

VIRAL AND AUTOIMMUNE HEPATITIS

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CAUSES OF ACUTE HEPATITIS

- Viral hepatitis
- Other infectious etiologies e.g. CMV, EBV, TB
- Alcoholic hepatitis
- Drug hepatitis
- Ischemic hepatitis
- Choledocholithiasis

Virus	Genome	Genome size (kb)	Envelope	Family / genus
HAV	RNA positive sense, single stranded, linear	7.5	-	Picornaviridae hepatovirus
HBV	DNA partially double stranded, circular	3.2	+	Hepadnaviridae
HCV	RNA positive sense, single stranded, linear	9.6	+	Flaviviridae hepacivirus
HDV	RNA positive sense, single stranded, linear	1.7	+	Unclassified (viroid), delta virus
HEV	RNA positive sense, single stranded, linear	7.5	-	Unclassified, togavirus and alpha virus-like

WHAT IS HEPATITIS ?

- Inflammation of the liver
- Almost always, inflammation implies elevation in liver enzymes
- AST and ALT are the key liver enzymes
- Other Liver Function Tests (LFTs) which can be abnormal in hepatitis include:
 - Bilirubin, albumin, alkaline phosphatase, gamma glutamyl transpeptidase

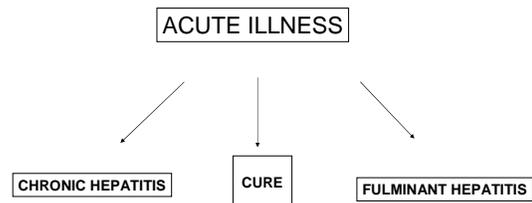
OTHER INFECTIOUS ETIOLOGIES OF ACUTE HEPATITIS

- CMV - cytomegalovirus;
immunocompromised host
- EPSTEIN-BARR – mononucleosis;
lymphadenopathy; splenomegaly
- TB and M. avium intracellulare (MAI)

SYMPTOMS OF ACUTE VIRAL HEPATITIS

- Fatigue, nausea, anorexia
- Jaundice
- Low-grade fever, abdominal pain
- Arthralgia, myalgia, headache

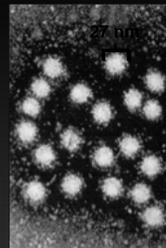
OUTCOMES OF VIRAL HEPATITIS



SIGNS OF ACUTE VIRAL HEPATITIS

- Fever – low grade
- Jaundice
- Hepatomegaly with RUQ tenderness
- Splenomegaly - infrequent

Hepatitis A Virus



- Nucleic Acid: 7.5 kb ssRNA
- Classification: *Picornaviridae*, *Hepatovirus*
- One serotype and multiple genotypes
- Nonenveloped, acid and heat stable
- In vitro model: monkey and human cell cultures
- In vivo replication: in cytoplasm of hepatocyte; human and other higher primates

LIVER BLOOD TEST ABNORMALITIES IN ACUTE VIRAL HEPATITIS

- AST AND ALT - 1000-5000 IU
- Bilirubin – generally elevated – both conjugated and unconjugated
- Alkaline Phosphatase – minimally elevated
- Bilirubin and urobilinogen increased in urine

Global Prevalence of Hepatitis A Infection

HAV Prevalence

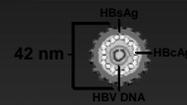
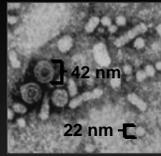
- High
- Intermediate
- Low
- Very Low



