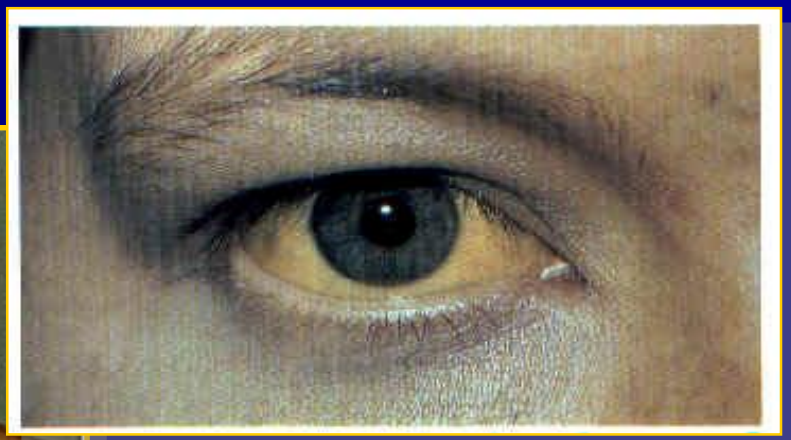
“VICTOR BABEŞ” UMP TIMIŞOARA

Course 6
Viral hepatitides

Emilian Damian Popovici,
M.D.,Ph.D.

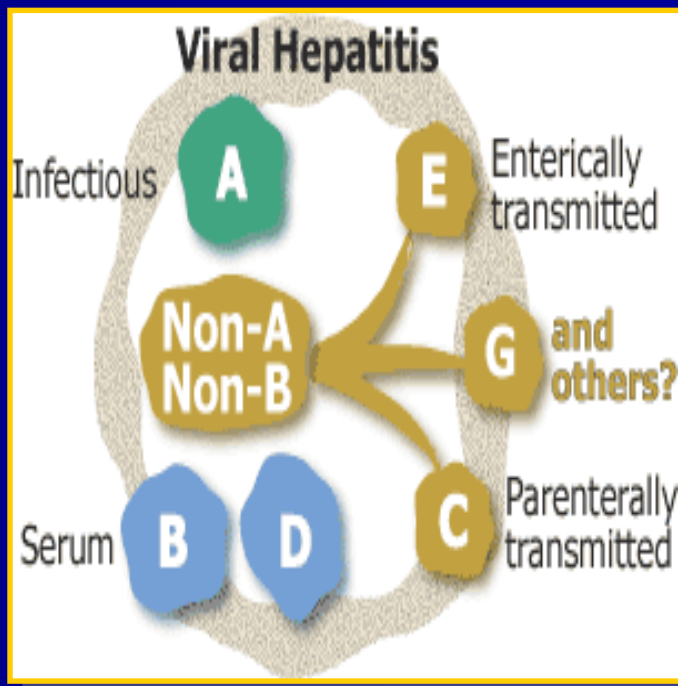
Definition

- **Viral hepatitides are human-specific infectious diseases with an endemic-epidemic evolution, spread over a wide geographical area and with clinical manifestations in an icteric or anicteric form.**



Viral hepatitides

- **The following entities are currently united under the name of viral hepatitides:**
  - **Viral hepatitis caused by the A virus;**
  - **Viral hepatitis caused by the B virus;**
  - **Viral hepatitis caused by the D virus;**
  - **Viral hepatitis caused by the C virus;**
  - **Viral hepatitis caused by the E virus;**
  - **Viral hepatitis caused by the G virus.**

