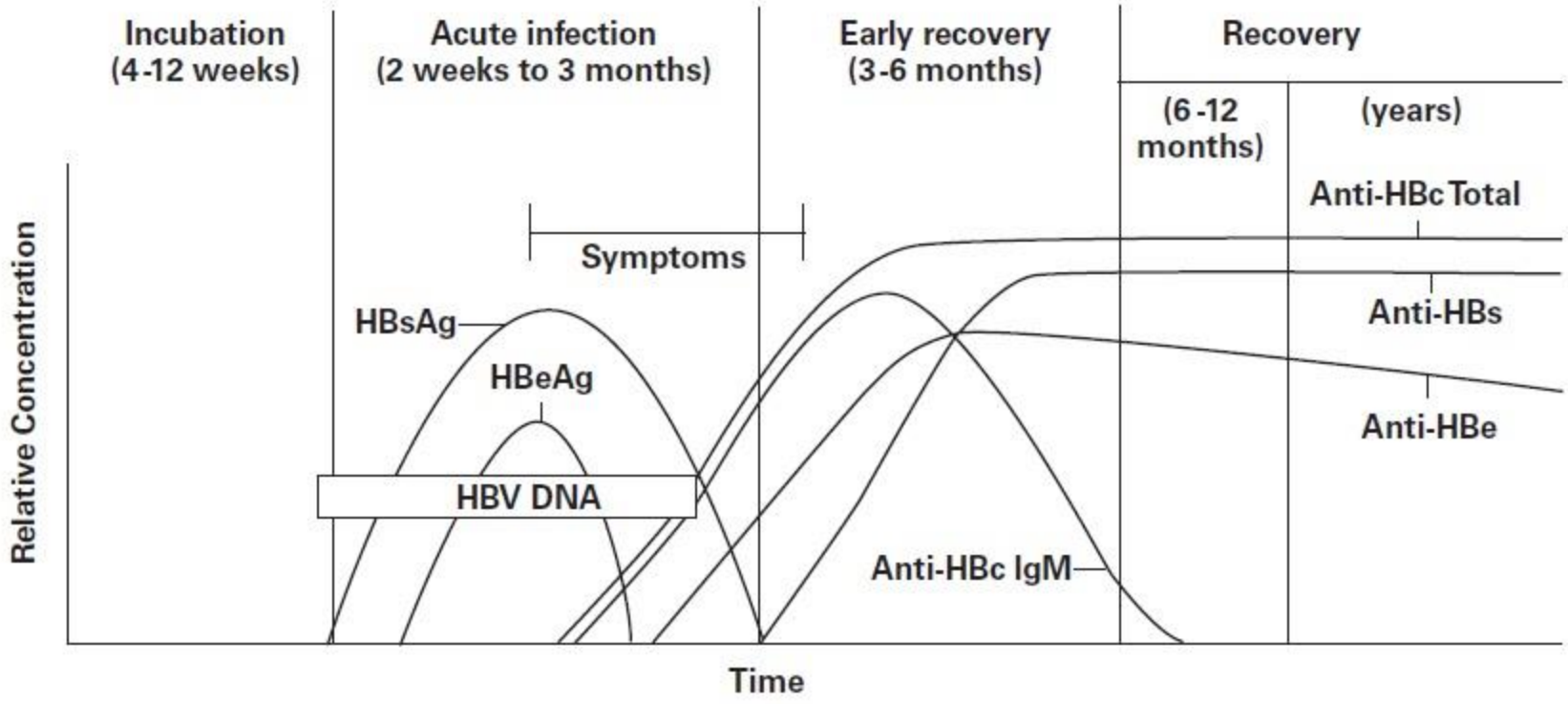
Clinical presentation

- Incubation 2-3 months
- Prodrome: anorexia, N/V, fever, arthralgia/myalgia, HA, pharyngitis, cough (Sx), dark urine/clay colored stool precedes jaundice (which is about 1-2 weeks into prodrome); RUQ pain, LFTs abnl
- Resolves over 3-4 month period
- Most HBV self-limited


