VIRAL HEPATITIS

Learning Objectives

- The student should recognizing the features of viral hepatitis in children
- The student be familiar with the important diagnostic test required to diagnose viral hepatitis
- The student should understand the preventive measures of viral hepatitis in community including vaccination

VIRAL HEPATITIS

Caused by at least 5 pathogenic hepatotropic viruses recognized to date: hepatitis A, B, C, D, and E viruses . Other viruses can cause hepatitis (HSV), (CMV), (EBV), varicella-zoster virus, HIV, rubella, adenoviruses, enteroviruses, parvovirus B19. The hepatotropic viruses cause similar acute clinical illness.

ž Morbidity is related to a rare cases of acute liver failure (ALF) in susceptible patients, and to chronic disease state and attendant complications (mainly HBV , HCV,HDV)

Issues Common to All Forms of Viral Hepatitis

- Jaundice which is a mixed or direct hyperbilirubinemia
- deep colour urine .
- Enlarged and tender liver
- Splenomegaly and lymphadenopathy may occure
- Extrahepatic symptoms are more readily seen in HBV and HCV infections (example :rashes, arthritis).
- Encephalopathy in ALF.

Pathogenesis

The acute liver injury is caused by 2 mechanisms , cytopathic and immune-mediated injury. The entire liver is involved. With recovery, the liver morphology returns to normal within 3 months of the acute infection. If chronic hepatitis develops, the inflammatory infiltrate settles in the periportal areas and often leads to progressive scarring.

Common Biochemical Profiles in the Acute Infectious Phase

- Rise serum ALT and AST. There is usually slow improvement over several weeks, Rapidly falling can predict a poor outcome . *The magnitude of enzyme elevation does not correlate with the extent of hepatocellular necrosis and has little prognostic value.*

- Cholestasis : Elevated serum conjugated bilirubin , Elevation of ALP , 5′-nucleotidase, γ-glutamyl transpeptidase (GGT), and urobilinogen

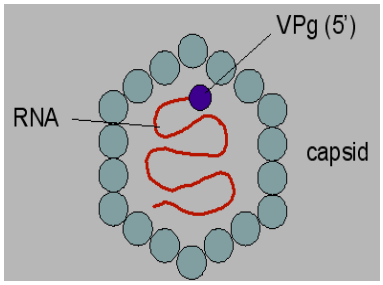
•Synthetic dysfunction is reflected by prolonged PT , high [INR], low serum albumin , metabolic disturbances (hypoglycemia, lactic acidosis, hyperammonemia), and encephalopathy (altered sensorium with increased deep tendon reflexes).

Altered synthetic function is the most important marker of liver injury. Monitoring of synthetic function should be the main focus in clinical follow-up to define the severity of the disease.

Table 350-1 -- FEATURES OF THE HEPATOTROPIC VIRUSES

VIROLOGY	HAV RNA	HBV DNA	HCV RNA	HDV RNA	HEV RNA
Incubation (days)	15-19	60-180	14-160	21-42	21-63
Transmission					
• Parenteral	Rare	Yes	Yes	Yes	No
• Fecal-oral	Yes	No	No	No	Yes
• Sexual	No	Yes	Yes	Yes	No
• Perinatal	No	Yes	Rare	Yes	No
Chronic infection	No	Yes	Yes	Yes	No
Fulminant disease	Rare	Yes	Rare	Yes	Yes

Hepatitis A



ž Responsible for most forms of acute and benign hepatitis. Transmission is by person-to person contact through the fecal-oral route..Infection has also been associated with contact with contaminated food or water and after travel to endemic areas.

Common cause of food or waterborne outbreak has occurred due to contaminated shellfish, frozen berries, raw vegetable.

The mean incubation period for HAV is ~3 wk.

Fecal excretion of the virus reaches its peak just before the onset of symptoms, and resolves by 2 wk after the onset of jaundice in older subjects.

Clinical Manifestations

•Acute febrile illness with an abrupt onset of anorexia, nausea, malaise, vomiting, jaundice and deep color urine . The typical duration of illness is 7-14 days

•Regional lymph nodes and the spleen may be enlarged.