HEPATITIS A

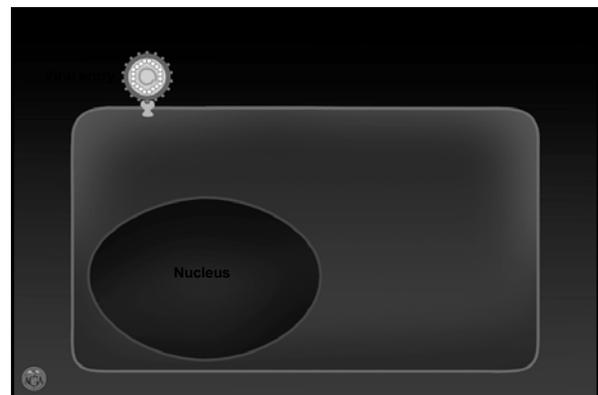
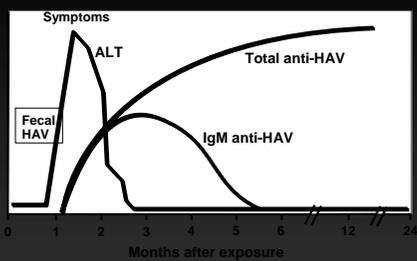
- Oral fecal route of transmission
- Excreted in stool about 2 weeks prior to clinical illness
- 1 month incubation period
- Children often asymptomatic
- Never causes chronic hepatitis

Hepatitis B Virus



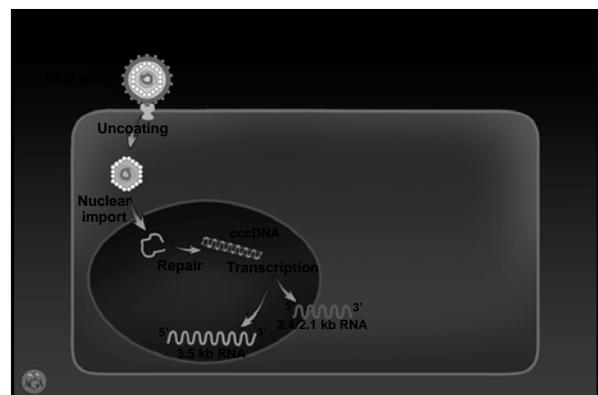
- Nucleic Acid: 3.2 kb DNA
- Classification: *Hepadnaviridae*
- Multiple serotypes and genotypes A-F
- Enveloped
- In vitro model: primary hepatocyte culture and transfection of cloned HBV DNA
- In vivo replication: in cytoplasm, cccDNA in nucleus; hepatocyte and other tissues, human and other primates

