Training workshop on screening, diagnosis and treatment of hepatitis B and C

World Health Organization

Session 5

Viral hepatitis
transmission and prevention

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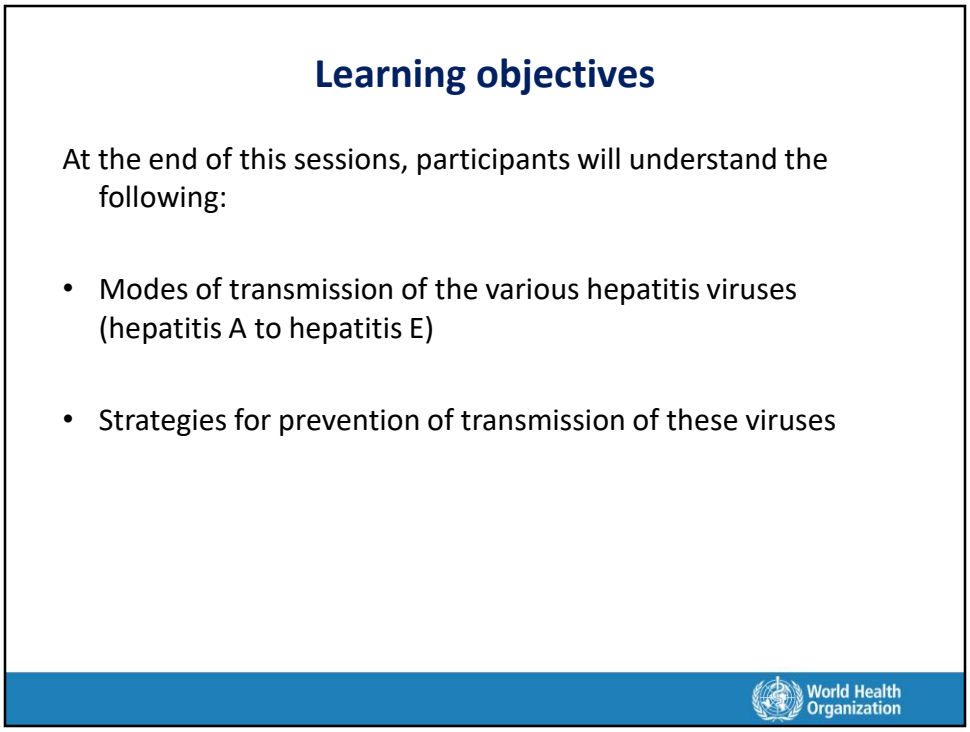

At the end of this sessions, participants should be able to understand the following:

- Modes of transmission of various hepatitis viruses (hepatitis A to hepatitis E)
- Strategies for prevention of transmission of these viruses

Main features of the hepatitis viruses

	HAV	HBV	HCV	HDV	HEV
Virus family	Picornaviridae	Hepadnaviridae	Flaviviridae	Deltaviridae	Hepeviridae
Chronicity rate	No	5% of adults 90% of infants	~75%	Co-infection of HBV; modifies course	Very rare
Hepatocellular carcinoma	No	Yes	Yes	Yes	No
Route of transmission	Person-to person Foodborne Waterborne	Perinatal Bloodborne Sexual	Bloodborne (perinatal) (sexual)	Bloodborne Sexual (perinatal)	Waterborne Foodborne Person-to-person
Vaccine	Yes	Yes	No	HBV vaccine	Not generally (licensed in China)
Treatment options	None	**Available - lifelong treatment**	**Available - CURE**	**No treatment, if HBV–HDV coinfected, treat as for HBV**	None

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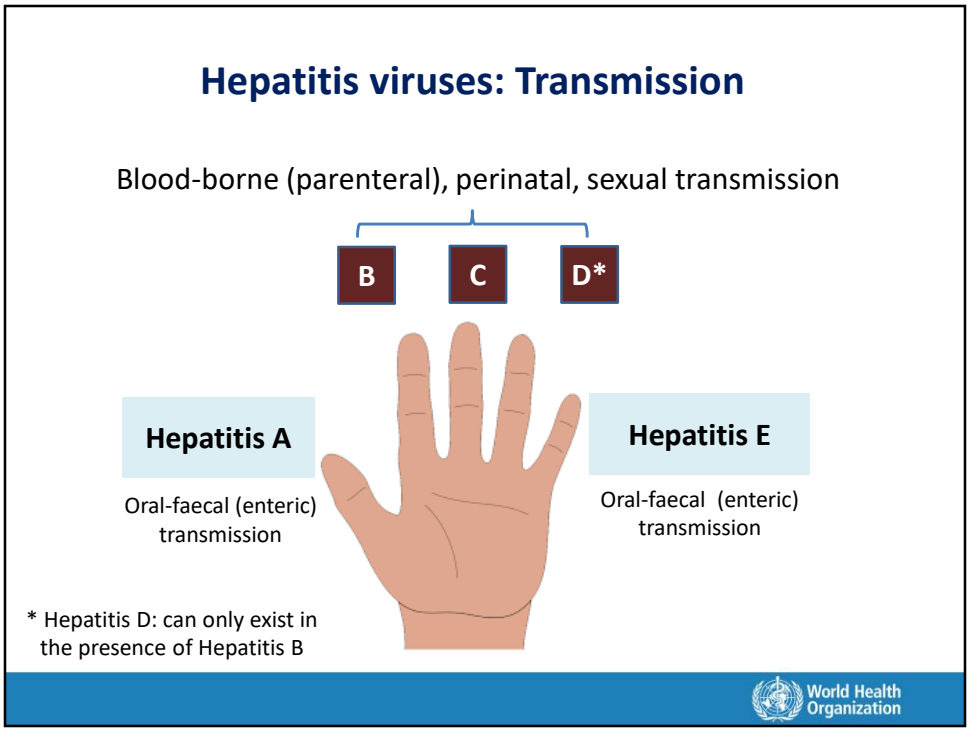
This slide summarizes the several clinical features of the hepatitis viruses from HAV to HEV in general.

There are some differences among these viruses regarding chronicity rate, complication of hepatocellular carcinoma and routes of transmission.

We shall see that only hepatitis B is a DNA virus; the rest are all RNA viruses.

Hence, hepatitis B virus, akin to other DNA viruses such as CMV, HSV, etc. if it enters the human body, its DNA gets integrated with human DNA and remains inside the host body for the rest of his/her life.



For ease of understanding, hepatitis A and E viruses can be grouped together because both of them are transmitted through the faecal–oral route by consumption of contaminated food and water; cause acute viral hepatitis and acute liver failure, and do not cause chronic viral hepatitis, liver cirrhosis or hepatocellular carcinoma. In rare cases, HEV can cause chronic hepatitis.

Similarly, hepatitis B, C and D can be grouped together because all of them are transmitted through the parenteral route; further, all these viruses cause chronic hepatitis, liver cirrhosis and hepatocellular carcinoma.

Parenteral transmission of hepatitis viruses

- Bloodborne
  - Transfusion: blood or blood products (and organ transplant)
  - Other nosocomial routes
    - Dialysis
    - Unsafe injections, needle-stick injury
    - Surgery, dental procedures, etc.
    - Organ transplantation
  - Sharing of needles among persons who inject drugs (PWID)
- Sexual
- Perinatal (mother to child)
- Possible horizontal transmission (children, household contacts)

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Parenteral transmission of viruses occurs following exposure through transfusion of contaminated blood or blood products, unprotected sex, in utero transmission from a pregnant woman to her baby, and possible horizontal transmission.

It is important to know that hepatitis viruses can be transmitted through transfusion, dialysis, unsafe injections, needle-stick injury, surgery, dental procedures, organ transplantation or sharing of needles among persons who inject drugs because these are also interventional points.

Enterically transmitted hepatitis

- Sporadic

  Occurrence of scattered cases at irregular intervals

- Epidemic (=outbreak*)

  Occurrence of a larger-than-usual number of cases of a disease in a community over a short period of time

*Sometimes, use of the term “epidemic” is limited to only larger outbreaks.

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Enterically transmitted viral hepatitis could present as either sporadic hepatitis, which means the occurrence of scattered cases at irregular intervals, or in the form of an epidemic, which means the occurrence of a large number of cases of a disease in a small geographical region over a short period of time.

