HEPATITIS VIRUSES

Viral hepatitis is a systemic disease primarily involving the liver. Medically important hepatitis viruses are: Hepatitis A virus (HAV); Hepatitis B virus (HBV); non-A, non-B viruses, of which Hepatitis C virus (HCV); Hepatitis D virus (HDV, delta agent) and Hepatitis E virus (HEV), Hepatitis G virus (table). Hepatitis viruses are taxonomically unrelated. Except for type B, which is a DNA virus, all the others are RNA viruses. The features common to them are their hepatotropism and ability to cause a similar icteric illness, ranging in severity from the unapparent to the fulminate fatal forms. As all types of hepatitis viruses cause a clinically indistinguishable acute illness, their differentiation is based on their serological and molecular markers. By epidemiological and clinical criteria, two types of viral hepatitis had been recognized forlong:

1. One type occurred sporadically or as epidemics, affecting mainly children and young adults, and transmitted by the fecal- oral route. This was called infectious hepatitis (HepatitisA).

2.A second type of viral hepatitis, transmitted mainly by inoculation, was originally observed in persons receiving serum inoculation or blood transfusion. This had been given various names such as homologous serum jaundice, serum hepatitis and transfusion hepatitis (Hepatitis B).

HEPATITIS A VIRUS

Hepatitis A (infectious hepatitis) is a subacute disease of global distribution, affecting mainly children and young adults.

HAV is a distinct member of the Picornavirus family. HAV is a 27-32 nm, non-enveloped, spherical virus. It has single stranded RNA positive polarity genome, icosahedral nucleocapsid and replicates in the cytoplasm of the cell. Only one serotype is known. HAV is stable to treatment with 20 per cent ether, acid and heat (60°C for one hour) and its infectivity can be preserved for at least one month after being dried and stored at 25^0 C and 42% relative humidity or for years at -20° C. The virus is destroyed by autoclaving (121°C for 20 minutes), by boiling in water for 5 minutes.

Transmission and Epidemiology:

Humans are the reservoir for HAV. Virus appears in the faeces roughly 2 weeks before the appearance of symptoms. Children are the most frequently infected group, and outbreaks occur in special living situations (kinder gardens, summer camps). Common-source outbreaks arise from faecal contaminated water or food such as oysters grown in polluted water and eaten raw. HAV is rarely transmitted via the blood, because the level of viremia is low and chronic infection does not occur.

Hepatitis A is an anthroponose infection. The source of infection is patient. HAV is transmitted by the faecal-oral route (infection is by ingestion). The primary reproduction in small intestine is occurs. Later the virus enters into the blood and spreads to the liver via the blood. For these viruses the target cells are hepatocytes and these cells are infected. The incubation period is 21-28 days but can last 50 days. The prodromal period lasts 5-7 days. Fever, anorexia, nausea, vomiting, and jaundice are typical. After 2-4 days urine becomes dark (like beer), the faeces is pale **(acholia),** and elevated transaminase levels are seen, increasing of Specific M immunoglobulins is detected which have differential diagnostic meaning. During this period the enlargement of liver is detected. The next is specific illness period, which lasts from 1 week to 1.5 months, jaundice develops, and the intoxication becomes weak. Jaundice begins from the oral cavity mucous layer, palate, frenula, sclera and then skin. The urine becomes darker **(urobilinuria, choluria)**, acholia isintensive.

Disappearance of the jaundice shows convalesces and it lasts from 2 to 6 months.

Post infectious immunity is stable depends on virus neutralizing antibodies, memory cells, and intestinal local immunity. There is no cross immunity between HAV and any of the other hepatitis viruses.

Prevention: General prophylaxis consists of improved sanitary practices and prevention of fecal contamination of food andwater.

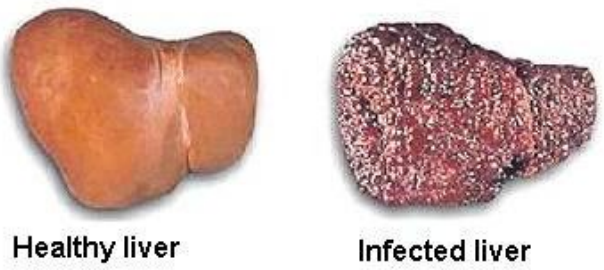
Specific prophylaxis: Specific **passive prophylaxis** by pooled normal human immunoglobulin IM, before exposure or in the early incubation period, can prevent or attenuate clinical illness, while not necessarily preventing infection and virus excretion. Specific **active prophylaxis** by inactivated cultural vaccine and recombinative vaccine areused.