INCUBATION PERIOD
ACUTE DISEASE
CONVALESCENCE AND RECOVERY
JAUNDICE
SYMPTOMS
Serum markers
HBeAg
HBV-DNA
HBsAg
IgM–anti-HBc
IgG–anti-HBs
IgG–anti-HBc
Serum transaminases
Anti-HBe
A
4–26 weeks (average 8)
4–12 weeks
4–20 weeks
Years
INCUBATION PERIOD
ACUTE DISEASE
CHRONIC DISEASE
JAUNDICE
SYMPTOMS
Serum markers
HBeAg
HBV-DNA
HBsAg
Serum transaminases
IgM–anti-HBc
IgG–anti-HBs
Anti-HBe
IgG–anti-HBc
B
4–26 weeks (average 8)
4–12 weeks
Months to Years

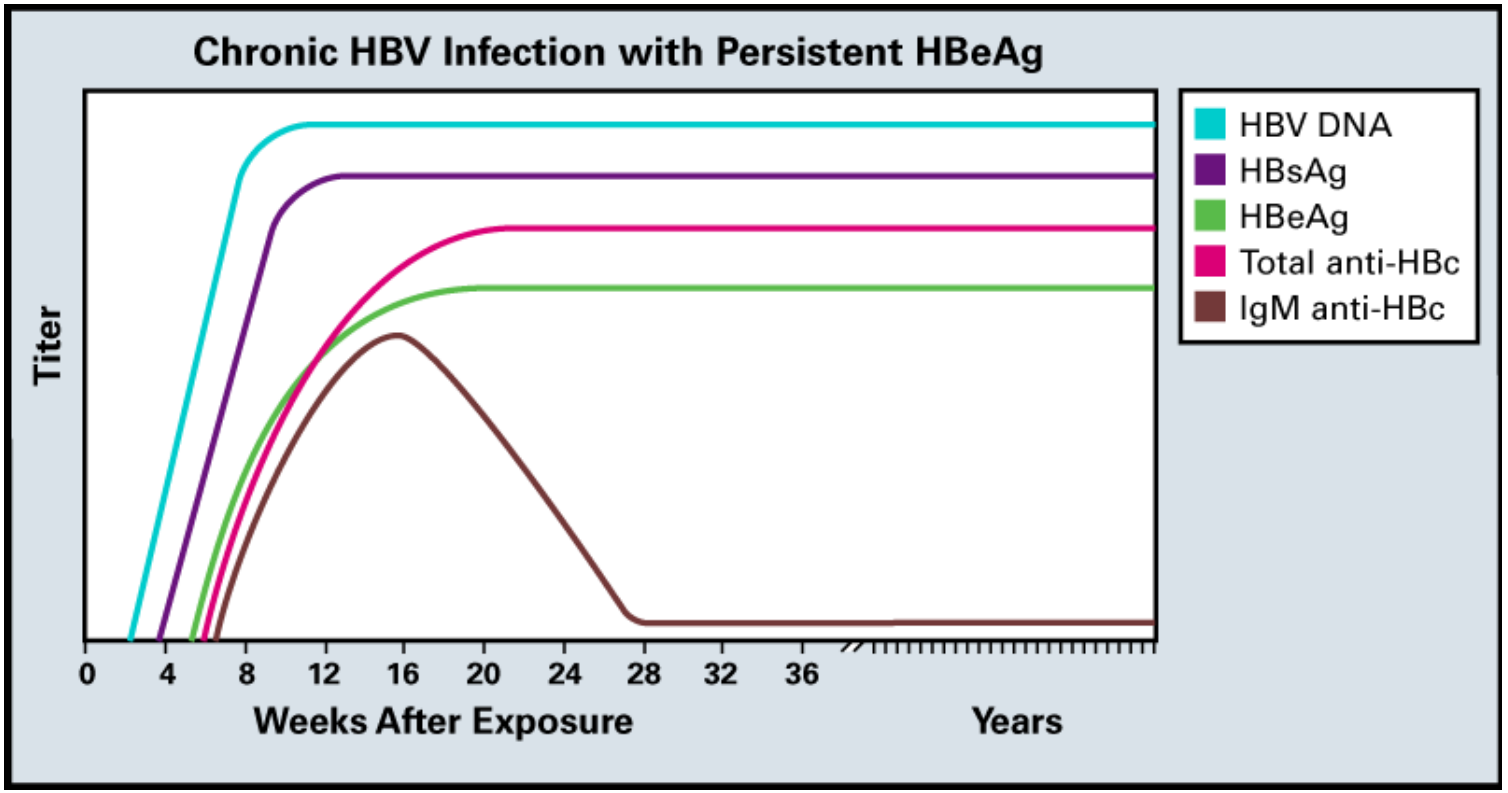
Serology

Acute infection which resolves



Serology

Chronic infection



Prevention

- Vaccines
  - Four: Engerix, Recombivax, Pediarix and TwinRix
- Series of 3 injections
- Interruptions?
- High dose Hep B vax
  - ESRD and other immunocompromised

Who should be vaccinated

- Pretty extensive list
  - All infants, beginning at birth and unvaccinated children aged <19 years
  - Susceptible sex partners of hepatitis B surface antigen (HBsAg)-positive persons
  - Sexually active persons who are not in a long-term, mutually monogamous relationship (e.g., >1 sex partner during the previous 6 months)
  - Persons seeking evaluation or treatment for a sexually transmitted disease
  - Men who have sex with men
  - Injection drug users
  - Susceptible household contacts of HBsAg-positive persons
  - Health care and public safety workers at risk for exposure to blood or blood-contaminated body fluids
  - Persons with end-stage renal disease, including predialysis, hemodialysis, peritoneal dialysis, and home dialysis patients
  - Residents and staff of facilities for developmentally disabled persons
  - Travelers to regions with intermediate or high rates of endemic HBV infection
  - Persons with chronic liver disease
  - Persons with HIV infection
  - Unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (discretion of clinicians for unvaccinated adults with diabetes mellitus who are aged ≥60 years)