Enterically transmitted hepatitis

- Endemic

  An infection is said to be endemic in a population when it is constantly maintained at a baseline level in a geographical area without external input

- Degree of endemicity of an infection may vary
  - Very highly endemic
  - Highly endemic
  - Intermediate endemicity
  - Low endemicity

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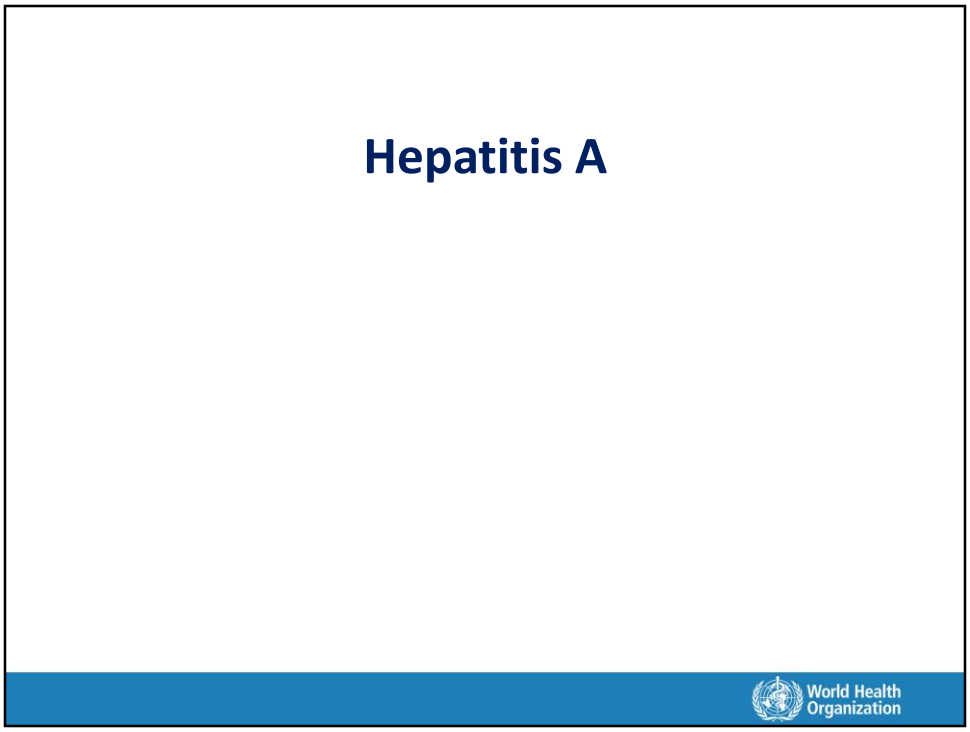
A health condition, specially those of infective etiology, in a geographical region is said to be endemic if it occurs commonly round the year without external input.

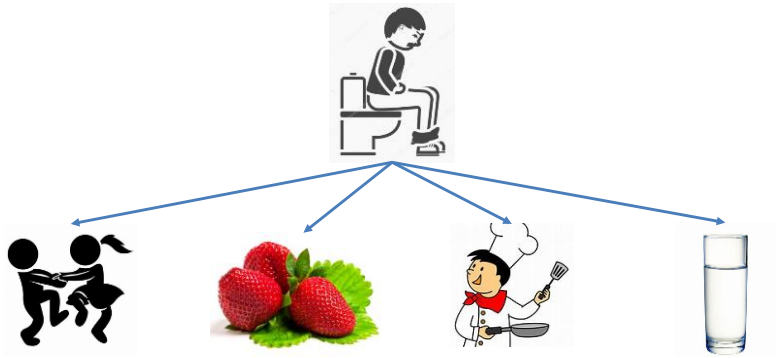
Depending upon the disease frequency in a region, the region may be categorized as low endemic, intermediate endemic, highly endemic and very highly endemic. The cut-offs to define these endemicity categories vary from disease to disease and are not universally constant.



Then, please let me explain some features of each virus. At first, about hepatitis A virus.

Hepatitis A virus

- Excreted in faeces of infected persons
- Enters a new host through the intestinal tract (enteric or faecal–oral transmission)



Close personal contact | Contamination of food (e.g. at farm level) | Contamination of food (e.g. food handlers) | Contaminated drinking water

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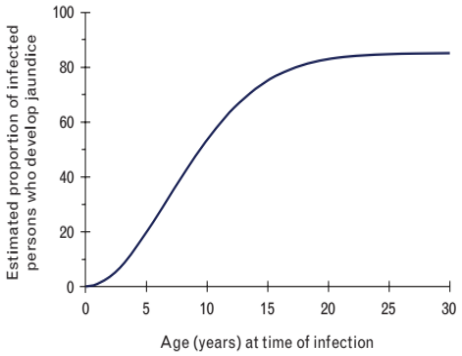
An infected person excretes hepatitis A virus in the faeces. If the water contaminated with the virus containing faeces comes in contact with food and water the virus can be transmitted to a non-infected person.

Faeces-contaminated water could come in contact with food at several points, such as during irrigation of crops, washing of raw food, contamination of drinking water because of a breach in safe water supply.

Further, hepatitis A can also be transmitted from person to person by close personal contacts.

Age and hepatitis A virus infection

- The outcome of HAV infection is determined primarily by the age at the time of infection
- In young children, the infection is usually asymptomatic
- Older children and adults: more likely to have symptomatic infection



Source: Aggarwal R and Goel A. Hepatitis A: epidemiology in resource-poor countries. Curr Opin Infect Dis 2015, 28:488–496

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All those infected with HAV do not develop clinical illness. The majority of HAV-infected persons remain asymptomatic or develop a non-specific minor illness that usually goes unnoticed.

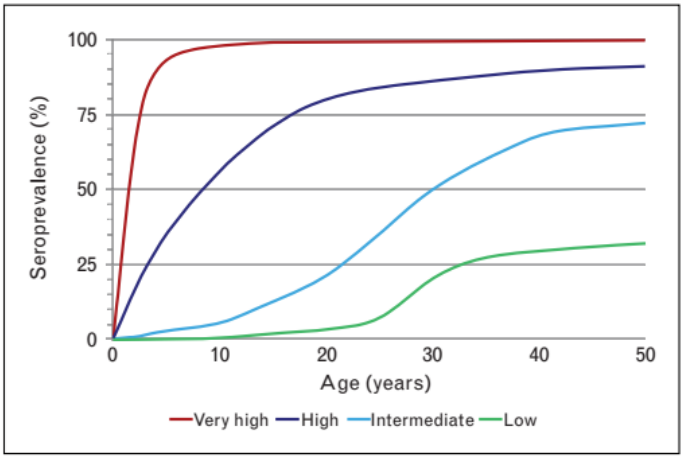
The clinical illness is marked by the development of jaundice coupled with a marked elevation of serum levels of liver enzymes, namely, ALT and AST.

The risk of developing clinical illness is primarily determined by the age of the person at the time of infection.

As the age of the host increases, the risk of clinical disease and severe illness increases.

Generally, in young children, the infection is usually asymptomatic, but older children and adults have symptomatic infection.

Age and hepatitis A virus



Source: Aggarwal R and Goel A. Hepatitis A: epidemiology in resource-poor countries. Curr Opin Infect Dis 2015, 28:488–496

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Anti-HAV antibody persists for life once it develops and hence the seroprevalence of anti-HAV antibodies keeps on increasing with age. The most likely reason for the lifelong presence of anti-HAV is repeated exposure to the virus, in particular, in those who are living in HAV-endemic countries where drinking water quality is compromised.

Based on the anti-HAV seroprevalence, countries in the world are divided into those with low, intermediate, high or very high endemicity. In highly endemic regions, almost 100% of children have been exposed to HAV by the age of 10 years. As we know, the majority of infections in children are asymptomatic. Hence, in highly endemic countries, the majority of infections occur in children and are not severe.

In countries with low endemicity, where exposure occurs mainly in adults, clinical disease usually occurs in adults and is severe.

Other routes of transmission

- Sexual activity (e.g. oral–anal sex)

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HAV can be transmitted by sexual activity. This mode of transmission is most common among adults in developed countries where endemicity of HAV infection is low. The reason for this we have just discussed in the previous slide.

