



Medical Virology for 2nd Year M.D. Students



Hepatitis Viruses (1)

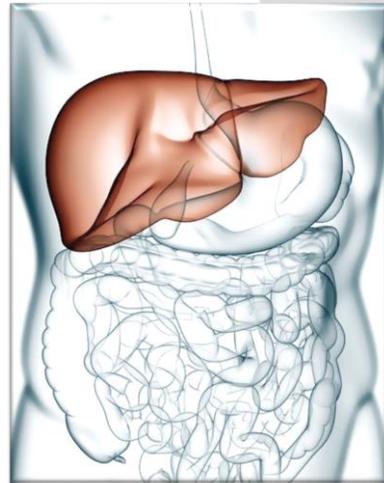
*University of Jordan
School of Medicine
Section of Microbiology & Immunology
Malik Sallam, M.D., Ph.D.*



Introduction



- Viral hepatitis is a systemic disease primarily involving the liver.
- Most cases of acute viral hepatitis are caused by one of the following agents: HAV, HBV, HCV, or HEV.
- Hepatitis viruses produce acute inflammation of the liver, resulting in a clinical illness characterized by fever, nausea, vomiting, and jaundice.
- Regardless of the virus type, **identical histopathologic lesions are observed in the liver during acute disease.**





Characteristics of Hepatitis Viruses



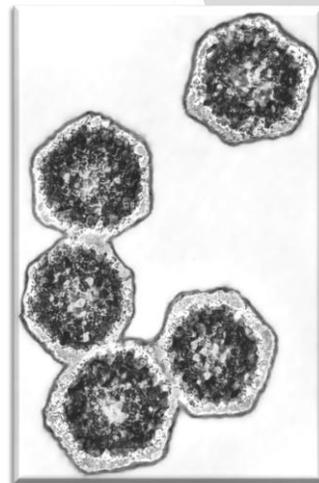
Virus	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Family	Picornaviridae	Hepadnaviridae	Flaviviridae	Unclassified	Hepeviridae
Genus	<i>Hepatovirus</i>	<i>Orthohepadnavirus</i>	<i>Hepacivirus</i>	<i>Deltavirus</i>	<i>Hepevirus</i>
Virion	27 nm, icosahedral	42 nm, spherical	60 nm, spherical	35 nm, spherical	30–32 nm, icosahedral
Envelope	No	Yes (HBsAg)	Yes	Yes (HBsAg)	No
Genome	ssRNA	dsDNA	ssRNA	ssRNA	ssRNA
Genome size (kb)	7.5	3.2	9.4	1.7	7.2
Stability	Heat and acid stable	Acid sensitive	Ether sensitive, acid sensitive	Acid sensitive	Heat stable
Transmission	Fecal–oral	Parenteral	Parenteral	Parenteral	Fecal–oral
Prevalence	High	High	Moderate	Low, regional	Regional
Fulminant disease	Rare	Rare	Rare	Frequent	In pregnancy
Chronic disease	Never	Often	Often	Often	Never
Oncogenic	No	Yes	Yes	?	No



Hepatitis A virus (HAV)



- An RNA virus that belongs to the *Picornaviridae* family.
- Positive-sense single-stranded RNA.
- Naked (non-enveloped).
- HAV is stable at low pH, heating.
- HAV has been found to survive for days to months in experimentally contaminated fresh water, seawater, waste water, soils, marine sediment and live oysters.





Features of HAV



- HAV is a 27- to 32-nm spherical particle with a linear single-stranded RNA genome with a size of 7.5 kb.
- **Only one serotype is known.**
- Genomic sequence analysis divided HAV isolates into seven genotypes.
- HAV is stable to treatment with 20% ether, acid (pH 1.0 for 2 hours), and heat (60°C for 1 hour), and its infectivity can be preserved for at least 1 month after being dried and stored at 25°C. The relative resistance of HAV to disinfection procedures **emphasizes the need for extra precautions in dealing with hepatitis A patients and their products.**



Pathogenesis of Hepatitis A



- HAV is spread by the **fecal-oral route**, most commonly by person-to-person contact. Common source outbreaks can occur.
- HAV is exceptionally stable at low pH.
- The primary site of replication for HAV is the liver, as demonstrated by virus detection in hepatocytes within days after infection.
- A relatively high concentrations of HAV are shed in the feces before the alanine aminotransferase (ALT) level initially becomes elevated and before the onset of clinical symptoms or jaundice.



Clinical and Laboratory findings in Hepatitis A



- Incubation period: 10–50 days (average, 25–30).
- Principal age distribution: Children, young adults.
- Seasonal incidence: Throughout the year but tends to peak in autumn.
- Route of infection: Predominantly fecal–oral.
- Occurrence of virus in blood: 2 weeks before to ≤ 1 week after jaundice.
- Occurrence of virus in stool: 2 weeks before to 2 weeks after jaundice.



Clinical and Laboratory findings in Hepatitis A



- Onset is abrupt (sudden) and fever is common.
- Duration of aminotransferase elevation: 1–3 weeks.
- **Complications are uncommon, no chronic state.**
- Patients with inapparent or subclinical hepatitis have neither symptoms nor jaundice. Other patients can develop anicteric hepatitis or icteric hepatitis.
- Symptoms ranging from mild and transient to severe and prolonged can accompany anicteric or icteric hepatitis. Most patients recover completely; however, some develop fulminant hepatitis and die.



