

# الجهاز الهضمي

علم الأحياء الدقيقة

رقم المحاضرة : 5



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# Hepatitis Viruses

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# Introduction

- Hepatitis: inflammation of liver; presence of inflammatory cells in organ tissue
- The causes of hepatitis are varied and include viruses, bacteria, and protozoa, as well as **non-infectious causes like** drugs and toxins (eg, isoniazid, carbon tetrachloride, and ethanol).

**In this lecture we will focus on viruses that cause hepatitis.**

- Acute hepatitis: symptoms last less than 6 months
- Viral Hepatitis: is inflammation of the liver induced by viral infections
- The clinical symptoms and course of acute viral hepatitis can be similar (**can't be distinguished from each other clinically(I mean the hepatitis viruses)**), regardless of etiology, and determination of a specific cause depends on laboratory tests.

**Usually liver enzyme tests test the serum enzyme increase (AST (Aspartate aminotransferase) and ALT (Alanine aminotransferase)) to allow the differentiation from other liver diseases.**

**The general rule that the ratio between ALT and over AST more than one usually indicate a cytoplasmic damage (viral hepatitis).**

**Viruses are the major cause of infectious liver diseases, there are other viruses that can cause sporadic cases of hepatitis, they can infect the liver as well as other sites of the body therefore they are not exclusively hepatitis viruses like the one we will talk about.**

**Example of these viruses: Cytomegalovirus , Ebstein Barr virus , Yellow fever virus, Herpes simplex virus, Rubella virus and other enteroviruses.**

**For hepatitis viruses:**

**The target organ for each of these viruses is the liver and the basic hepatitis symptoms are similar, they differ greatly in their structure, mode of replication, mode of transmission and in the time course as well as the sequelae of the disease they cause.**

# Viral hepatitis *types*:

**Most cases of acute viral hepatitis in children as well as in adults are caused by one of the following agents:**

- A: Picornavirus: +ssRNA, Non enveloped

**Previously known as infectious hepatitis**

- B: Hepadnavirus Ds DNA, Partial, has enzyme, enveloped

**Known as serum hepatitis**

- C: Flavivirus, +ssRNA genome, enveloped

**Common cause of post-transfusion hepatitis**

- D: Deltaviruses, Defective –ssRNA virus

**Always dependent on the co-infection with hepatitis B virus**

- E: Hepevirus, +ssRNA non enveloped

**Hepatitis E: agent for enterically transmitted hepatitis the same as hepatitis A virus**

**Regardless of the virus type, identical histopathological lesions are observed in the liver during the acute disease, these viruses are not cytopathic, it is an immunological response that leads to those lesions mainly.**

# Hepatitis A Virus

**Distinct member of the Picornaviridae family.**

- A typical Enterovirus , also known as enterovirus 72
- Naked Icosahedral nucleocapsid virus (Non enveloped) with a single stranded positive polarity RNA. No virion polymerase. One serotype.

**There are seven genotypes for HAV.**

- Enterically transmitted (fecal/oral route)

**There are always outbreaks that associated with contaminated food and water. Humans appear to be the major natural hosts of HAV.**

**HAV particles can be demonstrated in the feces by electron microscopy.**

- *Ingestion* > Multiplies in oropharynx and intestinal epithelial cells > blood > Liver > Periportal necrosis + mononuclear infiltrates
- Virus is not cytopathic but the CMI causes cell necrosis

## **HAV:**

**It replicates in liver, it is excreted in the bile and then excreted in the feces of infected persons for about two weeks before the onset of clinical illness and up to one week post symptoms in those affected patients.**