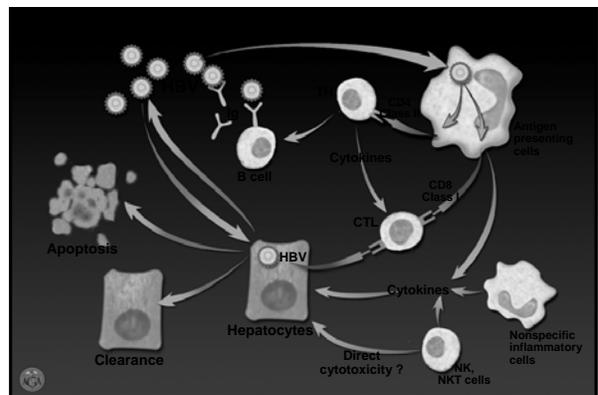
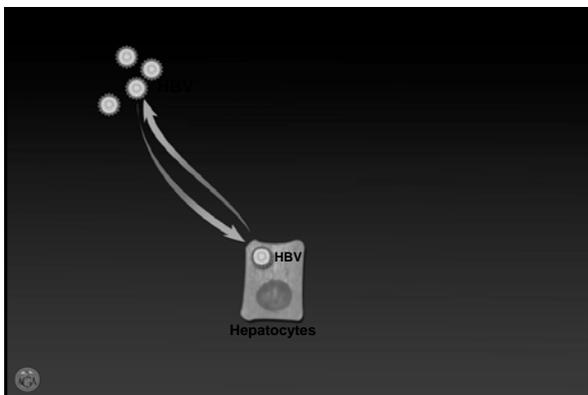
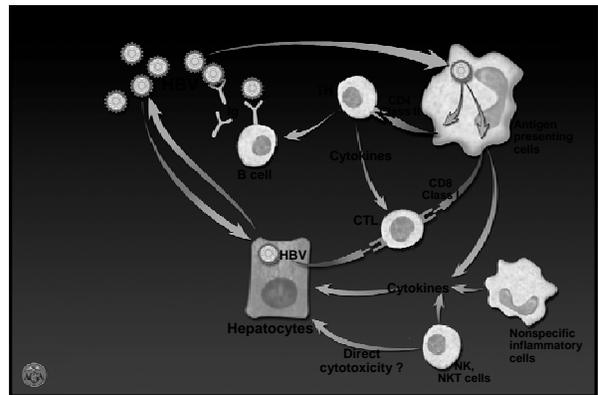
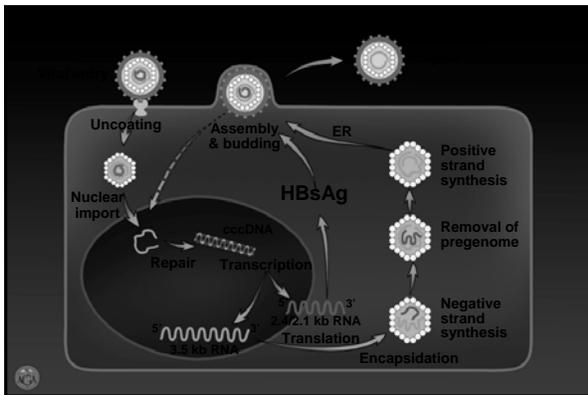
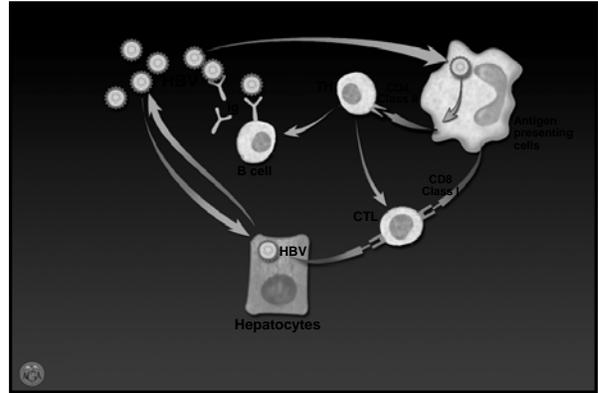
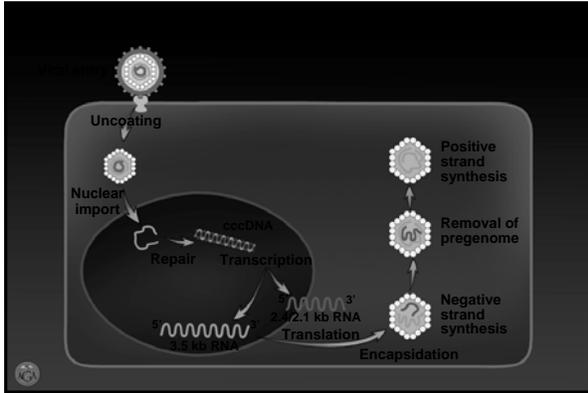
Typical Serologic Course of Acute Hepatitis A Virus Infection



HEPATITIS A PREVENTION AND TREATMENT

- No treatment of infection available
- Passive immunity with gamma globulin can ameliorate disease in early stages of the infection
- Gamma globulin can prevent disease pre-exposure
- Vaccine available to induce active immunity

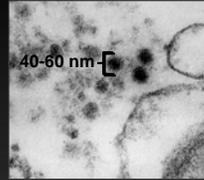




HEPATITIS B CLINICAL

- Transmission – parenteral, secretions, sexual mother to child (vertical)
- 6-8 week incubation
- 20% of patients have serum sickness prodrome
- 4% of patients develop chronic hepatitis
- Treatment and vaccine available

