

VIRAL AND AUTOIMMUNE HEPATITIS

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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

CAUSES OF ACUTE HEPATITIS

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

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

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

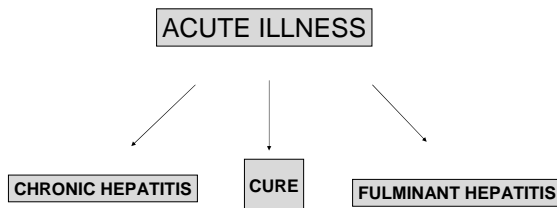
SIGNS OF ACUTE VIRAL HEPATITIS

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

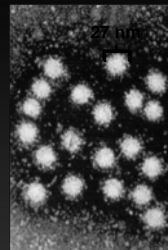
LIVER BLOOD TEST ABNORMALITIES IN ACUTE VIRAL HEPATITIS

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

OUTCOMES OF VIRAL HEPATITIS



Hepatitis A Virus



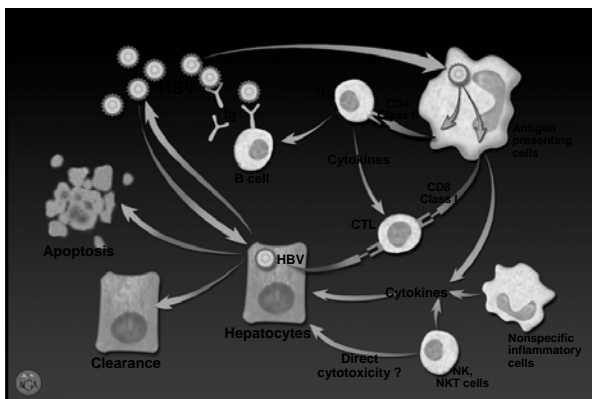
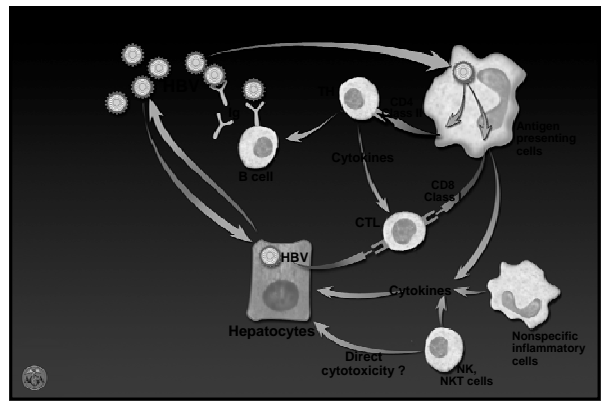
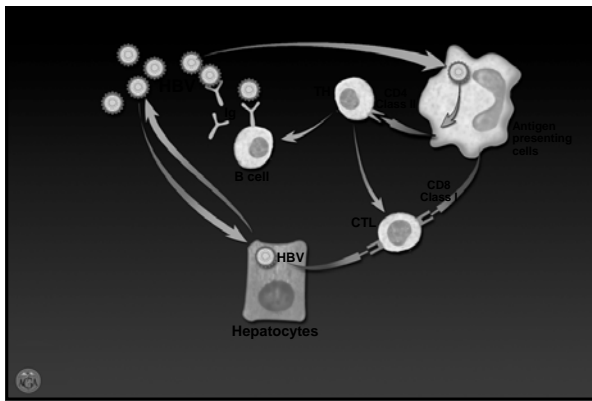
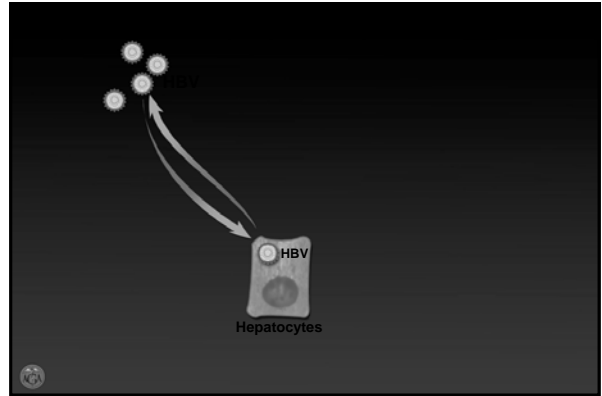
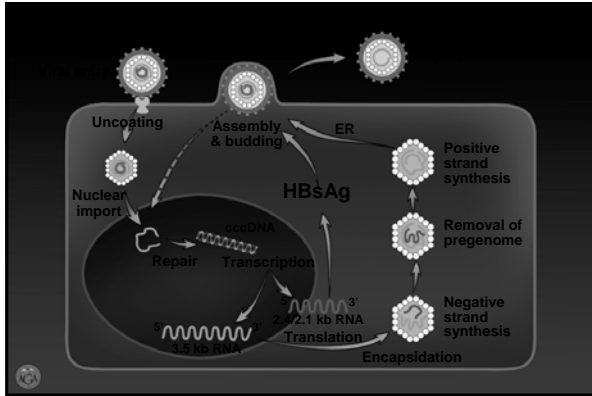
- Nucleic Acid: 7.5 kb ssRNA
- Classification: *Picornaviridae*, *Hepatovirus*
- One serotype and multiple genotypes
- Nonenveloped, acid and heat stable
- In vitro model: monkey and human cell cultures
- In vivo replication: in cytoplasm of hepatocyte; human and other higher primates