Prevention of hepatitis A

- Personal hygiene
  - Handwashing
- Food hygiene
  - Prevent faecal contamination
  - Food handlers need attention
- Prevention of water contamination

- Hepatitis A vaccine
  - Pre-exposure/universal childhood
  - Post-exposure

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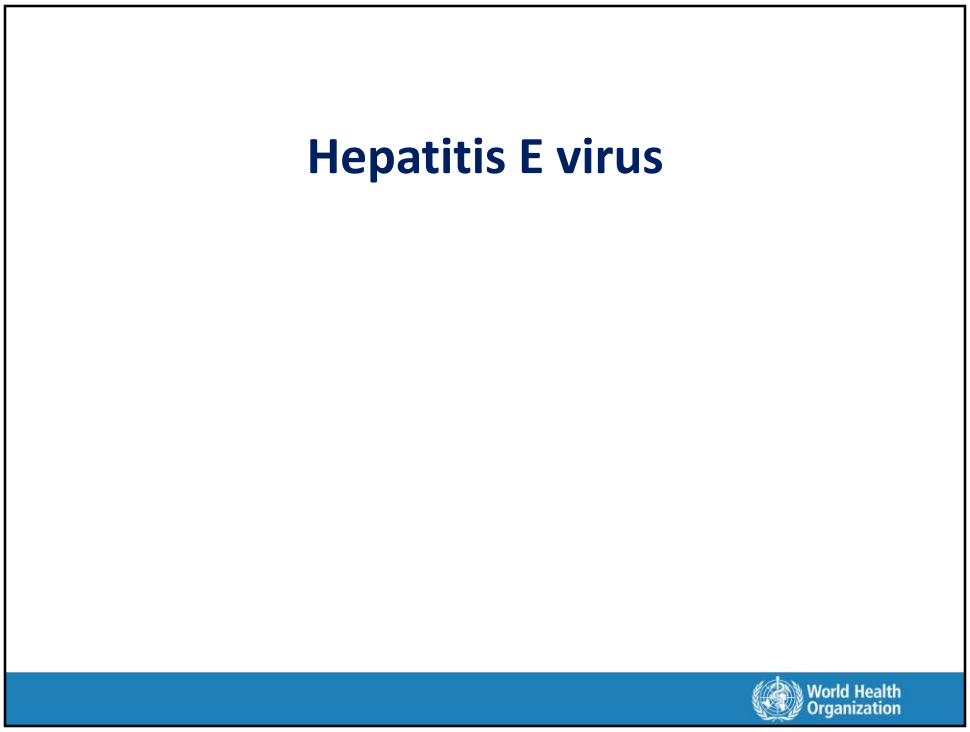
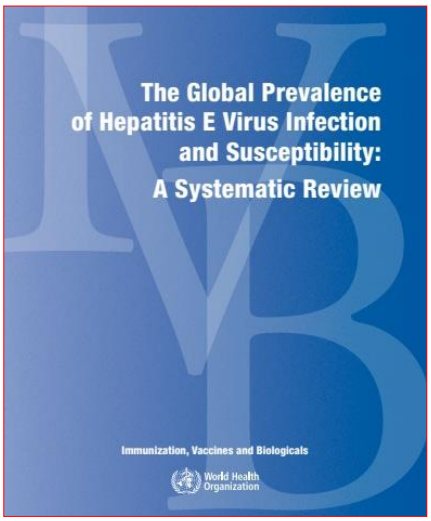
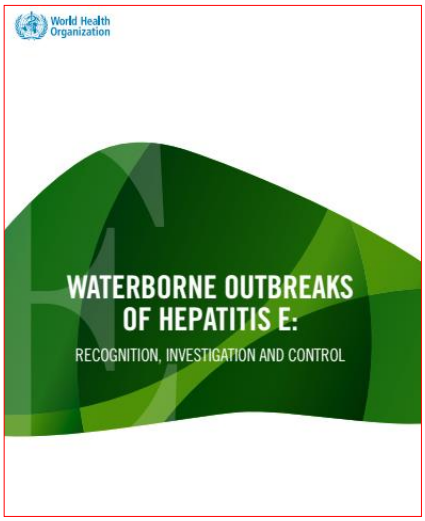
To prevent faecal–oral transmission, personal hygiene, food hygiene and prevention of water contamination is needed.
Vaccination is recommended for individuals without anti-hepatitis A antibody who plan to go to a highly endemic area.



Next is hepatitis E virus, which is also transmitted through consumption of contaminated food and water.

Hepatitis E virus





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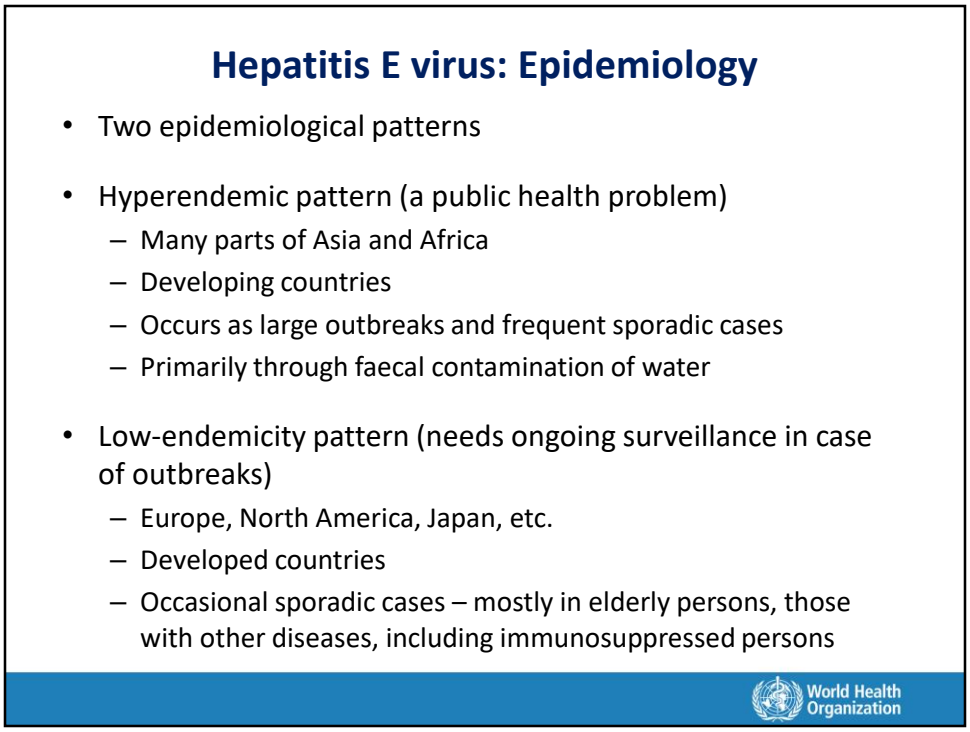
Recently, two detailed documents on hepatitis E virus infection have been published by WHO.

The first one contains a comprehensive description of the seroprevalence of HEV in different countries across the world.

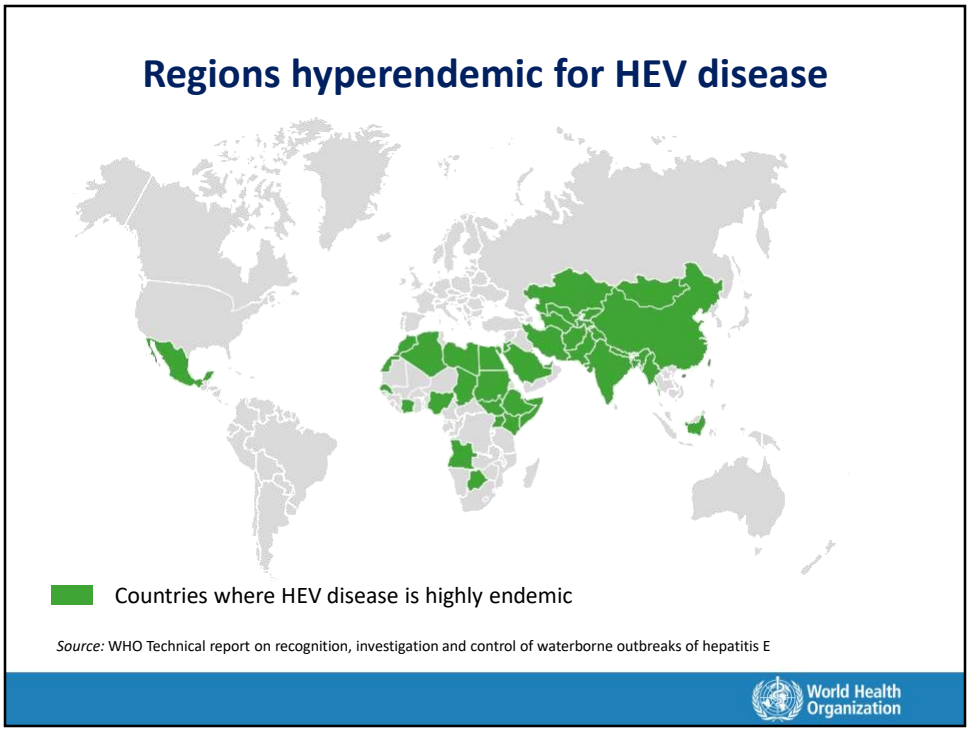
The second one is about HEV outbreak investigation and control. HEV outbreaks are very frequent in developing countries, in particular, in south Asian countries.



