HEPATITIS B

Virology	Hepnaviridae DNA small
Envelope proteins	pre-S1, pre-S2, **hepatitis B surface antigen (HBsAg)** glycoprotein in excess, circulating in blood independently from the virus major type: a determinant, main serotypes are *adw, ayw, adr* and *ayr.*
Nucleocapside antigens	**Hepatitis B core antigen (HBc)** not soluble, not circulating in blood; located in nucleus of infected hepatocyte **Hepatitis B e antigen (HbeAg),** derived from viral protein precursor not part of virion, secreted by infected hepatocytes
Hosts	Natural hosts: Only **humans**; Experimental hosts: Primates (chimpanzees, gorilla and gibbon)
Source Human	[HBV] blood of chronic carriers = 100 E6 - 10E9 /mL; internal fluids (CSF, pericardial, pleural, peritoneal, amniotic), semen, genital saliva and semen [HBV]= 1/1000th blood [HBV]; practically undetectable in stools and urine HbeAg+ :40% infection after needle stick; 2% infection; HbsAg+ ≤ lab detection threshold rarely infectious
Environment	HBsAg detected on contaminated surfaces; in dried blood at room temperature viable for 1 week;
Transmission	**Direct Parenteral exposure:** historically = serum hepatitis **Needle stick** main mode of transmission to HCWs; Mucosal exposure, non intact skin (eczema, dermatitis) **Parenteral drug users** **Human bites:** bite wounds inflicted by HBV infected patients ⇨ HBV prophylaxis; risk of infection very low. **STD**: 1/3 to 2/3 of HBV in USA from STD **Perinatal Transmission:** infants born to HBV-infected mothers = 70% (10% - 85%, f[viral DNA] mother & HbeAg status **In utero** small 5-10%; Infected newborns usually become HBV carriers; high risk for developing chronic liver disease **NOT transmitted:** aerosolized blood; Mucosal contact with saliva poses little if any risk **Households** of chronically infected, environment heavily contaminated with HBV: low transmission w toothbrushes, washcloths, close personal contact with blood or saliva contaminated fomites. **Environmental transmission:** clinical laboratory, hemodialysis unit **Inapparent transmission**: 40% HCW Inapparent exposure of skin or mucosal exposure

Risks	**Epi Situation**	**Low**	**Inter**	**High**	**Prevalence HbsAg %**	
Infants of mothers HbeAg+ = 70% infected, 90% infected ⇨ chronic carriers					North America	<2%
Infants of mothers HbsAg + = 10-20% infected	HBsAg	≤ 1%	1-7%	≥7%	Latin America, Caribbean	2-7%
Children 0-5 in household with HbsAg+ = additional 20-30%	anti-HBc or anti-HBs	5-15%	16-55%	40-90%	Western Europe	<2%
USA M: F 2:1;	Perinatal infection	<10%	10-20%	20% *		
US High risk groups	Early childhood infect	<10%	10-50%	60%	Eastern Europe	2-7 %
Parenteral drug abusers (10-15% of cases)	Adult infection	90%	20-50%	20%	Middle East	2-7%
Individuals with multiple sexual partners (15-40%)					Sub-Saharan Africa	≥8%
Homosexuals (15-20%)					Asia	2-7%
Before HB vaccine: HCW (dentists, hemodialysis, lab tech,surgeons)					China	≥8%
patients in hemodialysis, w blood transfusions or blood products					Australia /Oceania /SEAsia	<2%