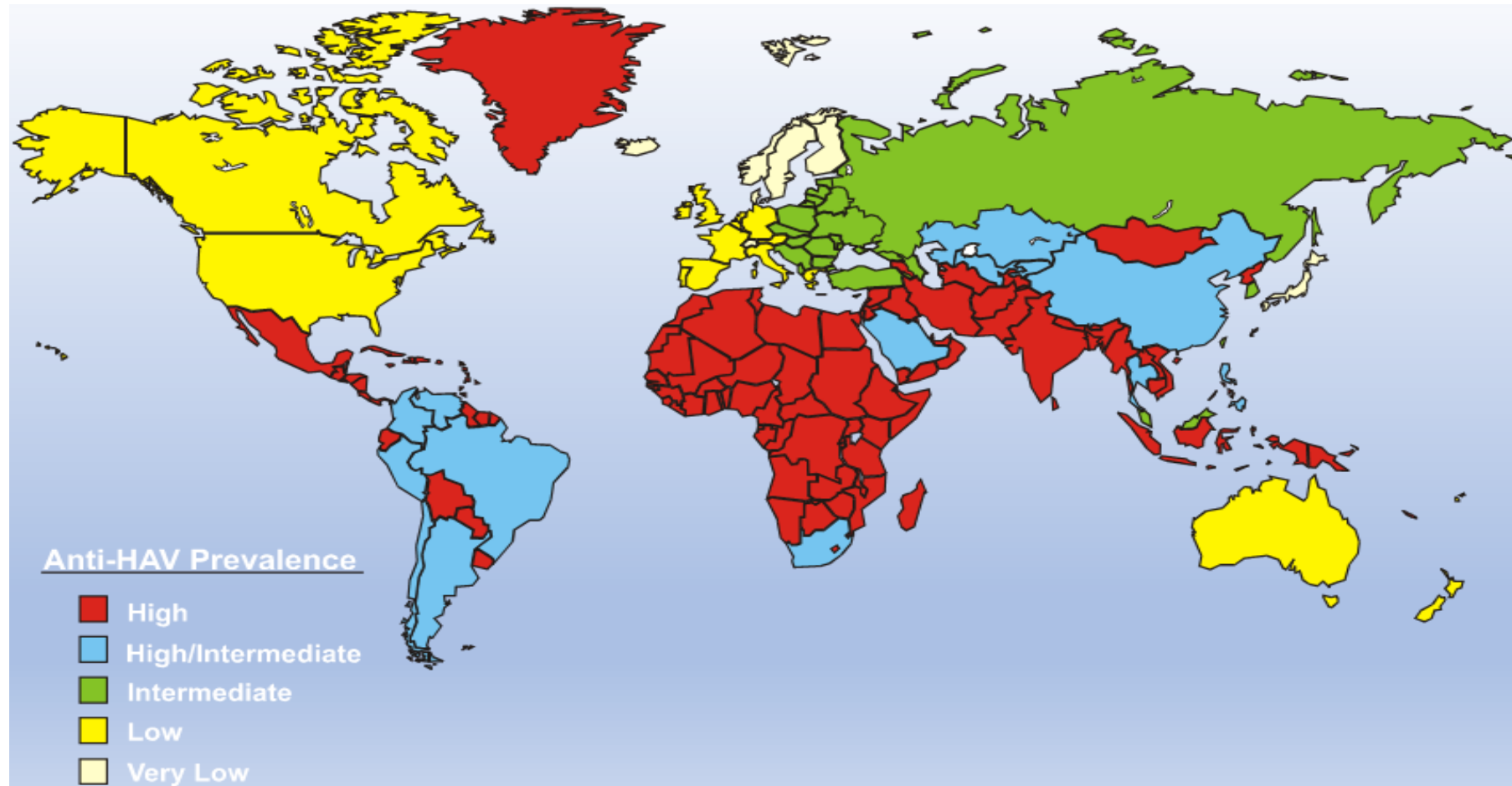
**Estimated to be the causative agent of more than 40%-50% of acute hepatitis cases.**

## **MOST COMMON VIRAL HEPATITIS !!!**

**There is no chronic infection with HAV and HEV, only initially IgM antibody response then followed by IgG antibody response and that usually give you a life long immunity post-infection with HAV.**



# Epidemiology of *Hepatitis A*



**We could see the prevalence of anti-hepatitis A (antibodies in red color), Jordan is considered high in the prevalence of HAV infection as well as in the antibodies against HAV.**

**Most common type viral hepatitis that occur worldwide, most often outbreaks or epidemics.**

**Commonly seen in children mainly as well as in young adults, 90% of infected children and up to 25%-50% of infected adults have inapparent but productive infection with HAV.**

**When we say that individuals have "inapparent but productive infection with HAV," it means they have an asymptomatic or subclinical infection with Hepatitis A virus (HAV) that is still actively replicating and capable of spreading to others.**

**The spread of infection mainly by fecal-oral route and arise from the ingestion of contaminated food and water, so overcrowding and poor sanitation facilitate the spread.**

**HAV cause infectious hepatitis (an acute disease that clinically milder or asymptomatic in young children, and there is no career or chronic state with HAV)**

**More than 90% of adult population in many developing countries show evidence of previous hepatitis A infection, and travelers from developed countries who enter those endemic areas they are particularly susceptible.**

**Patients are most contagious, primarily two weeks prior to the onset of clinical disease, which is mainly characterized by jaundice.**

# Clinical Manifestations

- Incubation period: 2-6 WEEKS
- Most HAV infections are asymptomatic.
- fever; anorexia; nausea, vomiting and jaundice .
- Abdominal pain, hepatomegally, splenomegally, Dark urine and clay-colored stools and elevated transaminase levels.
- Resolve spontaneously in 2-4 weeks.