Treatment is symptomatic. No specific antiviral drug is available.

Laboratory diagnosis: The detection of IgM antibody is the most important test. IgM and anti-HAV antibody appears during the late incubation period, reaches peak levels in 2-3weeks and disappears after 3-4 months. The IgG antibody appears at about the same time, peaks in 3-4 months and persists much longer, perhaps for life. Demonstration of IgM antibody in serum indicates current or recent infection, while the IgG antibody denotes recent or remote infection and immunity. ELISA kits for detection of IgM and IgG antibodies areavailable.

Hepatitis E virus (HEV)

HEV is spherical, non-enveloped virus. The genome is single stranded RNA positive polarity. The size is 32-34 nm in diameter.



Viral hepatitis E (synonym: viral hepatitis neither A nor B with fecal-oral infection) is an acute infectious disease with clinical manifestations similar to hepatitis A, usually with a benign course, but in pregnant women it is characterized by a severe course with the development of hepatic encephalopathy and high mortality.

Hepatitis E virus was identified in 1983. The name "E" was chosen to reflect the properties that reflect the epidemiology of the virus and the alphabetical order in which hepatitis viruses were already identified at that time as causing hepatitis in people: A, B, C and D.

Taxonomy. HEV belongs to the family Caliciviridae (from the Greek calyx-bowl), the genus Hepavirus.

Morphology. The HEV has a small size (32-34 nm), a spherical shape, just an organized structure (there is no supercapsid). The genome is represented by single-stranded RNA. It differs from hepatitis A viruses in antigenic properties.

Resistance In general, viral hepatitis E is less stable than hepatitis A. It is well preserved at a temperature of -20 ° C or lower. It quickly collapses during freezing-thawing, dies during boiling, under the influence of chlorine-containing or iodine-containing disinfectants. However, it can be stored for a long time in fresh water.

Cultivation. It is hardly cultivated in cell culture, pathogenic for monkeys (chimpanzees, macaques).

Epidemiology. Sources of infection are sick people. The infection mechanism is fecal-oral, the main route of transmission is water. Mostly young and middle-aged people (15-40 years old) are affected. The patterns of the epidemiological process resemble those of hepatitis A and are associated with a violation of the regime of chlorination of water, the use of contaminated water for drinking open water bodies. However, other transmission methods that are less common are possible: consumption of insufficiently cooked meat or meat products obtained from infected animals; transfusion of infected blood products; and vertical transmission from a pregnant woman to her fetus. In endemic areas, the source of sporadic cases may be the consumption of raw or non-cooked shellfish. Mostly, hepatitis B virus is detected in areas with a high incidence of hepatitis A. About 1 million people get hepatitis E each year, and in Asia, it accounts for more than half of all cases of acute hepatitis. Large water outbreaks (with the number of cases of 15-20 thousand) occurred in India, Burma, Algeria, Nepal, the republics of Central Asia of the former USSR (Turkmenistan, Tajikistan, Uzbekistan, Kyrgyzstan).

Pathogenesis. It has not been fully studied, it is believed that the pathogenesis of hepatitis E is close to the pathogenesis of hepatitis A. The virus selectively infects hepatocytes, which leads to

impaired liver function and the development of intoxication.

Clinic. The clinical course is similar to hepatitis A. The incubation period is from 2 to 8 weeks. In most cases, the disease begins acutely. The initial (preicteric) period, as with hepatitis A, is characterized by dyspeptic manifestations, sometimes asthenovegetative signs are observed. During jaundice, intoxication is moderate. The course of the disease is favorable.

The most dangerous viral hepatitis E in the II and III trimesters of pregnancy. In this case, the course of the icteric period is transient, it quickly passes into acute hepatic encephalopathy. The phases of acute hepatic encephalopathy quickly succeed each other and patients fall into a deep coma. Hemorrhagic syndrome is pronounced. Mortality among patients with hepatitis E during pregnancy is high, can reach 30-40%, and at 40 weeks of pregnancy - 70%. Fetal death occurs before birth.

Immunity. Post-infectious immunity is strong, lifelong, due to virus-neutralizing antibodies and immune memory cells.

Laboratory diagnostics. The material for the study is the blood serum of patients. Diagnosis of HEV is carried out by the method of elimination of viral hepatitis A and B. Use methods: Immune electron microscopy.

Serological method (detection of antibodies to the pathogen - immunoglobulins IgM, IgG in RIA or ELISA reactions.

Treatment. See treatment for viral hepatitis A. Treatment of patients with mild and moderate forms of viral hepatitis E is carried out according to the generally accepted scheme, while diet, medical and protective regimen are of great importance, and, if necessary, detoxifying agents.