  - All other persons seeking protection from HBV infection — acknowledgment of a specific risk factor is not a requirement for vaccination

Boosters?

- Immunocompromised based on serology?
  - ESRD on HD
  - Consider in setting of lost Hbsurf Ab and ongoing risk
  - ? HIV+, other immunocompromise in particular cell mediated immunity

Post exposure prophylaxis

- HBIG and vaccination
  - Perinatal (mom known HBsAg+ or unknown)
    - 0.5mL HBIG (IMMEDIATE)
    - Start vax in (1st 12 h life)
  - Needle stick/other
    - 0.06mL/kg IM in 14 days post exposure
    - Start vax series
    - Give vaccine and HBIG in separate sites

Neonatal infection

- BSAg and BEnvAg risk of perinatal infxn 70-90%
  - Most infxn during birth process
  - 90% infants develop chronic HBV
- Chronic subclinical disease with persistent BSAg and elevated LFTs
- Increased risk liver disease (Cirrhosis, ESLD, HCCA)
- No treatment → prevention is key
- Pregnant women tested for HBsAg at early prenatal or at delivery if not done
- Some HBsAg + women are treated with lamivudine or telbivudine during the 3rd trimester to prevent Tx

Treatment

- Most don’t need it (95-99% clearance rates)
- Nucleoside analogues
  - Lamivudine, tenofovir (DF and AF), entecavir
- Replicates in nucleus/incorporates into host genome (similar HIV)

NC epidemiology

A	B	C	D	E	F	G
Communicable Disease Counts for 2016, by Month and Disease Group						
Disease	**Number of Cases in June, 2016**	**Number of Cases January-June, 2016**	**Average Number of Cases January-June, 2011-2015**	**Number of Cases in 2015**	**Average Number of Cases Per Year, 2011-2015**	**How does the number of January-June 2015 cases compare to January-June 2011-2015*?**
Diphtheria	0	0	0	0	0	
Hepatitis B - Acute	4	39	54	166	131	
Hepatitis B - Chronic	27	241	514	988	1180	
Hepatitis B - Perinatal	0	0	1	1	1	
Measles	0	0	5	0	5	
Mumps	1	25	2	4	6	HIGHER
Pertussis	16	165	190	439	585	
Polio	0	0	0	0	0	
Rubella	0	0	0	0	0	
Rubella - congenital	0	0	0	0	0	
Tetanus	0	0	0	3	1	