Pathogenesis	Viral replication in hepatocytes. HBV not directly cytotoxic for hepatocytes. damage due to immune reactions: cytotoxic T lymphocytes attack hepatocytes
Incubation	45-180 days (average 60-90 days)
Communicability	Variable; may start weeks before onset; during HBsAg carriage; chronic carriers; anti-HBc usually not infectious
Definition	
HBV acute hepatitis	Clinical case: An acute illness with a) discrete onset of symptoms and b) jaundice or elevated serum aminotransferase levels Laboratory criteria: IgM-antiHBc positive (if done) or HBsAg positive and IgM antiHAV negative (if done) Confirmed: a case that meets the clinical case definition and is laboratory confirmed
Chronic HBV	Confirmed: HBsAg Pos on two occasions at ≥6 months interval; Probable: HBsAg Pos and anti-HBc IgM Neg Persons w chronic hepatitis or HbsAg+ **not** to be reported as acute viral hepatitis unless evidence of acute viral hepatitis
Perinatal HBV Infection	Clinical Perinatal hepatitis B in newborn range from asymptomatic to fulminant hepatitis Laboratory criteria: Hepatitis B surface antigen (HBsAg) positive
Clinical	Asymptomatic infection: mostly childhood infections
Acute Hepatitis B	Prodromal phase: malaise, weakness, anorexia, myalgia and arthralgia, macular rash (30%) Few days: 30% jaundice; persist for weeks;. Hepatocyte lesions: Liver enzyme abnormalities
Fulminant hepatitis	1% of adults with jaundice
Chronic infection	Risk f[age]: 90% in newborns; 30% in children ≤5 years of age; 2 to 10% in older age groups 5-10% Chronic active hepatitis or cirrhosis; Primary Hepatocellular carcinoma (PHC)

Serology		
HBsAg	↑ during incubation period, before onset; persists from week 4 to 8, (2 week - 16 weeks); present 95% in acute phase 70% at time of resolution of sx; wanes during convalescence; HbsAg- primary infections: no detectable levels although antibodies develop (usually asymptomatic) Immuno-diffusion (old), reversed passive hemagglutination (RPHA less sensitive) , radio-immuno assay (RIA) or enzyme-immuno assay (EIA)	
anti-HBs	after HBsAg waned; after clinical recovery, ↑ 6- 12 months; persist for life; Associated with protection against reinfection titers above 10 mIU/ml OK; rapid anamnestic response may protect individuals with prior levels ≥10 mUI/ml	
50-70%	Typical	weeks to months between disappearance of HBsAg and apparition of antiHBs
10%	No antibody	HbsAg last 2-4 months, then no anti-HBs
10%	HBsAg Neg Primary Infection	AntiHBs ↑ in few weeks
10%	Complexes	antigen-antibody immune complexes; with arthritis /rashes; few without imm/complex disease
10%	HbsAg Carriers	
anti-HBc	onset of symptoms, rises to a maximum in about 6 weeks, decreases but persists from 5 years to a lifetime IgM arises early at the onset of disease and persists a few months (6, maximum 24 months) then IgG for lifetime **window period** w anti-HBc only marker present between HbsAg decline and anti-HBs appearance antiHBc alone over a long time period may represent either a false positive test or a decay of the anti-HBs titer	
HBeAg	↑ very early, at onset of disease; lasts only 1-2 weeks; appears few days after HbsAg; rise and fall parallels HBsAg HBeAg = marker of viral replication and high infectivity	
Anti HBe	Develop after HbeAg gone; anti HBe = viral multiplication peaked and infection ↓;lasts 1-2 years	
HBV-DNA	High in HbeAg+; 20% of chronic carriers with HbeAg neg tests	
chronic HBsAg carriers	95% w DNA polymerase activity, HBcore antigen or virion DNA = persistence of viremia 05% non infectious chronic carriers: HBsAg without active virions persistent high levels of anti-HBc; 25% have persistent HBeAg in the serum, and the others have anti- Hbe Persistent infections ↓ over years with HBsAg, HBeAg and virions DNA titers falling slowly. # 2% of patients lose HBsAg /year	
HbsAg- chr carrier	rare HBsAg negative persistent HBV infections; high anti-HBc titer; HBsAg titers undetectable; may transmit HBV to blood recipients	
Viral isolation	cultures difficult, not routine; Identification of HBV-DNA and polymerase chain reaction testing available not routine	

Serologic markers

Clinical									
HbsAg		**+++**	**++**	**+**	chronic carriers				
AntiHBs									
antiHbc			**++**	**+++**	**++**	**++**	**++**	**+**	
HbeAg			+	+++					
antiHBe									
	4 weeks	8	12	16	26 weeks	1 Yr	2	5	10