Prevention. General prevention consists in compliance with sanitary standards. Raw water should not be consumed, especially in regions where hepatitis E is recorded. Specific prophylaxis is carried out by the introduction of a whole-virion vaccine for risk groups.

PICORNAVIRUS

There are 120 viruses, which cause acute intestinal infections. These viruses are: Enteroviruses; Rotaviruses; Coronaviruses. The **Picornaviridae** family (pico-small; rna-RNAviruses) includes two groups of medical importance: **Enteroviruses** and **Rhinoviruses.** Among the major Enteroviruses are Poliovirus (types1-3), Coxsackievirus A(types1-24), Coxsackievirus B (types1-6); ECHOvirus (types 1-34) and Hepatitis A virus.

Enteroviruses:

There are common properties for Enteroviruses: the virion is spherical, about 28-30 nm in diameter; non-enveloped viruse composed of an icosahedral nucleocapsid and single stranded RNA genome, which has positive polarity, isn't sensitive to ethers

In human organism they cause various illnesses ranging from neural infections to infections in several organ-systems.

Poliomyelitis:

Poliomyelitis is an acute infectious disease which affects the central nervous system. The destruction of motor neurons in the spinal cord results in flaccid paralysis (polios GK grey; myelitis-inflammation of spinal cord).

Properties of the virus (In 1908-1909, K. Landstainer and E. Popper proved poliomyelitis to be of viral aetiology) are common to Picornavirus.

Cultivation: The poliomyelitis virus is cultivated on kidney cells of monkeys and on diploid human cells (HeLa). The cytopathogenic effect is attended by destruction and the formation of granules in the infectedcells.

Antigenic structure: By antigenic structure they are subdivided into three groups: I, II, III. During epidemic outbreaks, type I is most frequently isolated (65-95 per cent of cases). Paralytic forms of the disease are more frequently produced by the type I organism.

Resistance: The virus survive in sterile water at room temperature for a period of more than 100 days, in milk 90 days, in faeces in the cold for more than 6 months, and sewage for several months. It withstands exposure to 0.5-1 per cent phenol solutions. The poliomyelitis virus is sensitive to calcium chlorate lime, chloramine, formalin, hydrogen peroxide and potassium permanganate solutions,

Pathogenesis and pathology: Natural infection occurs only in humans (experimentally, monkeys may be infected by intracerebral or intraspinal inoculation). The virus is transmitted by the fecal-oral route through ingestion. Air droplet route is possible too. Primary multiplication of virus takes place in the oropharynx or intestine. In incubation period the virus reproduced in the lymphoid substances of the throat and intestine. Later they enter into the blood and viremia occurs. Poliovirus can spread along axons of peripheral nerves to the central nervous system, where it continues to progress along the fibres of the lower motor neurons to increasingly involve the spinal cord or the brain. Poliovirus invades certain types of nerve cells, and in the process of its intracellular multiplication it may damage and completely destroy these cells. The anterior horn cells of the spinal cord are most prominently involved, but in severe cases the intermediate grey ganglia and even the posterior horn and dorsal root ganglia are often involved. In the brain, the reticular formation, vestibular nuclei, and deep cerebellar nuclei are most often affected. The cortex is virtually spared, with the exception of the motor cortex along the precentral gyrus. In addition to pathologic changes in the nervous system, there may be myocarditis, lymphatic hyperplasia, ulceration of Peyer's patches, prominence of follicles, and enlargement of lymphnodes.

The incubation period is usually 7-17days, but it can range from 3 to 35 days. The clinical forms are: 1. inapparent asymptomatic infection; 2. abortive poliomyelitis; 3. nonparalytic poliomyelitis; 4. paralytic poliomyelitis. Only about 1 per cent of infections are recognized clinically.

Abortive poliomyelitis: This is the most common form of the disease. The patient has only the minor illness, characterized by fever, malaise, drowsiness, headache, nausea vomiting, constipation, and sore throat in various combinations. The patient recovers in a few days spontaneously.

Non-paralytic poliomyelitis manifests as aseptic meningitis with fever, headache, and a stiff neck. The disease lasts 2-10 days, and recovery is rapid and complete. In a small percentage of cases, the disease advances to paralysis.

Paralytic poliomyelitis: The major illness may follow the minor illness described above. In paralytic poliomyelitis flaccid paralysis is the predominant finding resulting from lower motor neuron damage. Painful muscle spasms also occur. The motor nerve damage is permanent, but some recovery of muscle function occurs as other nerve cells take over. Muscle atrophy and loss of neuromuscular functions can occur.