Hepatitis C Virus



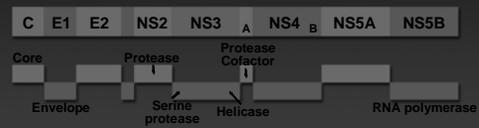
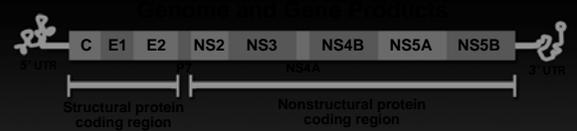
- Nucleic Acid: 9.6 kb ssRNA
- Classification: *Flaviviridae*, *Hepacivirus*
- Genotypes: 1 to 6
- Enveloped
- In vitro model: primary hepatocyte and T cell cultures; replicon system
- In vivo replication: in cytoplasm, hepatocyte and lymphocyte; human and other primates

Serological Markers

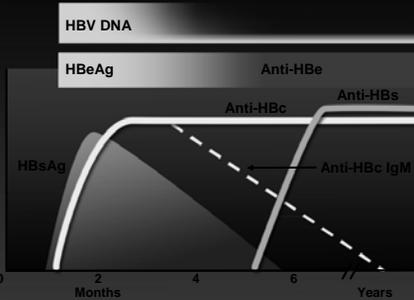
HBsAg
Anti-HBc IgM
HBeAg
Anti-HBe
Anti-HBs
Anti-HBc IgG and HBsAg
Anti-HBc IgG and anti-HBs

Clinical Significance

Acute/Chronic infection
Acute infection
High infectivity
Low infectivity
Immunity
Chronic infection
Resolved infection