**The infectious dose for HAV is <100 particles (enough to establish infection). And the contagiousness as well as the communicability is usually 2 weeks before the onset of clinical symptoms that are usually characterized by the onset of jaundice.**

**Jaundice is usually observed in almost 70-80% of adults, meanwhile in only maybe 10% of children, especially of an age less than 6 years.**

**So, the most common presentation of HAV infection is asymptomatic, and that's the case with most children. Meanwhile in adults, it's usually symptomatic, usually including two phases:**

- **Pre-Icteric phase, where there is an abrupt flu-like illness associated with nausea, vomiting, anorexia**
- **Icteric phase, characterized by jaundice, abdominal pain, hepatosplenomegaly, pale stool, dark-color urine (especially noticed in patients 1-5 days before the onset of clinical jaundice). Sometimes a sudden onset of fever, anorexia, pain especially in the right upper quadrant of the abdomen within several days (classical history of HAV infection in symptomatic patients). The liver is enlarged and tender.**

- Many individuals are asymptomatic or only mildly ill **without jaundice**.
- **Recovery occurs in days or weeks usually. 99% of HAV cases are self-limiting, no chronic hepatitis, no carrier state with HAV infection. However, <1% of patients might develop fulminant hepatitis, with mortality rate of (0.1-0.2)%.**
- **(To emphasize, again) Unlike HBV, HAV they can't initiate chronic infection, and are not associated with hepatic cancer.**

★ Abrupt means sudden, opposite of gradual. Fulminant means severe and sudden.

★ Icteric means jaundice-associated.

★ Jaundice is the yellow discoloration of the skin that is seen when bilirubin levels go above the normal concentration, can also be seen particularly well in the sclera. Watch this neat 5-minute video if you like: <https://youtu.be/5QN5OhEXyno?si=usTspAhFO4qJHYal>

# Hepatitis A Diagnosis:

- Clinically

We look for history, or perform physical examination. Once we check the liver biochemistry, we notice an elevation in liver function (enzymes)

- Liver enzyme: High AST and ALT, mild elevation of bilirubin. These usually proceed in the icteric stage. So, we might also notice high levels of bilirubin in serum.

- Serology(viral markers): IgM, IgG (life long immunity)

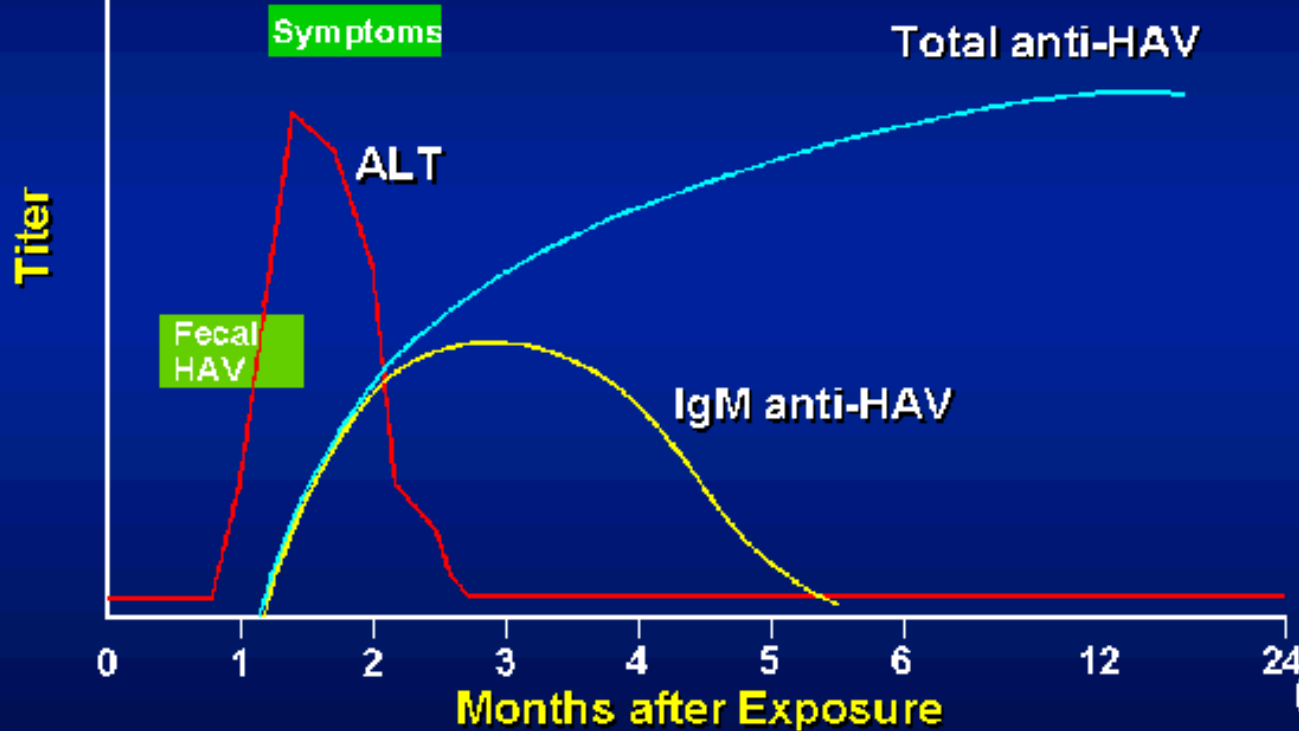
- IgM: Acute infection remains high for 3-6 months, followed by:

- IgG: Past infection or vaccine. Become predominant afterwards and it's common in the general population over the age of 50 years.