There are two epidemiological patterns of hepatitis E virus.

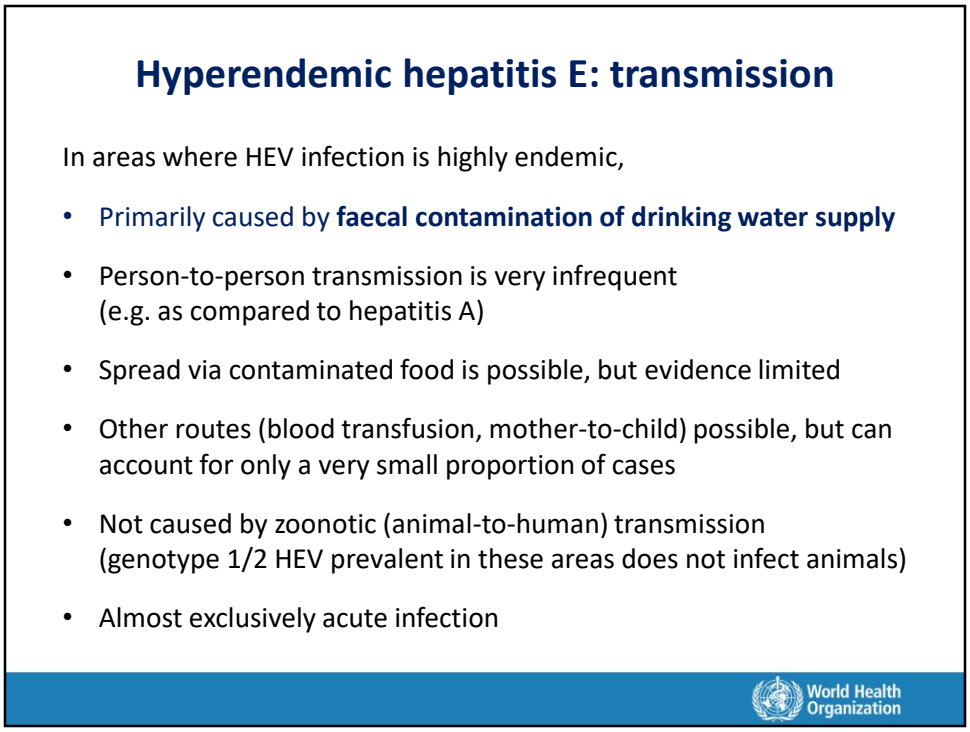
In Asian and African countries, where HEV is hyperendemic, large outbreaks are frequent. In these regions, sporadic cases occur throughout the year. These epidemics and sporadic cases occur because of faecal contamination of the water.

On the contrary, in developed countries where HEV is not endemic, only occasional sporadic cases have been seen and are primarily caused by zoonotic transmission of HEV. Ongoing surveillance is required in case of outbreaks.



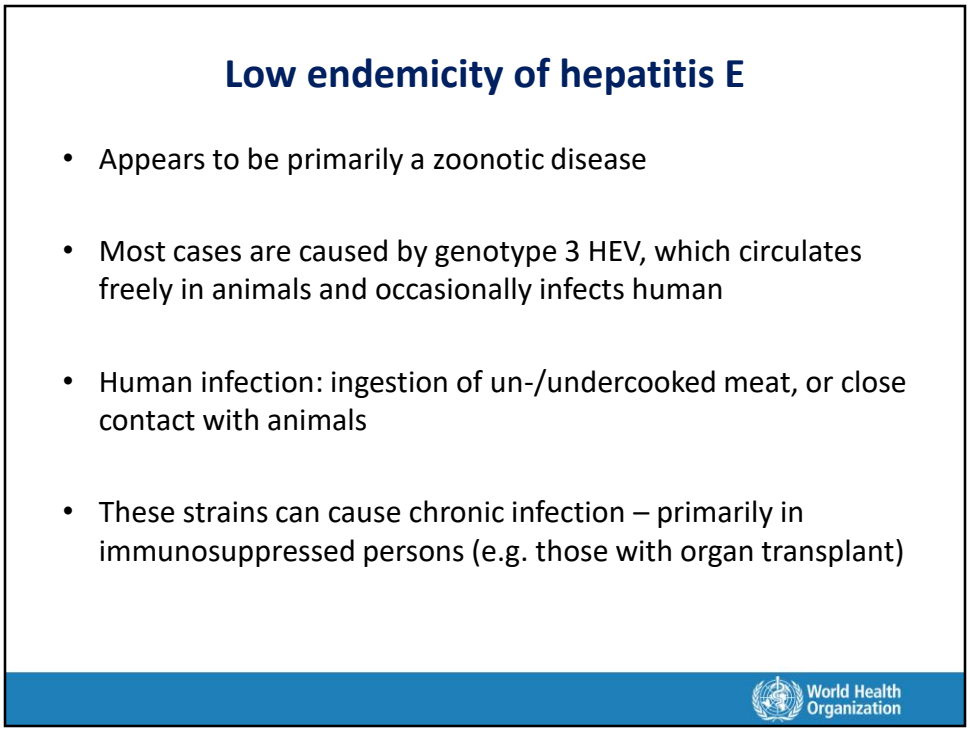
In the world map shown in this slide, the green areas shows countries where HEV disease is highly endemic.

Many parts of Asia and North Africa are hyperendemic zones.



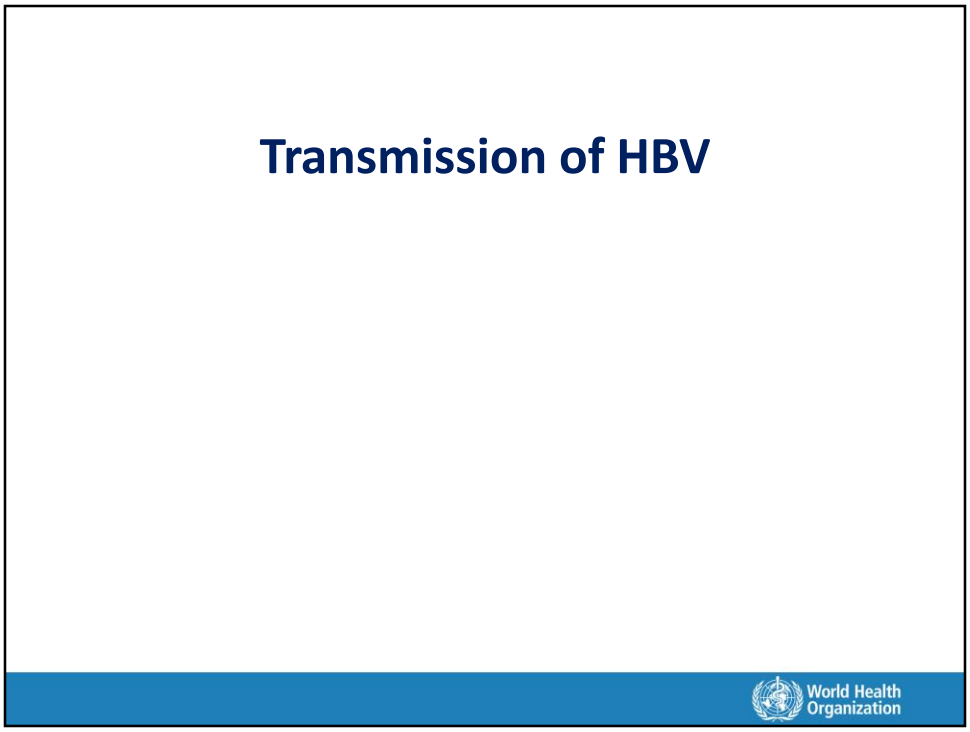
In areas where HEV infection is highly endemic,

- primarily caused by faecal contamination of drinking water supply
- person-to-person transmission very infrequent (e.g. as compared to hepatitis A)
- almost exclusively acute infection