- Ulceration of the GIT can occur, especially in fatal cases.
- Acute pancreatitis and myocarditis have been reported. Rarely nephritis, arthritis, vasculitis, and cryoglobulinemia

Diagnosis

- Detecting anti-HAV (IgM) by radioimmunoassay when the symptoms are clinically apparent ,it remains positive for 4-6 mo
- A neutralizing anti-HAV (IgG) detected within 8 wk of symptom onset. Anti-HAV (IgG) confers long-term protection
- Rarely, by identifying viral particles in stool.
- A viral polymerase chain reaction (PCR) assay
- Rises in serum levels of ALT, AST, bilirubin, ALP, 5′-nucleotidase, and GGT are almost universally found

DIAGNOSTIC BLOOD TESTS: SEROLOGY AND VIRAL PCR

- ACUTE INFECTION : Anti-HAV IgM^{+ve} , Blood PCR positive
- PAST INFECTION (RECOVERED) : Anti-HAV IgG^{+ve}
- VACCINE RESPONSE : Anti-HAV IgG^{+ve}

Complications Although most patients achieve full recovery, two distinct complications can occur.

a. ALF from HAV infection is a rare <1% (mainly In adults)

b. HAV can progress to a prolonged cholestatic syndrome

Treatment

- There is no specific treatment for hepatitis A.
- Supportive treatment consists of intravenous hydration as needed and antipruritic
- fat-soluble vitamins for the prolonged cholestatic form
- Serial monitoring for signs of ALF and, if ALF is diagnosed, a prompt referral to a transplantation center can be lifesaving.

Prevention

- Patients infected with HAV are contagious for 2 wk before and 7 days after the onset of jaundice and should be excluded from school, child care, or work
- Careful hand washing is necessary, particularly after changing diapers and before preparing or serving food.
- In hospital settings, contact and standard precautions are recommended for 1 wk after onset of symptoms.

Vaccine

- Two inactivated HAV vaccines are approved for children >1 yr of age. They are administered intramuscularly in a 2-dose schedule, with the 2nd dose given 6-12 mo after the 1st dose. Seroconversion after 2 doses is 100% protective antibody titer persists at least for 10 yr.

Vaccine Indication :

- Child >1y : Endemic area and out break
- Chronic liver disease
- Occupational risk of exposure
- Patient with clotting factor and immune disorder
- In the USA universal vaccination for all children >1 yr of age.

Immunoglobulin

- Pre-exposure prophylaxis for susceptible travelers to countries where HAV is endemic. IG ensures an appropriate prophylaxis in children <1 yr of age, patients allergic to a vaccine component, or those who elect not to receive the vaccine. If travel is planned in <2 wk, older patients, immunocompromised hosts, and those with chronic liver disease or other medical conditions should receive both IG and the HAV vaccine.
- Post exposure IG prophylaxis for : children <12 mo of age, immunocompromised hosts, those with chronic liver disease or in whom vaccine is contraindicated.
- IG is optional in healthy persons 12 mo-40 yr, in which HAV vaccine is preferred.

[redacted] Hepatitis A Virus Prophylaxis

PREEXPOSURE PROPHYLAXIS (TRAVELERS TO ENDEMIC REGIONS)

AGE	EXPECTED EXPOSURE DURATION	DOSE
<1 year of age	<3 months	Ig 0.02 mL/kg
	3-5 months	Ig 0.06 mL/kg
	Long term (>5months)	Ig 0.06 mL/kg at departure and every 5 mo thereafter
≥1 year of age	Healthy host	HAV vaccine
	Immunocompromised host, or one with chronic liver disease or chronic health problems	HAV vaccine and Ig 0.02 mL/kg

POSTEXPOSURE PROPHYLAXIS*

EXPOSURE	RECOMMENDATIONS
≤2 wk since exposure	<1 year-old: Ig 0.02 mL/kg Immunocompromised host, or host with chronic liver disease or chronic health problems: Ig 0.02 mL/kg and HAV vaccine >1 year and healthy host: HAV vaccine, Ig remains optional Sporadic non-household or close contact exposure: prophylaxis not indicated*
>2 wk since exposure	None

Prognosis of Hepatitis A virus: is excellent, with no long-term sequele. The only feared complication is ALF.

Hepatitis B

- HBV has a circular, partially double-stranded DNA genome.
- HBV is present in high concentrations in blood, serum, and serous exudates and in moderate concentrations in saliva, vaginal fluid, and semen.
- Efficient transmission occurs by blood exposure and sexual contact.