Immunity: Stable immunity is produced. Virus-neutralizing antibody forms soon after exposure to the virus, often before the onset of the illness, and apparently persists for life.

Treatment: There is no antiviral therapy. Treatment is limited to symptomatic relief and respiratory support, if needed. Physiotherapy for the affected muscles is important.

Prevention: Poliomyelitis can be prevented by both the killed vaccine (Salk vaccine, inactivated vaccine, IPV) and alive, attenuated vaccine (Sabin vaccine, oral vaccine, OPV). Both vaccines induce humoral antibodies. A. A. Smorodinzev and M. P. Chumakov prepared alive vaccine, which is currently preferred for two main reasons: It interrupts faecal-oral transmission by inducing secretory IgA in the gastrointestinal tract. 2. It is given orally and so is more readily accepted than the killed vaccine, which must be injected.

Passive immunization is accomplished by injecting human immunoglobulins. Passive immunity lasts 3-4 weeks.

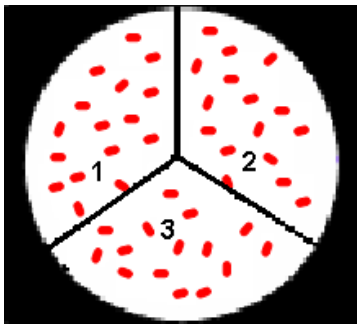
Laboratory diagnosis (picture):

1.Virological method: isolation of the virus. Virus can be recovered from the throat, stool, or spinal fluid by inoculation of the cell cultures. The virus causes cytopathic effect and can be identified by neutralization of the CPE with specific antisera.

2.Serological method: CFR, virus neutralization reaction. Precipitation reaction.

3.Biological method.

4.Immunofluorescence.



POLIOVIRUSES

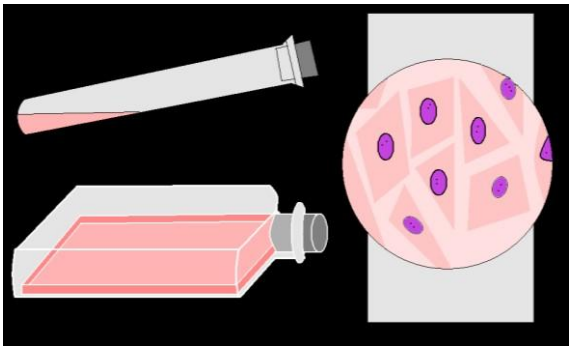
METHODS

Virological

Serological

Virological method

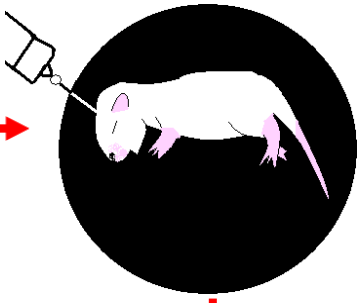
Isolation of enteroviruses



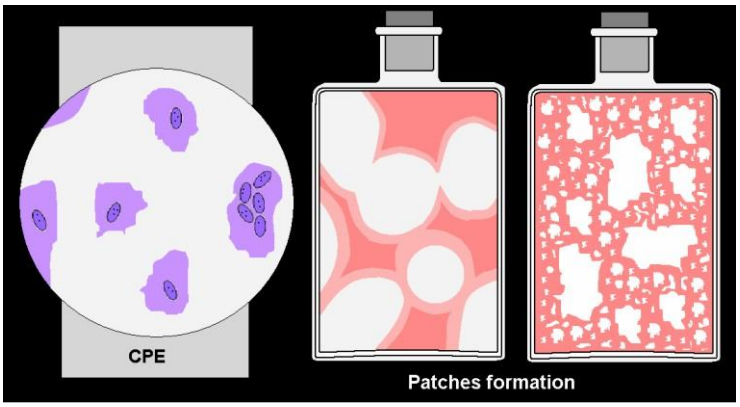
Investigated material:

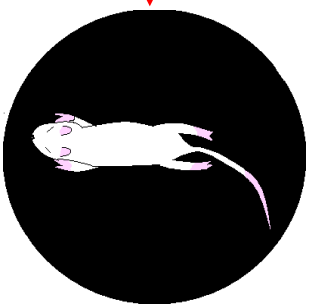
feces,
smear
from

nasopharynges,



INDIC ATION





Paralysis death, pathomorphological changes of organs

IDENTIFICATION (BNR, CFR, HAIR)

Biological neutralization test