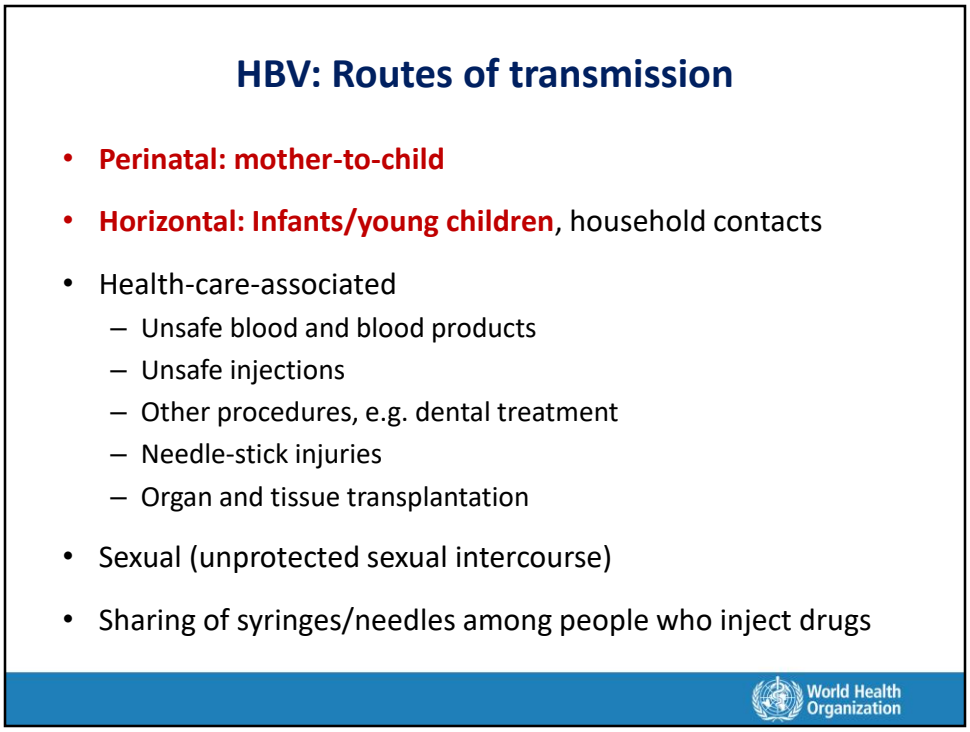


On the other hand, in areas where endemicity of HEV infection is low,

- hepatitis E virus infection appears to be primarily a zoonotic disease
- most cases are caused by genotype 3 HEV, which circulates freely in animals and occasionally infects humans
- human infection: ingestion of un-/undercooked meat, or close contact with animals
- these strains can cause chronic infection – primarily in immunosuppressed persons (e.g. those with organ transplant).



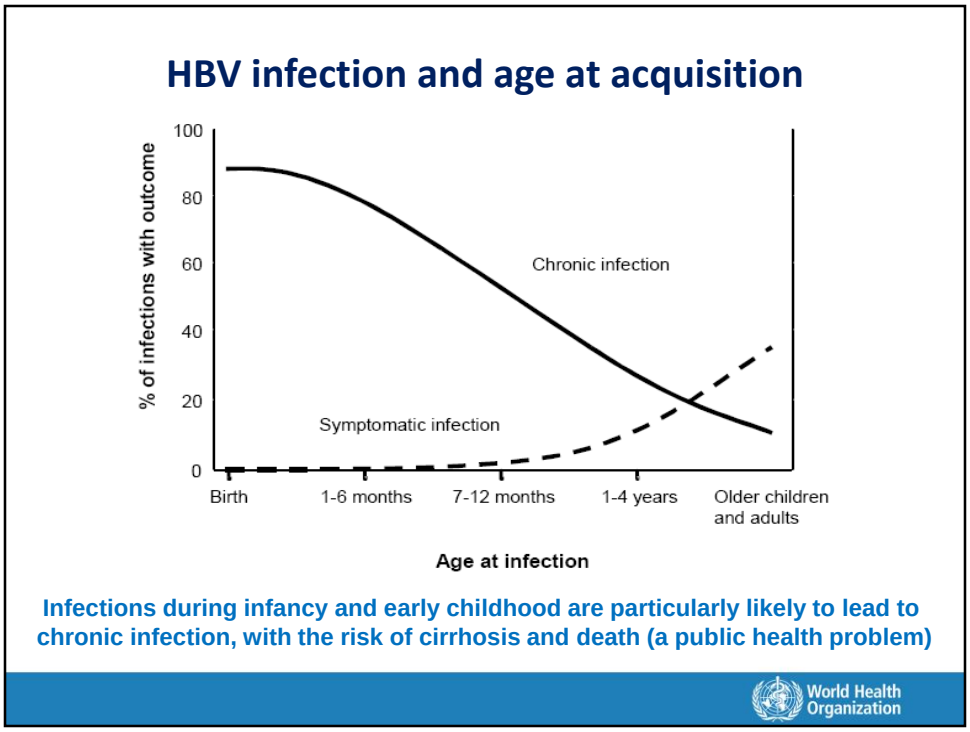
Next is hepatitis B virus.



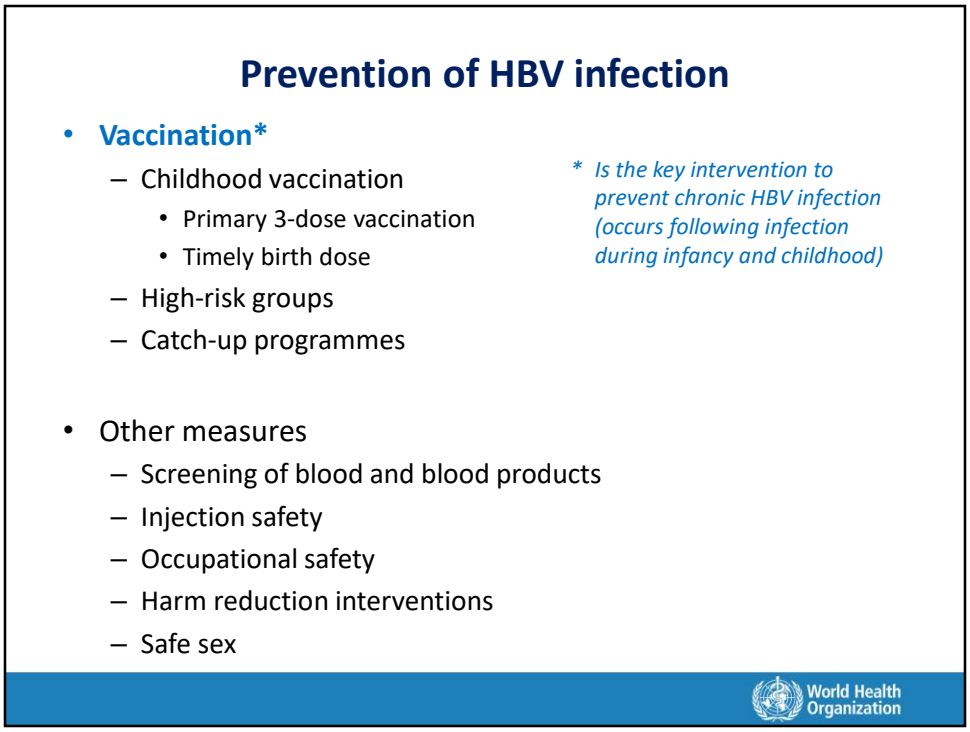
HBV is transmitted through the parenteral route. The most important of these are perinatal mother-to-child transmission, horizontal transmission in infants or young children in whom it leads to chronic infection, consequent cirrhosis and liver cancer.

On the other hand, horizontal transmission in older children or adults causes acute hepatitis, and most of them are asymptomatic, although in rare cases they may have fulminant hepatitis, which is fatal.
More than 95% of adults with acute hepatitis B clear the virus within six months.

Horizontal transmission occurs in health-care-associated transmission, sexual transmission, or through sharing of syringes/needles among PWID.