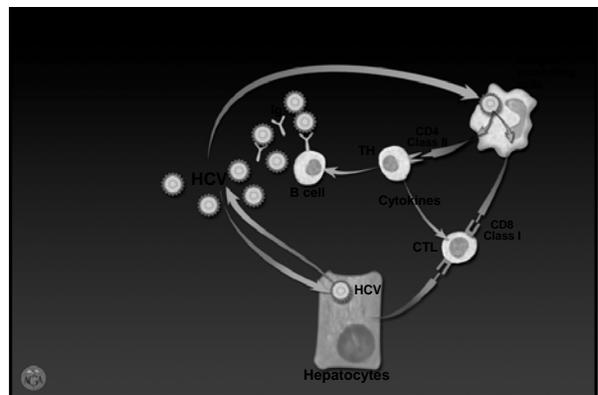
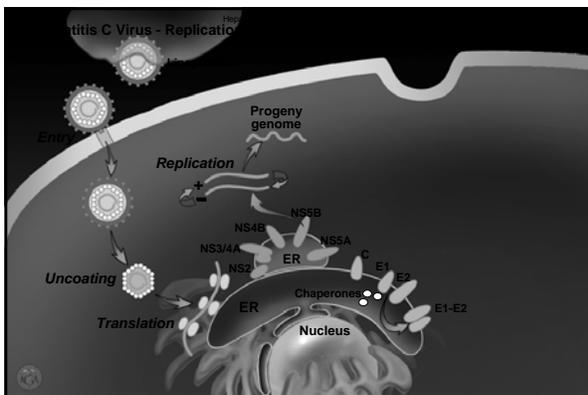
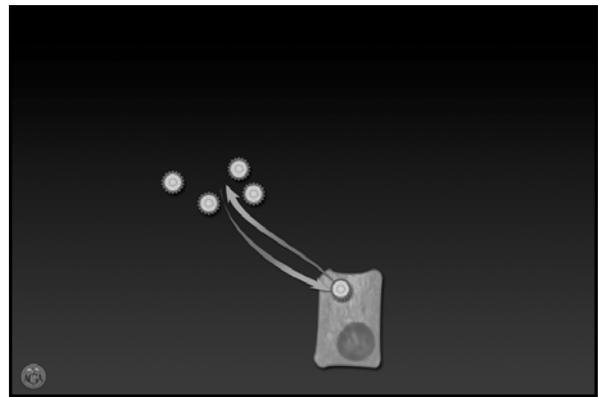
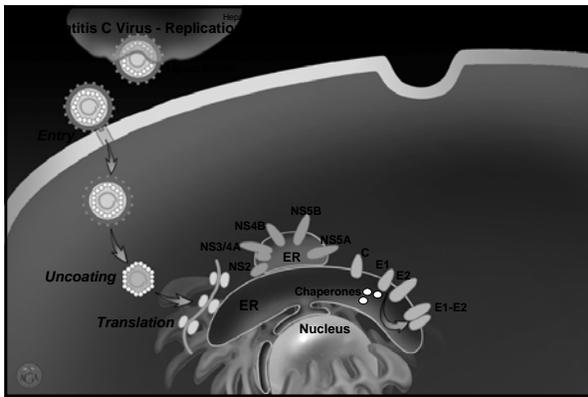
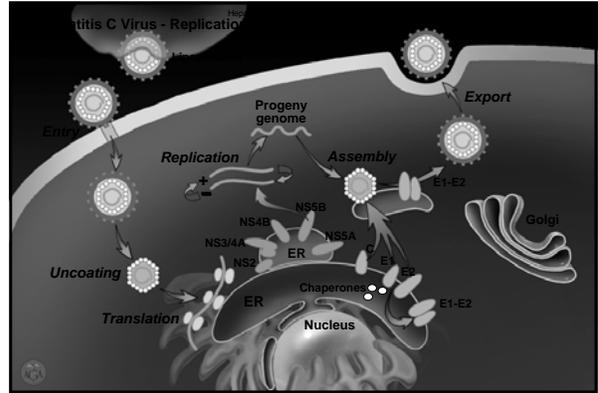
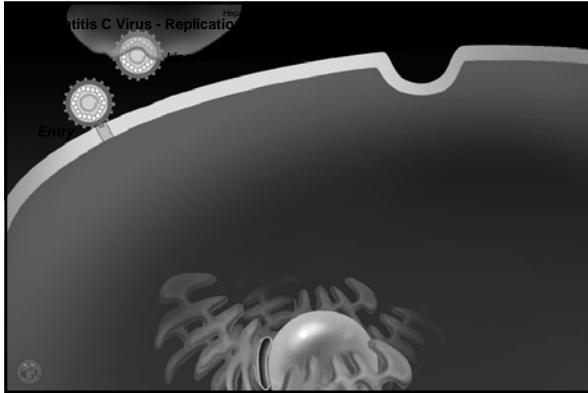