Global Prevalence of Hepatitis A Infection



HEPATITIS A

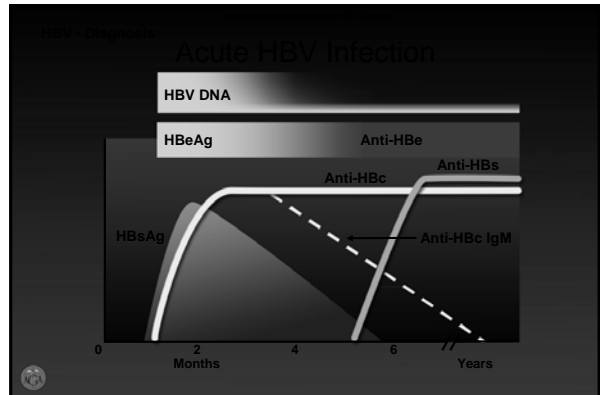
- Oral fecal route of transmission
- Excreted in stool about 2 weeks prior to clinical illness
- 1 month incubation period
- Children often asymptomatic
- Never causes chronic hepatitis



**HEPATITIS B VIRUS
NATURAL HISTORY**

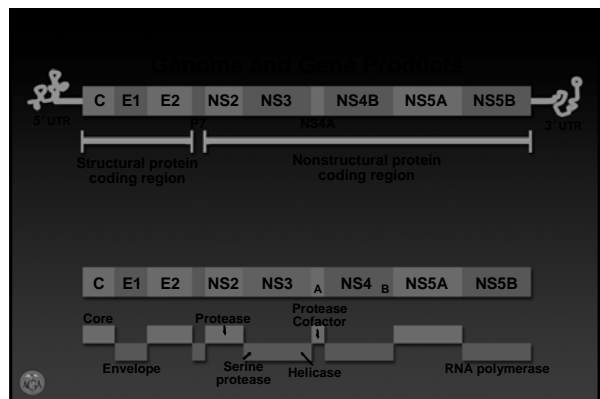
- Transmission – parenteral, secretions, sexual mother to child (vertical)
- 6-8 week incubation
- 20% of patients have serum sickness prodrome
- 4% of patients develop chronic hepatitis
- Treatment and vaccine available

Serological Markers	Clinical Significance
HBsAg	Acute/Chronic infection
Anti-HBc IgM	Acute infection
HBeAg	High infectivity
Anti-HBe	Low infectivity
Anti-HBs	Immunity
Anti-HBc IgG and HBsAg	Chronic infection
Anti-HBc IgG and anti-HBs	Resolved infection