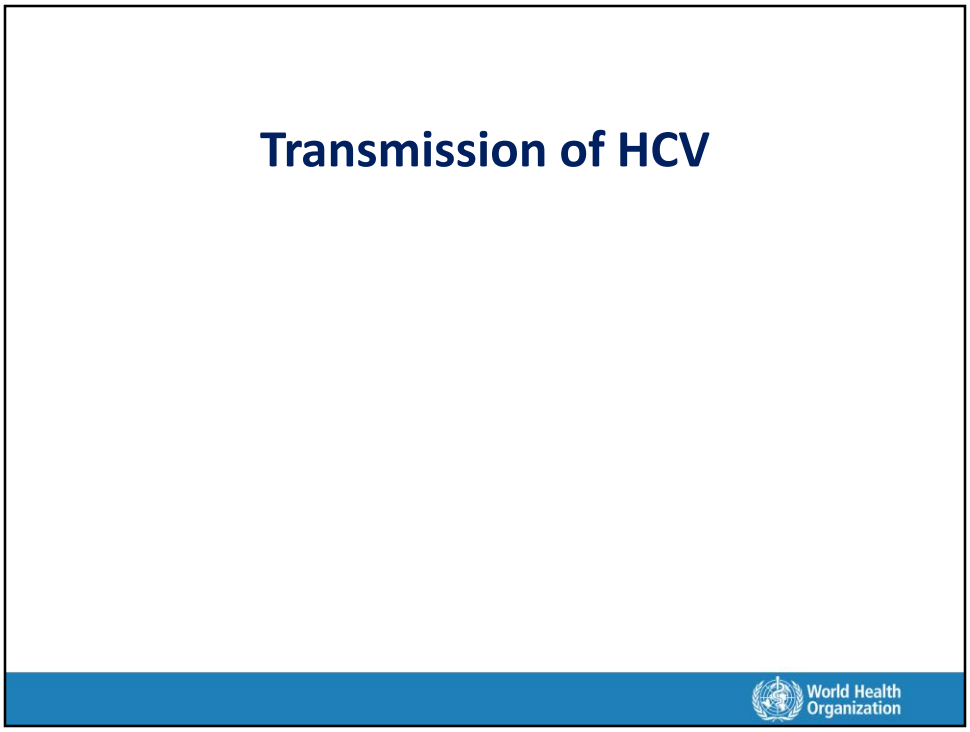


The natural history of HBV infection depends upon the age of the host at the time of infection. There is an inverse relationship between the risk of developing acute hepatitis and its progression to chronic infection and the age of the host.
Infections during infancy remain asymptomatic and carry more than 90% chance of progressing to chronic infection.
By the age of 5 years, about 20% develop chronic infection.
After the age of 5 years and particularly in adults, more than 90% develop acute hepatitis and clear the virus within six months.



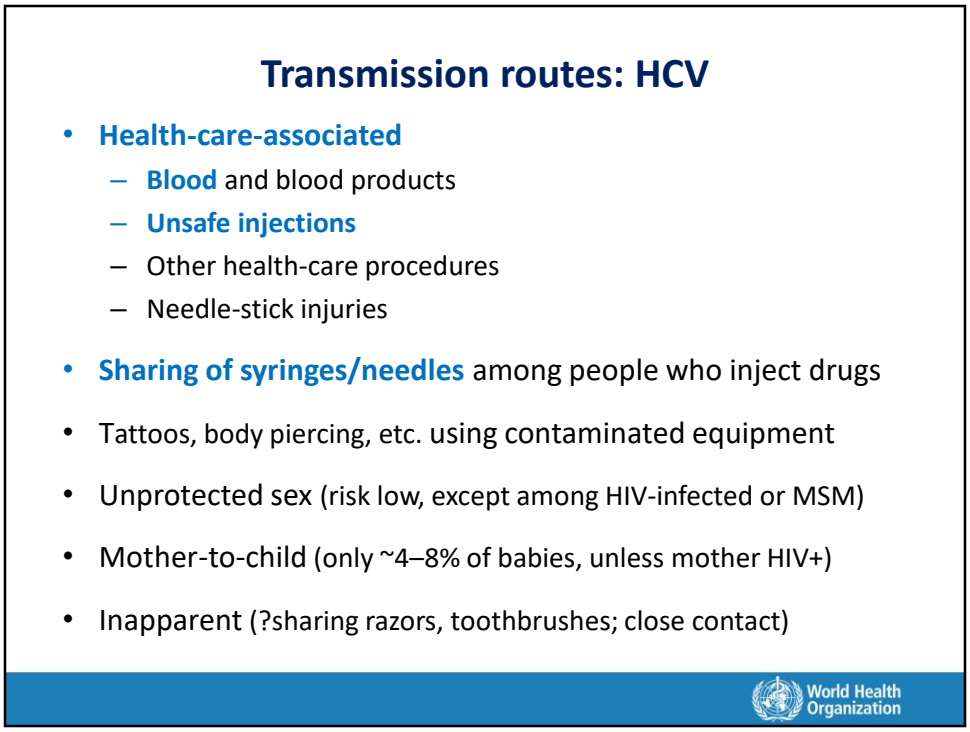
Because the majority of chronic HBV infections occur following infection during infancy and childhood,

- Vaccination is the key intervention to prevent chronic HBV infection.
- Adequate coverage of hepatitis B vaccination could be achieved through birth dose vaccination, routine childhood vaccination, vaccination of high-risk groups, and catch-up programmes to vaccinate susceptible adults. Among the various strategies for hepatitis B vaccination, childhood vaccination is the most important because children are at the maximum risk of developing chronic infection and also have the longest period of risk of developing the complications of chronic HBV infection such as cirrhosis or liver cancer.
- Other prevention measures are screening of blood and blood products, injection safety, occupational safety, harm reduction interventions and safe sex, etc.

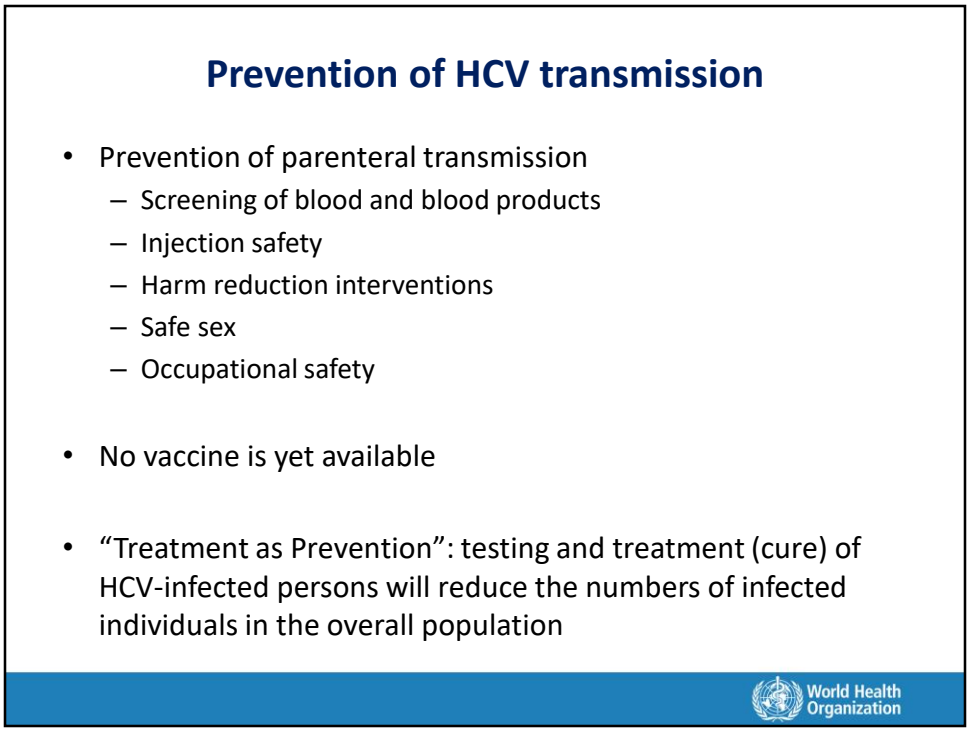


Another hepatotropic virus which is transmitted through the parenteral route.

In the past few years, the treatment of HCV infection has seen a major change in terms of efficacy, safety, cost and ease of administration.
Actually, it is the recent game change in HCV treatment which has led to the enhanced global response against viral hepatitis.



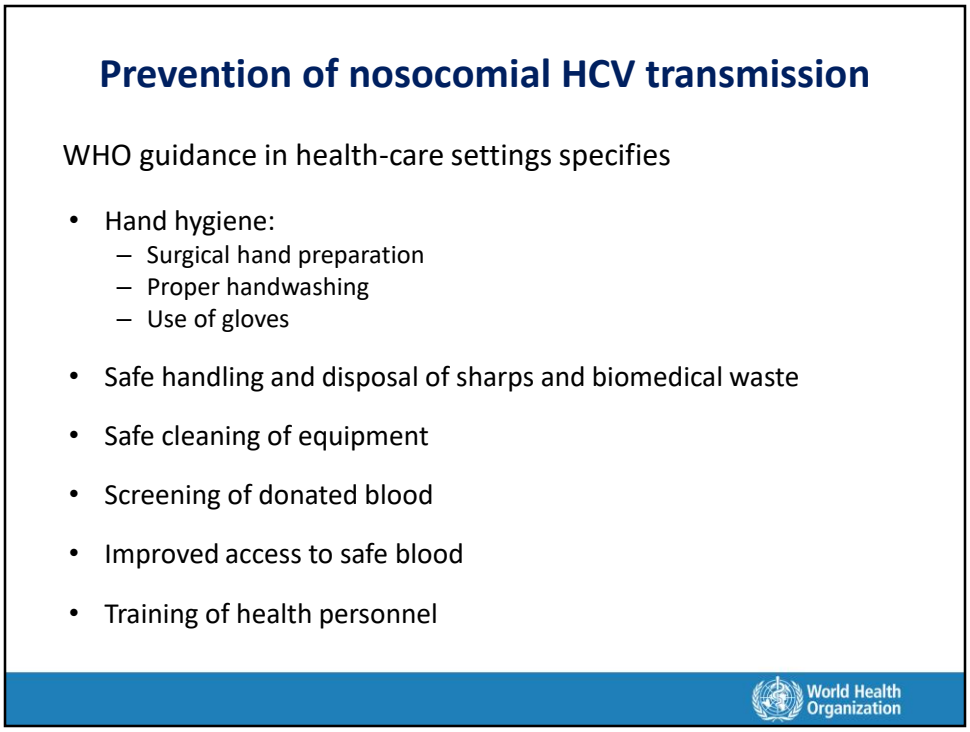
HCV infection also has several transmission routes.
Similar to HBV, the main routes of HCV transmission are health-care activities such as blood transfusion, unsafe injections, needle-stick injuries or other healthcare procedures.
As well as HBV, sharing of syringes/needles among PWID, unprotected sex, mother-to-child transmission also can cause HCV transmission.