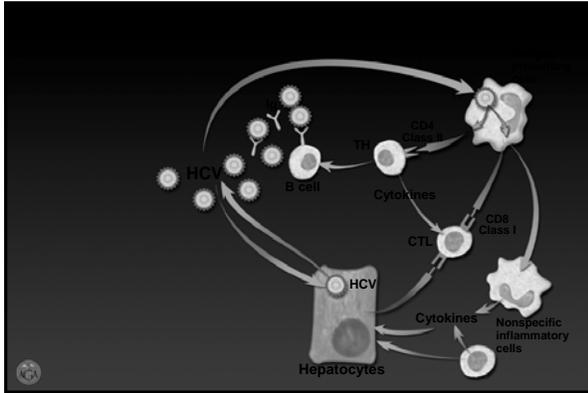
Acute HBV Infection



Gene Products and Functions

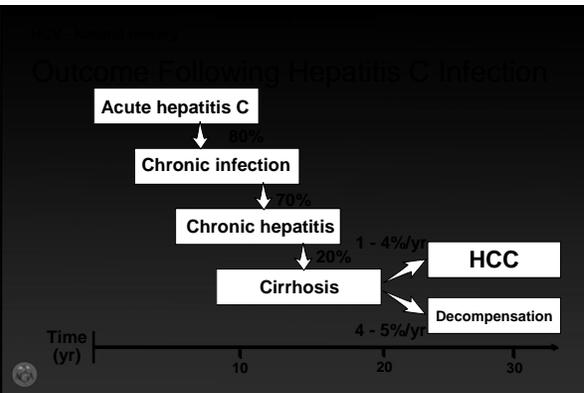
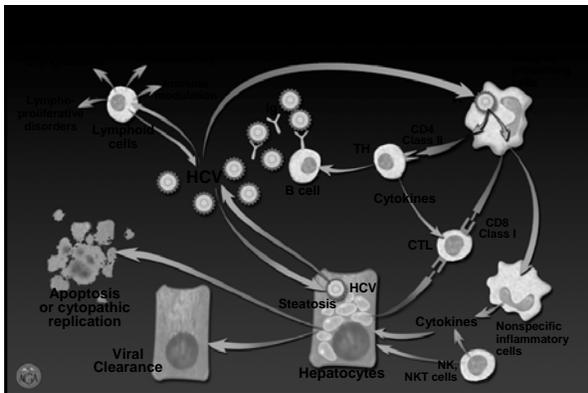
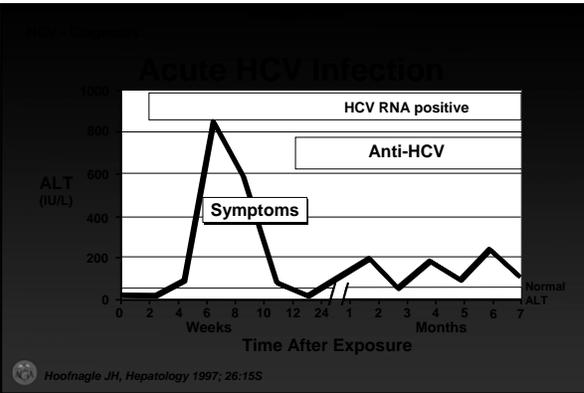
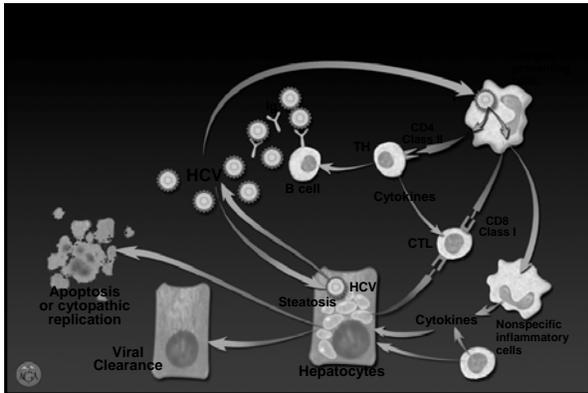
Core (C)	Nucleocapsid
E1 and E2	Envelope proteins hypervariable region in E2
p7	Nonstructural, ion channel (?)
NS 2	NS 2-3 protease
NS 3	Protease, nucleotide triphosphatase, and RNA helicase
NS 4	Cofactor for NS 3 protease activity
NS 4B	Formation of membranous web
NS 5A	Interferon sensitivity sequence
NS 5B	RNA-dependent RNA polymerase