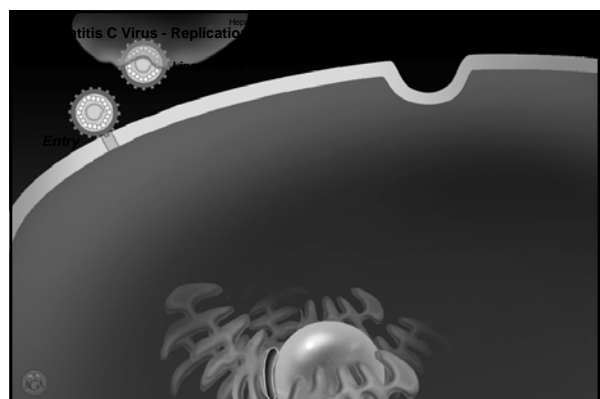
Hepatitis C Virus

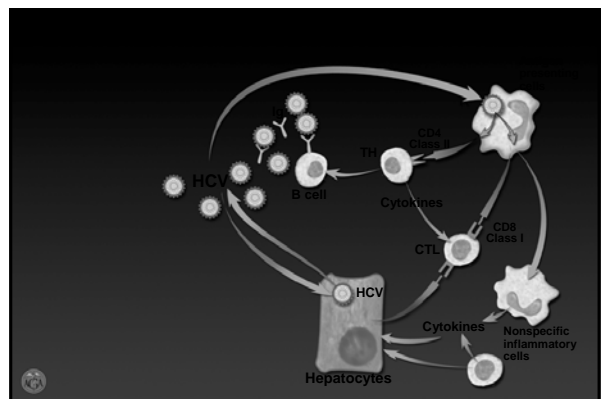
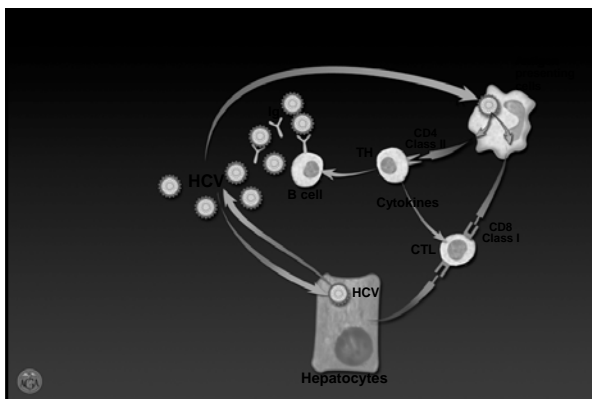
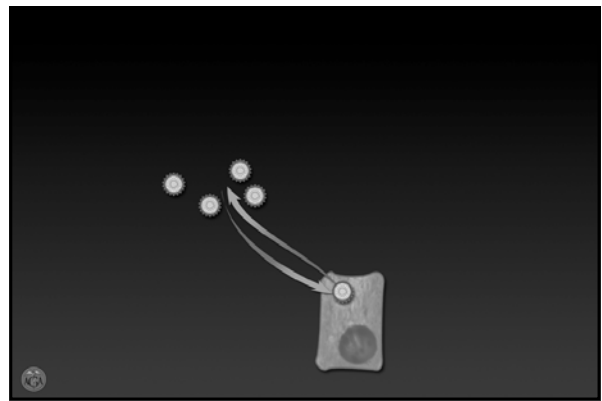
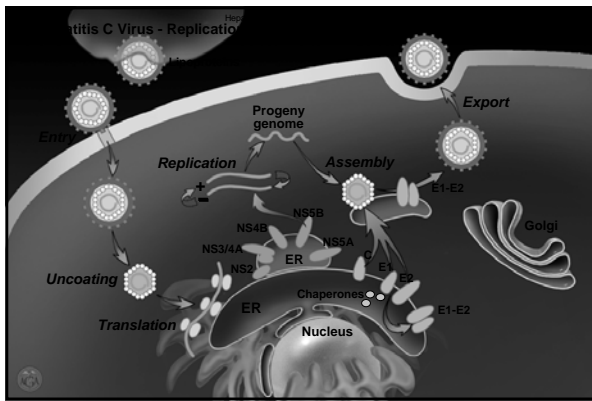
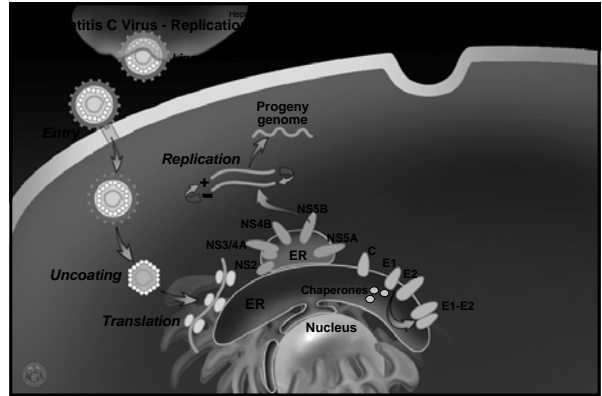
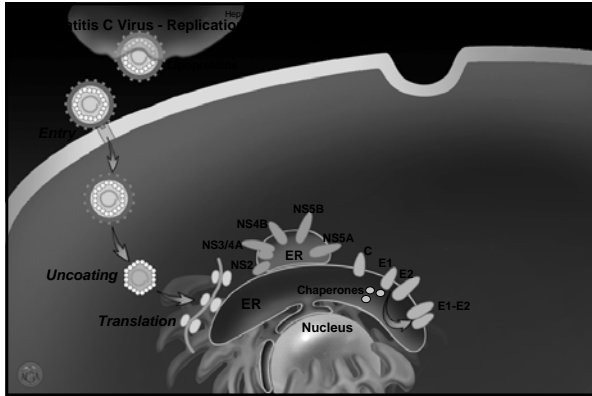
- Nucleic Acid: 9.6 kb ssRNA
- Classification: *Flaviviridae*, *Hepacivirus*
- Genotypes: 1 to 6
- Enveloped
- In vitro model: primary hepatocyte and T cell cultures; replicon system
- In vivo replication: in cytoplasm, hepatocyte and lymphocyte; human and other primates