There is no vaccine

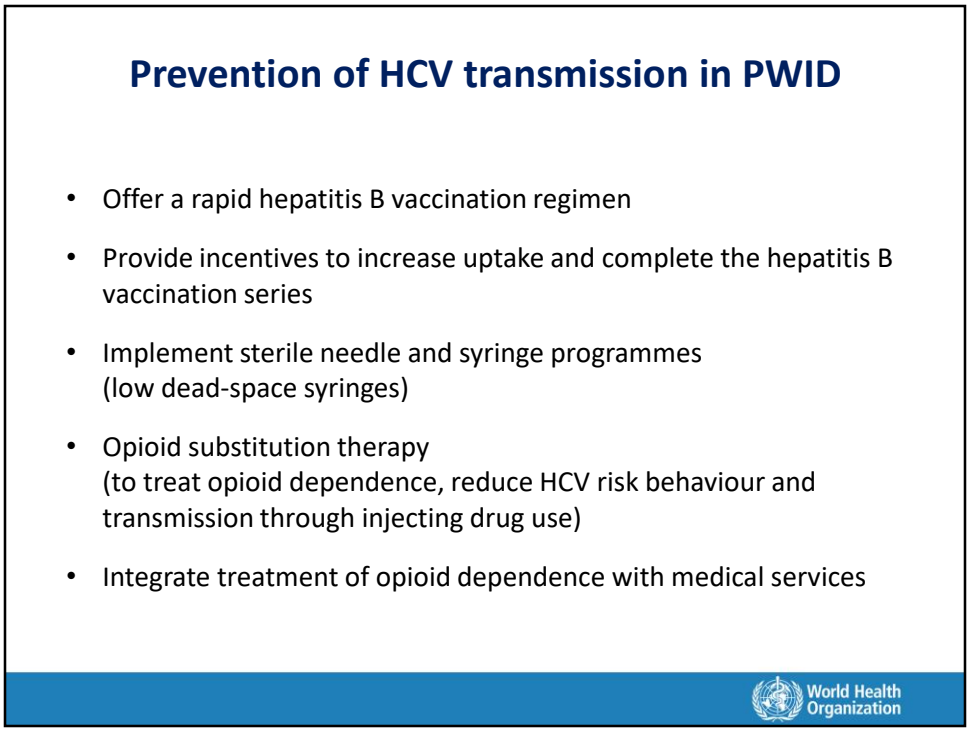
As a way of preventing parenteral transmission mainly to health-care providers, it is important to do the following:

- Screening of blood and blood products
- Injection safety
- Harm reduction interventions
- Safe sex
- Occupational safety.



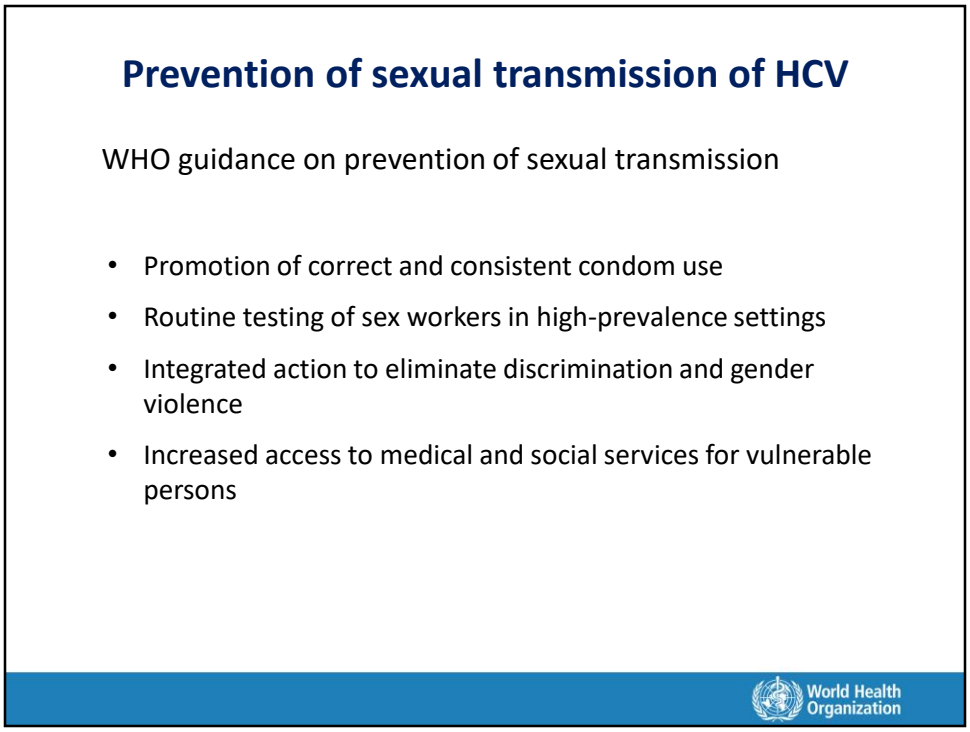
To prevent nosocomial HCV transmission, WHO guidance recommended

- Hand hygiene:
  - ✓ Surgical hand preparation
  - ✓ Proper handwashing
  - ✓ Use of gloves
- Safe handling and disposal of sharps and biomedical waste
- Safe cleaning of equipment
- Screening of donated blood
- Improved access to safe blood
- Training of health personnel



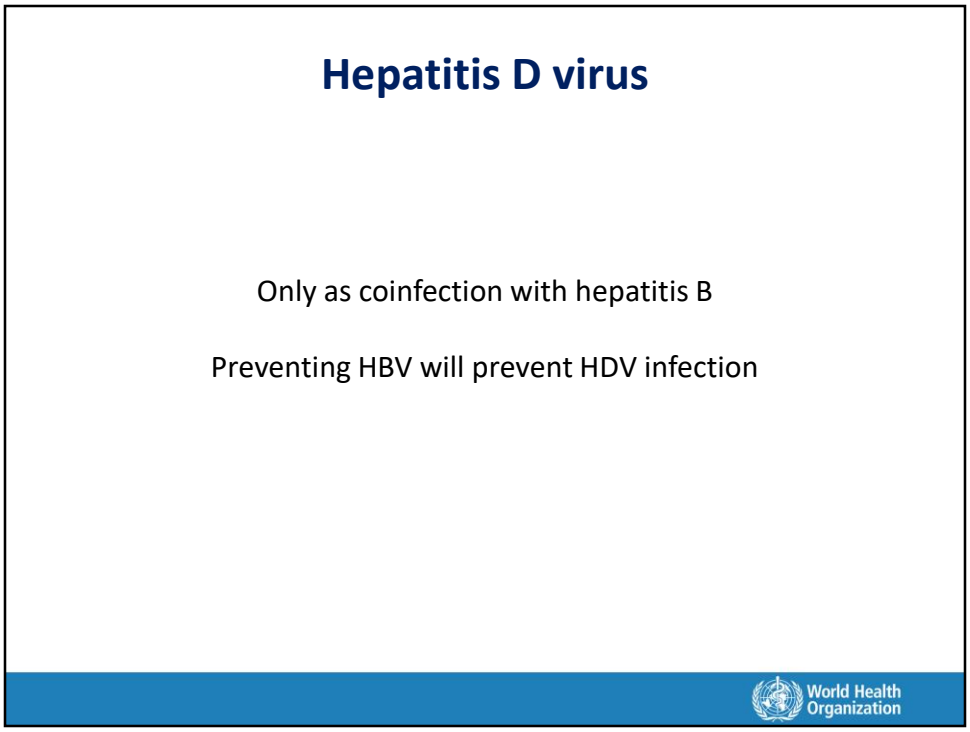
To prevent HCV transmission in PWID,

- Offer a rapid hepatitis B vaccination regimen
- Provide incentives to increase uptake and complete the hepatitis B vaccination series
- Implement sterile needle and syringe programmes (low dead-space syringes)
- Opioid substitution therapy (to treat opioid dependence, reduce HCV risk behaviour and transmission through injecting drug use)
- Integrate treatment of opioid dependence with medical services



To prevent sexual transmission of HCV

- Promotion of correct and consistent condom use
- Routine testing of sex workers in high-prevalence settings
- Integrated action to eliminate discrimination and gender violence
- Increased access to medical and social services for vulnerable persons



The last hepatitis virus is hepatitis D virus.