- **Hematological test: leukopenia with relative lymphocytosis in the affected patients. Also, the ESR (erythrocyte sedimentation rate) is raised.**
- **Using an immune electron microscope, you can identify the virus particles in the fecal specimen. The isolation of the virus in cell cultures is considered a research tool.**

# Hepatitis A

## Hepatitis A Virus Infection Typical Serologic Course



-This slide shows the typical serology course of infected patients with HAV. Which, as we said, can be identified in the stool and can be noticed by a raised liver function test (ALT and AST) followed by the anti-HAV: IgM that starts rising usually one month post-exposure and peaks in the third month post-exposure before being replaced by IgG anti-HAV. -Previous infection and vaccine can both give life-long immunity to the virus.



- *Rx: Usually full recovery in 90% of patients in 3-6m*

➤ *Acute:*

- *Supportive: Do not give Paracetamol and Alcohol*

- *Immunoglobulins*

➤ *Fulminant hepatitis:*

- *Supportive, but may need liver transplantation*

- *Prevention:*

- *Hygiene, Vaccine: killed, IM 2 doses separated by 3- 6 months*

- ◆ **There is no specific treatment for patients with acute hepatitis A.**
- ◆ **Supportive measures include adequate nutrition and bed rest.**
- ◆ **Avoidance of exposure of contaminated food and water is an important measure to reduce the risk of hepatitis A infection.**
  
- ◆ **There are two terms you should be familiar with regarding the treatment:**
  - **Passive immunization: prophylaxis with immune serum globulin given usually before or early in the incubation period. In other words: less than 2 weeks post-exposure. Usually 80-90% effective in preventing clinical illness.**
  - **Active immunization: vaccine against HAV (formalin-killed vaccine) that usually induces anti-HAV, similar to those infected with the wild virus type, usually 100% protective.**
- ◆ **For preventive measure, the spread is reduced by interrupting the feco-oral route, which is usually accomplished by avoiding potentially contaminated water and food (especially undercooked shellfish) and proper handwashing (especially in care centers, mental hospitals...Etc)**
- ◆ **It is vitally important that chlorine treatment of drinking water is generally sufficient to kill the virus.**

# Hepatitis E Virus

- Hepatitis E virus is a none enveloped, single stranded RNA virus.
- The viral particles in stool are spherical, 27 to 34 nm in size, and unenveloped and exhibit spikes on their surface.
- Feco-oral transmission
- Waterborne epidemics of hepatitis
- High mortality rate in pregnant women.
- No chronicity , No carrier state.

**Now, let's talk about HEV since it's similar to HAV:**

- **It is the cause of another form of hepatitis that spreads by the feco-oral route, therefore resemble hepatitis A.**
- **The viral particles in the stool are spherical, 30 nm in size, unenveloped and exhibit spikes on their surface.**

- **Like HAV, infection with this virus is usually subclinical(children). However, symptomatic causes only acute disease that may fulminate.**
- **Acute hepatitis E is clinically similar to hepatitis A infection EXCEPT that the bilirubin levels are usually higher in HEV and the jaundice is deeper and more prolonged.**
- **In endemic and developing areas, it has the highest attacking rate in young adults.**
- **Most cases have been identified in developing countries with poor sanitation. Recurrent epidemics have been described in these areas**
- **Infection is usually associated with contaminated food and water. It doesn't appear to spread from one person to another.**
- **Incubation period: approximately 40 days, usually 2-8 weeks. And the diagnosis may be confirmed by demonstrating the presence of specific IgM antibodies.**
- **High risk group: pregnant women and malnourished individuals. The normal- case fatality rate is 1-2% but usually becomes higher to reach up to 10-20% in the high-risk group.**
- **No treatment is available. Treatment is supportive in (like HAV).**
- **No chronic stage or carrier state (like HAV).**
- **Diagnosis is done by excluding other types as well as molecular real-time PCR.**

- [https://docs.google.com/forms/d/e/1FAIpQLSdN9YK7ry3f5EtqmJAzL1lqa9ogsCGEEVrFH9DfBd8lIAN1Eg/viewform?usp=sf\\_link](https://docs.google.com/forms/d/e/1FAIpQLSdN9YK7ry3f5EtqmJAzL1lqa9ogsCGEEVrFH9DfBd8lIAN1Eg/viewform?usp=sf_link)

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***The End***  
***Thank you!!***