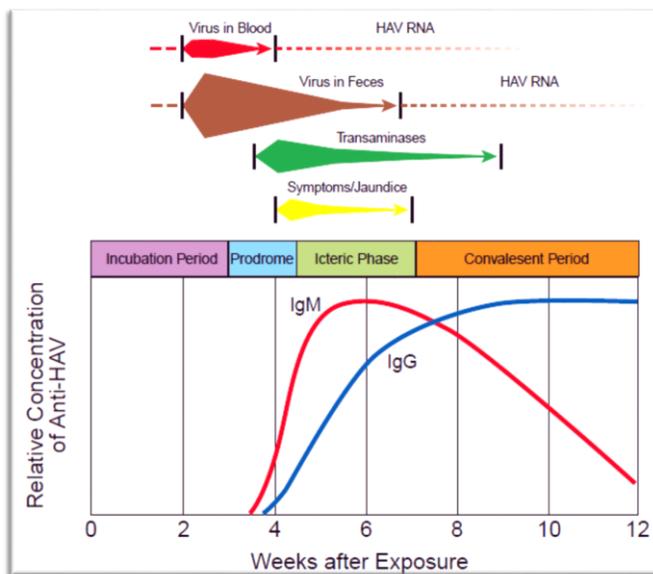
Clinical and Laboratory findings in Hepatitis A



- Occasionally, more extensive necrosis of the liver occurs during acute viral hepatitis A, leading to severe impairment of hepatic synthetic processes, excretory functions, and detoxifying mechanisms.
- This entity, designated fulminant hepatitis if hepatic encephalopathy occurs during the first 6 to 8 weeks of illness or within 1 to 4 weeks after jaundice, is characterized by the sudden onset of high fever, marked abdominal pain, vomiting, and jaundice followed by the development of encephalopathy associated with deep coma and seizures.



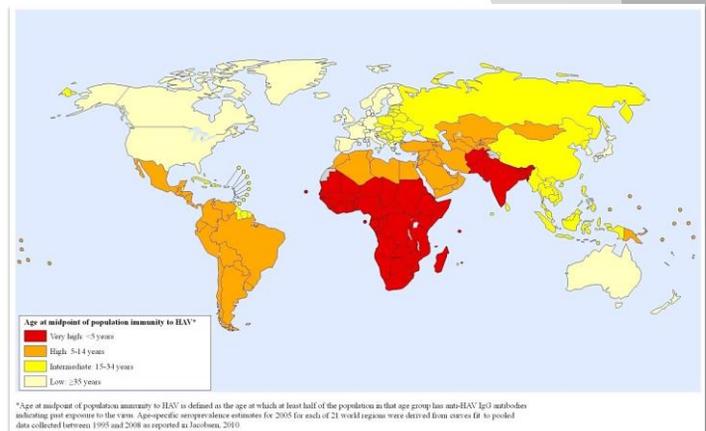
Markers of Hepatitis A





Epidemiology of Hepatitis A

- Hepatitis A is one of the most common causes of infectious jaundice in the world today and is frequently associated with recurrent epidemics.
- HAV communicability is apparently highest during the clinically silent incubation period when virus replication reaches a peak.

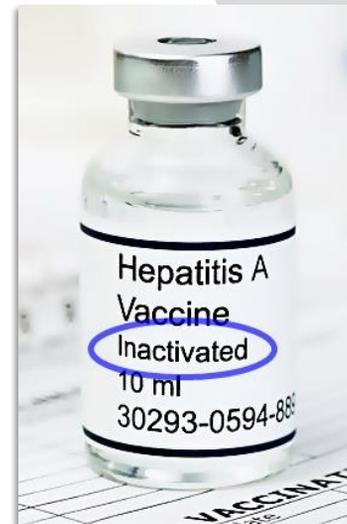




Diagnosis, Treatment & Prevention of Hepatitis A



- Liver function tests, IgM anti-HAV.
- No specific treatment for acute viral hepatitis exists, and hospitalization is not ordinarily indicated.
- Therapy should be supportive and aimed at maintaining comfort and adequate nutritional balance.
- Formaldehyde inactivated vaccines are available worldwide.





Hepatitis E virus (HEV)



- HEV is an enterically transmitted virus that occurs primarily in India, Asia, Africa, and Central America; in those geographic areas, HEV is the most common cause of acute hepatitis.
- This agent, with epidemiologic features resembling those of hepatitis A, is a 32- to 34-nm, non-enveloped, HAV-like virus with a 7.6 kb, single-strand, positive-sense RNA genome.
- All HEV isolates appear to belong to a single serotype, despite genomic heterogeneity of up to 25% and the existence of five genotypes.
- Contributing to the perpetuation of this virus are animal reservoirs, most notably in swine.



Hepatitis E virus (HEV)



- Although resembling caliciviruses, it is distinct and is classified in the genus, *Hepevirus*, within the *Hepeviridae* family.
- Entry of the virus into the host is by the oral route with incubation period ranging from 2 weeks to 2 months.
- Mortality of hepatitis E has varied in different reports but has been as high as 1%, compared to 0.2% for hepatitis A. More important, however, is the severity of hepatitis E in pregnant women, which may reach 20%.
- The reason for the excessive mortality of hepatitis E in pregnancy is unknown, although a high viral load and abnormalities of progesterone signaling pathways have been suggested.



Hepatitis E virus (HEV)

- Individual cases of hepatitis E cannot be differentiated from other cases of hepatitis on the basis of clinical presentation.
- Diagnosis can be achieved using serology and RT-PCR.
- No specific treatment exists for acute hepatitis E.
- Candidate recombinant vaccines in trials.