HDV infection is established only as a coinfection with hepatitis B.

If we can prevent transmission of HBV, we can also prevent HBV infection.

Hepatitis D virus (HDV)

- First discovered by Mario Rizetto in 1977
- Defective/incomplete, requires HBsAg for outer coat and hence entry/exit from cells
- HDV is estimated to infect 10–20 million people worldwide (5% HBsAg-positive carriers)
- Transmitted by exposure to infected blood or body fluids
  - High transmission in intravenous drug users
  - Some sexual transmission
  - Some intrafamilial spread but perinatal transmission is uncommon
- Low infectious dose

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This slide provides general information about HDV.

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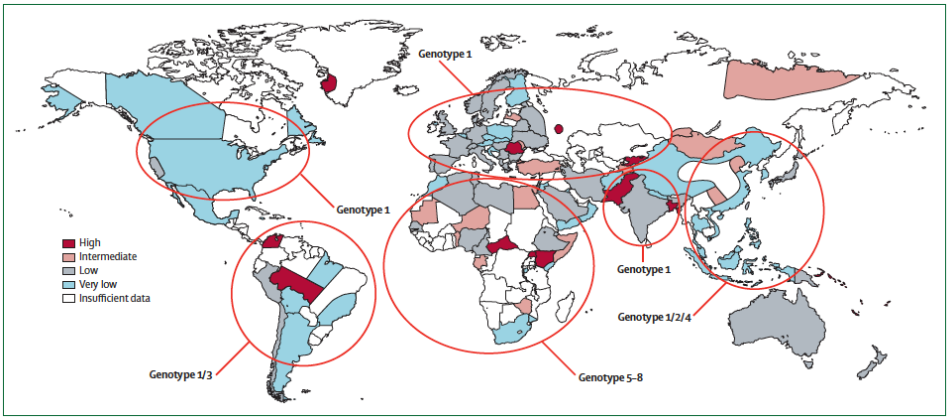
Hepatitis D – global epidemiology



Hughes et al. 2011 Lancet

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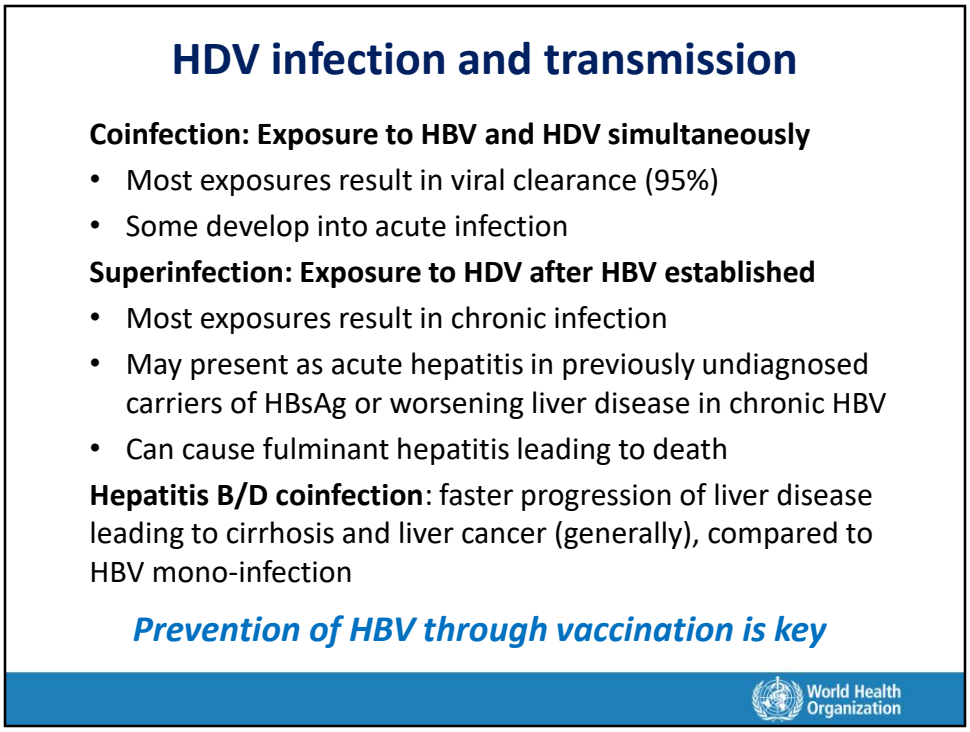
This slide shows the distribution of hepatitis D virus.

You can see that some areas of the Western Pacific Region have intermediate endemicity.



There are two patterns of HBV and HDV infection.

One is coinfection in those exposed to HBV and HDV simultaneously.

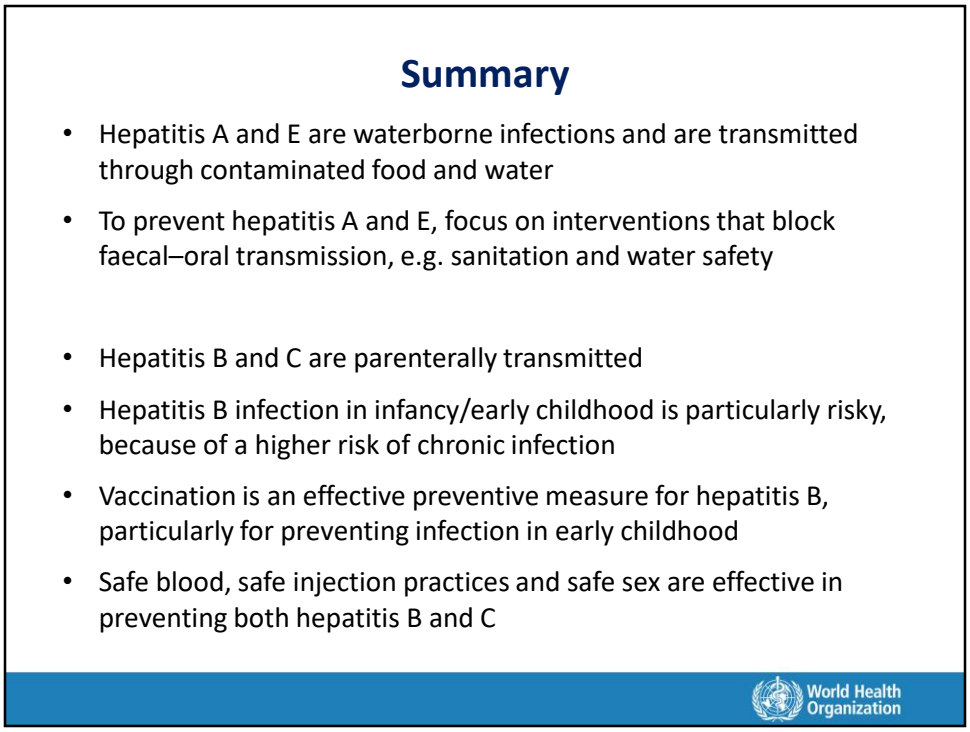
This form of transmission can cause acute hepatitis but mostly results in viral clearance.

Another is superinfection, in which patients with chronic HBV infection or HBV carriers are exposed to HDV.

This way of transmission can cause fulminant hepatitis leading to death.

It is important to know that hepatitis B and D coinfection leads to faster progression of liver disease to cirrhosis and liver cancer compared to HBV mono-infection.

Whatever the infection patterns, prevention of HBV through vaccination is key to preventing HDV infection.



In summary,

- Hepatitis A and E are waterborne infections and are transmitted through contaminated food and water

✓ To prevent hepatitis A and E, focus on interventions that block faecal–oral transmission, e.g. sanitation and water safety

- Hepatitis B, C and D are parenterally transmitted

✓ Hepatitis B infection in infancy/early childhood is particularly risky, because of a higher risk of chronic infection

✓ Hepatitis D only occurs if a person has hepatitis B.

- Vaccination is an effective preventive measure for hepatitis B, particularly for preventing infection in early childhood

- Safe blood, safe injection practices and safe sex are effective in preventing both hepatitis B and C.