PH Lab Testing OK			
	Dx in symptomatic	Confirm HBV, r/out other	HBsAg; anti-HBcIgM; anti-HAVIgM
	Followup of previous HBsAg+ pt	Confirm resolution or carrier state	HBsAg; anti-HBs
	Prenatal screening	Identify HBsAg+ pregnant woman	HBsAg; if positive: anti-HBcIgM;
	Followup of infant born to infectious mother	Monitor effectiveness of HBvaccine & HBIG	HBsAg; anti-HBs;
	Refugee screening	Identify HBsAg+ carrier; contact inv	HBsAg; if positive: anti-HBcIgM;
	Sexual or needle sharing ctc on infected ind	Identify new infection	HBsAg; anti-HBs; if positive: anti-HBcIgM
	Household contact of HBV carrier	Identify new infection	HBsAg; anti-HBs; if positive: anti-HBcIgM
	Source patient of percutaneous exposure	Identify source of infection	HBsAg; if positive: anti-HBcIgM
	HDept HCW w percutaneous exposure	Identify antibody level	Anti-HBs
NOT for	**NOT:** screening of HCW; post vaccine immune status of HDept employee		
Collection	Whole blood in red-top tube or serum separator tube		

Treatment	
Lamivudine 1998 3TC = Efavirenz	Action: HBV polymerase integrates 3Tc into the DNA chain and inhibits viral replication usual dosage = 150 mg bid, for HBV infection 100 mg bid improves necroinflammatory activity, reduces progression of fibrosis, converts HbeAg carriers (16%), reduces HBV DNA carrier state (98%), ALT normalization (72%)

HEPATITIS B

Vaccine	
Recombinant vaccines	**Engerix-B** (Smith-Kline), **Recombivax** (Merck); Yeast genetically modified to produce purified vaccine anitgen Store in refrigerator at 2-8 °C;
Eligibility	**ALL NEWBORNS** soon after birth, then at 2 months and at 6-12 months; availableto all in 1991; legal requirement in 1995 **Sex**: Sex/active homosexual /bisexual men, ≥1 sex partner in the preceding 6 months, STD patients, sexual contacts of infected, **HH**: household contacts of HBV carriers, **HCW:** College students in BBF exposed occupation, HCW w BBF exposure, **ParDU:** inmate in long term correctional facilities, parenteral drug users, **Patients:** Clients of institutions w disabled student w behavior or problems increasing risk of BBF exposure, hemodialysis patients
Schedules	3 doses of vaccine at 0, 1 and 6 months; Engerix-B also as 4 dose vaccine alternative schedule of 0, 1, 2, and 12 months also has been approved for one vaccine
Dose	Check vaccine info: formulation for infant /adults; 0.5 mL in infants (for Recombivax higher for infant of +mother); 0.5 to 1 mL for adults
Administration	administered IM in the deltoid - not in a buttock;
Protection	90% in adults, 95% in infants & children; ≥10 years after primary series; protected even if no detectable antibodies (40% after 5 years) because of rapid anamnestic response if challenged with live virus
Contraindications	Pregnancy OK
Precautions	**HIV infection:** impaired response; test for anti-HBs 1-2 months after 3rd vaccine dose; revaccination of non-responders more likely to become chronic carriers
Safety	20 million in USA; 500 million persons worldwide [thimerosal] in new pediatric/adolescent formulation of vaccines (<1 µg of thimerosal/0.5 mL vaccine) reduced by > 96%.
Adverse reactions	pain at the injection site, mild to moderate fever no confirmed scientific evidence of multiple sclerosis, chronic fatigue syndrome, rheumatoid arthritis, or autoimmune disorders Guillain-Barré syndrome, transverse myelitis, optic neuritis, and seizures 1 in 600,000 anaphylaxis (hives, difficulty breathing, shock); 1 /150,000 in Canada & NZ; rare reports of hair loss expected 4,000 to 5,000 HBV-related liver disease deaths would occur without immunization, # 5% lifetime risk of HBV infection.
Immune Globulin	Postexposure prophylaxis with 0.06 mL/kg of Hepatitis B immune globulin (HBIG) in a single IM dose within 14 days of last exposure Adult 60kg = 3.6mL; 5mL max; $150 /mL; medicaid covered; not supplied by HDept;