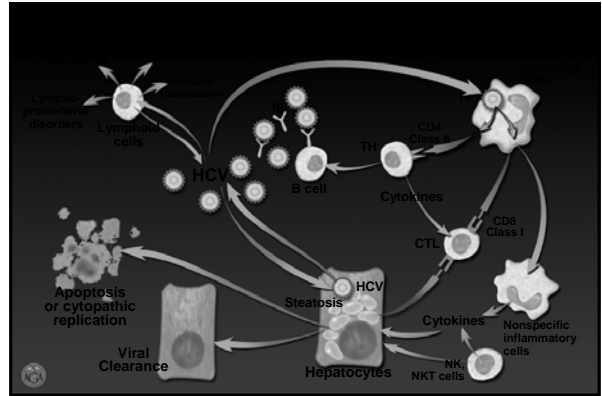
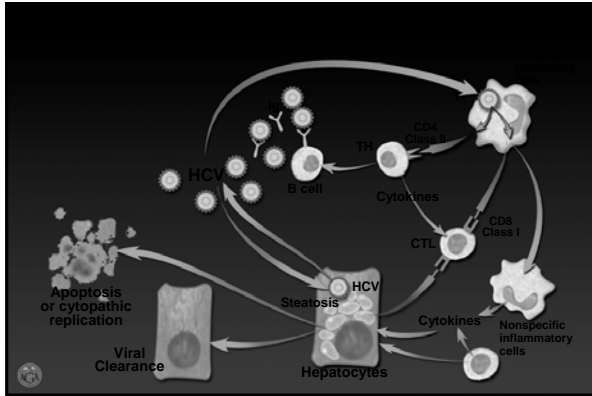