Risk factors for HBV infection in children and adolescents

Intravenous drugs or blood products, contaminated needls used by acupuncture or tattoos, sexual contact, institutional care , intimate contact with carriers. In children, the most important risk factor for HBV is perinatal exposure to an HBsAg+ve mother.

Perinatal exposure to an HBsAg positive mother.

Transmission occur if the mother is HBSAg is positive

Chronic HBV infection

Defined as being positive for HBsAg for >6 month . Complication of chronic hepatitis includes chronic liver disease and hepatocellular carcinoma.

Clinical Manifestations

Many acute cases of HBV infection are asymptomatic

The usual acute symptomatic episode is similar to that of HAV and HCV infections but may be more severe and is more likely to include involvement of skin and joints .

The illness may preceded by a serum sickness–like prodrome marked by arthralgia or skin lesions, including urticarial, purpuric, macular, or maculopapular rashes.

Diagnosis

Acute HBV infection : HBsAg +ve , IgM anti-HBc +ve, Anti-HBs –ve and PCR

Chronic HBV infection : HBsAg +ve , IgG Anti-HBc +ve , IgM anti-HBc -ve,Anti-HBs –ve

Complications

Mortality is >30% .Acute liver failure , coagulopathy, Encephalopathy, and cerebral edema, Membranous glomerulonephritis , Chronic hepatitis which can lead to cirrhosis, end-stage liver disease, and primary hepatocellular carcinoma .

Treatment

- Treatment of *acute* HBV infection is largely supportive.
- Treatment of *chronic* HBV infection.
  - ✓ Interferon-α-2b (IFN-α2b) S.C , duration of treatment for 24 weeks,
  - ✓ Oral Lamivudine : In children >2 yr, used for ≥6 mo after viral clearance.
  - ✓ Infants of $HBsAg^{+ve}$ women: at Birth HBIG (1^{st} 12hr) + vaccine at birth , 1 and 6 mo
  - ✓ OTHERS: Adefovir use in children >12 yr of age. Peginterferon-α2 used SC once weekly.

Prevention of HBV:

- Universal vaccination.
- HBV is not spread by breast-feeding, kissing, or sharing water or utensils.
- Children with HBV should not be excluded from school, play, child care, or work, unless they are prone to biting.

Prognosis of HBV :

- In general, the outcome after acute HBV infection is favorable, despite a risk of ALF. The risk of developing chronic infection brings the risks of liver cirrhosis and hepatocellular carcinoma to the forefront.
- Perinatal transmission leading to chronicity

Hepatitis C

- HCV is a single-stranded RNA virus, It has 6 major genotypes, Genotype 1b is the most common in the United States

Risk factors for HCV transmission

Blood or blood products transfusion, illegal drug use, Sexual transmission
Other risk factors include occupational exposure. In children perinatal transmission is the most prevalent mode of transmission, and vertical transmission occurs in up to 5% of infants born to viremic mothers.

Clinical Manifestations

Acute HCV infection tends to be mild and insidious in onset.
HCV is the most likely hepatotropic virus to cause chronic infection.
In pediatric studies, 6-19% of children achieved spontaneous sustained clearance of the virus during a 6 yr follow-up

Diagnosis of HCV :

- ✓ Detection of Anti-HCV antibodies to HCV antigens or detection of viral RNA
- ✓ (The most commonly used **virologic assay** for HCV is a PCR assay, The quantitative PCR aids in identifying patients who are likely to respond to therapy and in monitoring response to therapy.
- ✓ Determining HCV **genotype** is also important
- ✓ A liver biopsy is indicated only before starting any treatment and to rule out other causes of overt liver disease

Complications

- Chronic hepatitis is high
- In adults, Progression to cirrhosis or Hepatocellular carcinoma.

Treatment

- Peginterferon or IFN-α2b, and ribavirin are approved by the FDA for use in children older than 3 yr of age with HCV hepatitis of genotypes 2 and 3, and, genotype 1b,
- Treatment consists of 48 wk of IFN and ribavarin .A liver biopsy was recommended before treatment.

Prognosis

- Viral titers should be checked yearly to document spontaneous remission.
- Most patients develop chronic hepatitis