PUBLIC HEALTH			
Case Management	See below		
Blood , organ, semen donation	Blood & blood products donor screening; required by law		
Pregnancy &NBorn	Screening during pregnancy and immuno-prophylaxis of newborns of infected mothers		
Immunization pgm	See Vaccine		
HCW BBFE	Screening; Immunization; Post exposure prophylaxis		
IControl	Prevention of environmental transmission		
Screening programs	Immigrants, refugees, children adopted from high risk areas		
Tatoo, body piercing	Regulation		
Surveillance			
Acute HBV infection **Chronic carrier**	**Report;** Fill CDC Form; verify lab tests; **Exposure Hx:** Contact w HBV pt; travel outside US; parenteral drug use; multiple sex partners; blood recipent, dental procedure; **Risk factors:** close ctc w babies or children at home or work; employment in food svcs or health care; **Vaccine & serologic testing Hx**; hx of blood donation rejection		
Exclusion	None		
Isolation Precaution	**Universal precautions** sufficient		
Case management			
	1-Refer to PMD for case management; 2-Investigate source of disease; 3-Test & counsel contacts; 4-HBIG /Vaccine for susceptible contacts; 5-Retest annually for 2 years to assess new exposure;		
Source Investigtn	Personal contact; Sexual partner; Blood product; Transplant; Dialysis; injectable Drug use; Occupational exp to BBF; Tatoo, bodypiercing;		
Ctc investigation	ID contacts (see source) Test contacts; HBIG /Vaccine for susceptible contacts Other cases in outbreak		
Sex exposure **Inj DU exposure**	**HBIG + vaccination** administered ≤ 14 days of exposure. **HBIG + vaccination** administered ≤ 7 days of exposure.		
Household Contact	Education ; All household contacts should be evaluated and if susceptible, immunized.		
Pregnancy & NB			
Screen pregnant F **Vaccine + HBIG** **Postvaccin. testing** **Incomplete vacc inft**	**Required by law;** all mothers; HbsAg at first prenatal visit; re-screening at 32 wks for new /continuous exposure, sx, newborns whose mothers have hepatitis B or are carriers of hepatitis B: HBIG is administered at the dose of 0.5ml IM as early within the first 24 hours of life Hep B vaccine at 0.5ml (low risk newborn only 0.25 ml) at same time at different site Universal precautions; Newborn should be bathed thoroughly with soap and water, removing all external traces of blood for antibody to HBsAg recommended from 3 to 6 mos following completion of vaccine series If HBIG and initial vaccine delayed for >1 month after birth, testing for HBsAg may determine if infant is already infected. **HBIG:** Incomplete vaccination because age < 1yr and mother or primary care giver with acute infection		
HCW BBF Exposure	Exposed employee	Source patient is HBsAg carrier	Source patient HBsAg neg or unknown
	Not immunized	HBIG *1 & start HBV immunization	Start HBV vaccine
	Previously Immunized, known responder	AntiHBs: Pos⇨No action; Neg⇨HBV booster	No action
	Non responder	HBIG *1 & HBV booster	No action
	Immunized but response unknown	AntiHBs: Pos⇨No action; Neg⇨HBIG & HBV booster	No action
Environmental Contamination	**Use common sense: 1-Know what is clean;2- Know what is contaminated; 3-Keep the two separate; 4-Disinfect**		
Information	Hepatitis Hotline of the Hepatitis Branch, CDC at 1-888-4HEP-CDC (or 1-888-443-7232)		
	National Immunization Program, CDC Information Hotline at 1-800-232-2522; CDC Hepatitis Branch website at http://www.cdc.gov/ncidod/diseases/hepatitis/ CDC National Immunization Program website at http:/www.cdc.gov/nip		