Gene Products and Functions

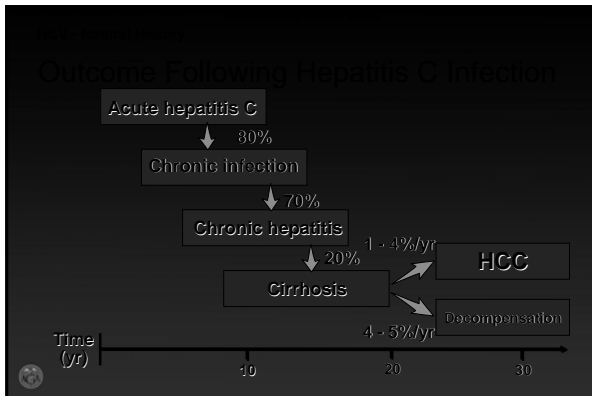
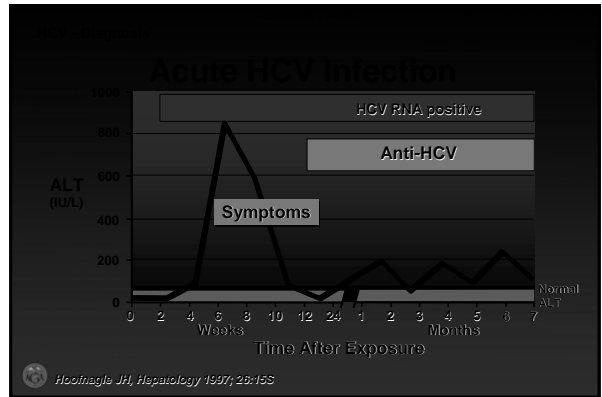
Core (C)	Nucleocapsid
E1 and E2	Envelope proteins hypervariable region in E2
p7	Nonstructural, ion channel (?)
NS 2	NS 2-3 protease
NS 3	Protease, nucleotide triphosphatase, and RNA helicase
NS 4	Cofactor for NS 3 protease activity
NS 4B	Formation of membranous web
NS 5A	Interferon sensitivity sequence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



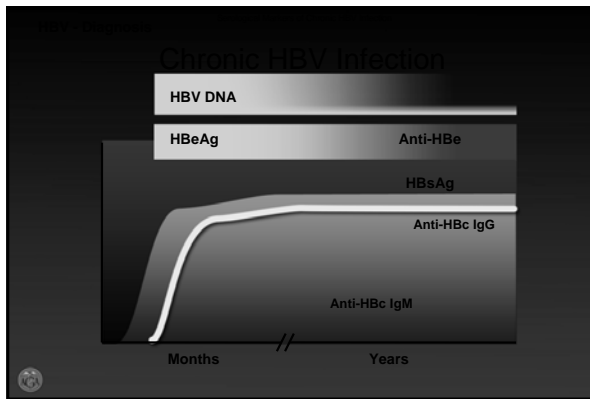
- ### HEPATITIS D AND E
- **HEPATITIS D**
 - Also known as delta agent
 - Uses the HBsAg protein coat
 - Hepatitis B must be present – coinfection or preexist
 - **HEPATITIS E**
 - Water borne virus resembling hepatitis A
 - Rarely seen in USA

CHRONIC HEPATITIS

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

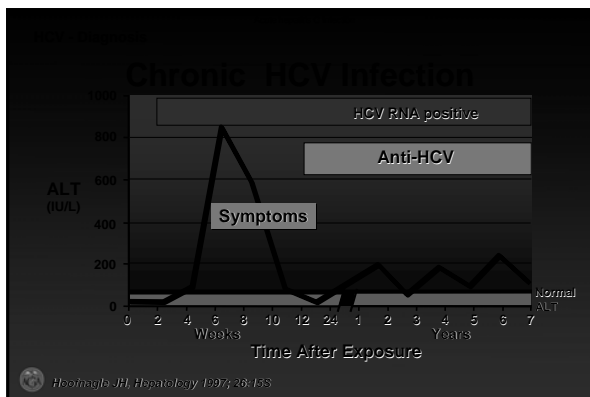
CHRONIC HEPATITIS B AND C

- 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



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



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
- Lab - presence of associated autoantibodies – ANA, thyroid antibodies, LKM, smooth muscle
- Diagnostic liver biopsy – interface hepatitis and plasma cell infiltration
- Treatment - steroids and immunosuppressants

END