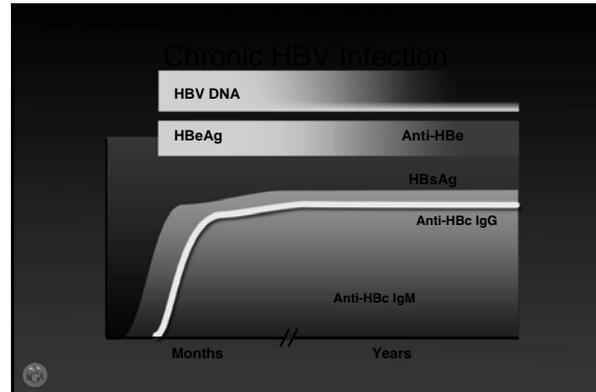
HEPATITIS C CLINICAL

- Most common cause of chronic hepatitis in USA
- 1.5% of population in USA carries the virus
- Parenteral transmission – blood, sexual
- 6-8 week incubation period
- Acute infection generally mild
- 80% of acute develop chronic disease
- No vaccine available
- Treatment – 40-80% cure rate



HEPATITIS D AND E

- HEPATITIS D
 - Also known as delta agent
 - Uses the HBsAg protein coat
 - Hepatitis B must be present – coinfection or preexist
- HEPATITIS E
 - Water borne virus resembling hepatitis A
 - Rarely seen in USA



CHRONIC HEPATITIS

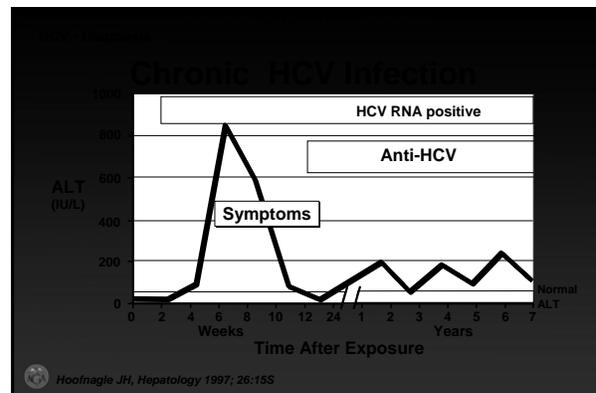
- Fatty liver
- Viral – B and C
- Autoimmune
- Drugs
- Alcohol
- Metabolic
- Others – CHF, hemochromatosis, vasculitis, IBD, celiac disease, neoplasia, etc.

Serologic events in HBV infection

	HBsAg	anti-HBs	HBeAg	Anti-Hbe	Anti-HBc IgG	anti-HBc IgM	HBV DNA	ALT
Acute HBV Infection	+	-	+	-	+	+	+	↑↑
Vaccine Responder	-	+	-	-	-	-	-	Normal
Exposure with Immunity	-	+	-	+/-	+	-	-	Normal
Chronic HBV (Wild Type)	+	-	+	-	+	-	+	↑/N
Chronic HBV (Precore Mutant)	+	-	-	+	+	-	+	↑/N
Inactive Carrier	+	-	-	+	+	-	+/-	Normal

CHRONIC HEPATITIS B AND C

- Cirrhosis develops in 20% of patients
- Liver failure and hepatoma develop in about 1/2 of cirrhotics
- Diagnosis of chronic hepatitis made on basis of:
 - chronic AST and ALT elevations
 - positive serology
 - positive DNA or RNA in blood
 - some patients have normal liver enzymes
- Treatment available with varying success rates



AUTOIMMUNE HEPATITIS

- Genetically predisposed host exposed to an environmental agent triggering an autoimmune response directed at liver antigens leading to a necroinflammatory response
- Associated with other autoimmune diseases - thyroid disease, colitis, hemolytic anemia, ITP, diabetes, celiac disease, polymyositis, pericarditis, SLE, MCTD

AUTOIMMUNE HEPATITIS

- Clinical presentation – generally female, fatigue, jaundice, hypergammaglobulinemia, elevated AST and ALT
- Presence of associated autoantibodies – ANA, thyroid antibodies, LKM, smooth muscle
- Diagnostic liver biopsy – interface hepatitis and plasma cell infiltration
- Treatment - steroids and immunosuppressants

END