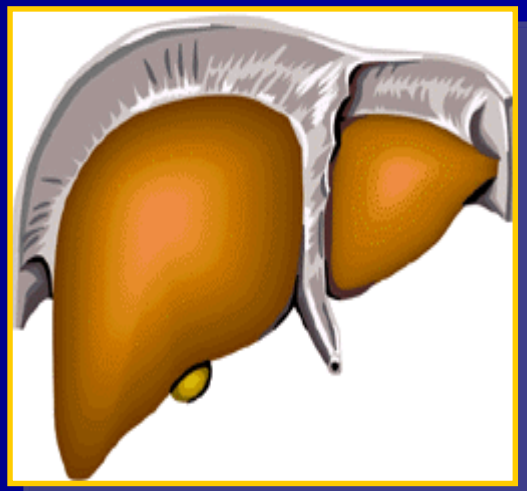


Brief history

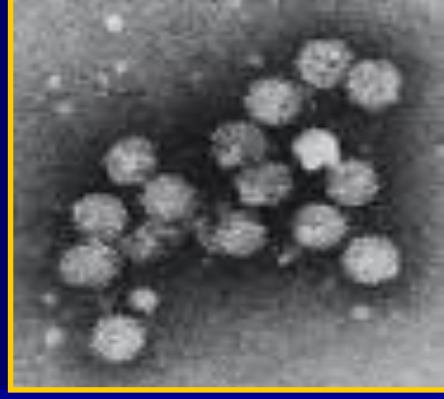
- **The discovery of the Australia antigen by Blumberg, in 1965, has led to the discovery of all the aspects of these diseases, which, in time, has led to:**
  - **A differentiation of hepatitis B from the other types;**
  - **A more accurate identification of anicteric forms and of chronic HBAg carriers;**
  - **The demonstration of hepatitis B transmission through other routes than the parenteral one;**
  - **The clarification of some pathogenicity aspects in hepatitis B;**
  - **The demonstration of the antigenic heterogeneousness of HBAg's, which has led to the identification of significant variation in the geographical distribution of HBAg types.**

The epidemiological importance

- **Generally speaking, viral hepatitides are a serious public health issues due to:**
  - **Their high morbidity;**
  - **The deaths they generate;**
  - **Their impairing sequelae;**
  - **The costs of medical care;**
  - **The proportion of hepatitis B**
  - **and of the non-parenteral transmission routes.**



Features of the pathogens



Hepatitis A virus

- **It is part of the *Picornaviridae* family, *Hepatovirus* genus;**
- **Seroepidemiologic studies have highlighted the presence of anti-VHA antibodies in an average percentage of 70% of the population;**
- **In our geographic area, most individuals go through an icteric/anicteric form of the disease by the age of 20;**
- **There are very big differences among geographic areas.**

Features of the pathogens

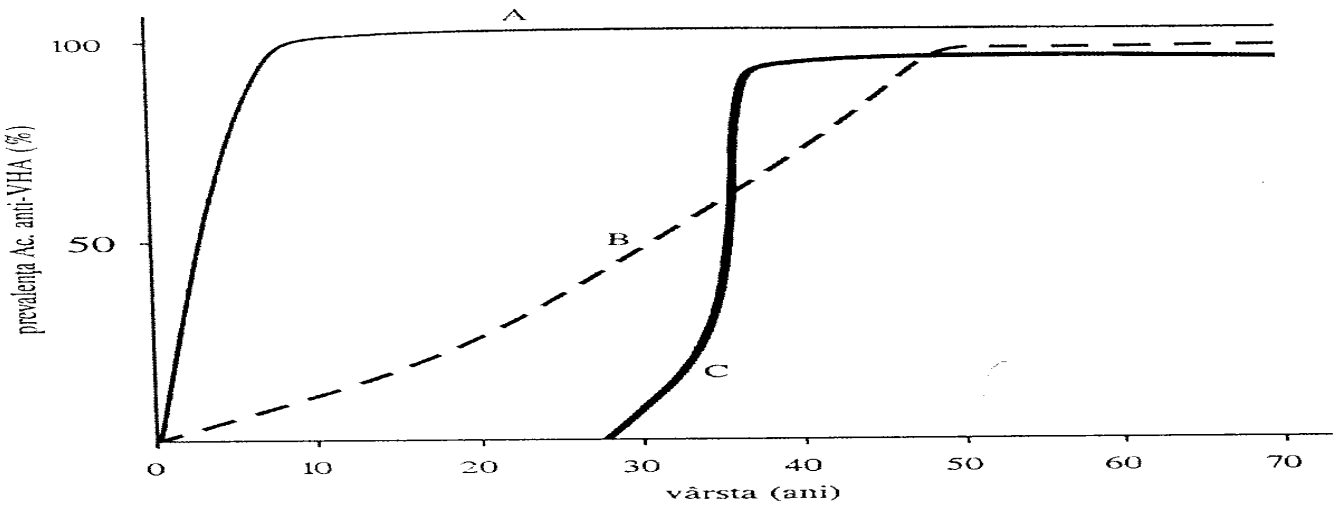
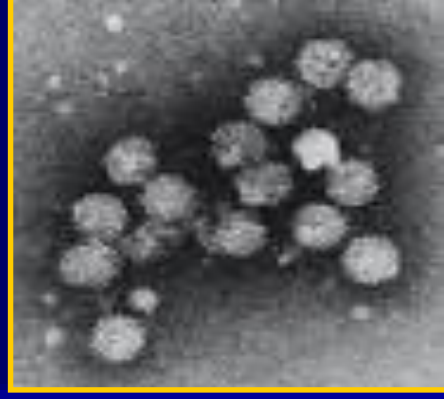


Fig. 2. *Modelele de prevalență ale anticorpilor anti-VHA, în raport cu vârsta*

- **A – A pattern characterizing intensely endemic areas**
- **B – A pattern characterizing medium endemicity area**
- **C - A pattern characterizing low endemicity areas**

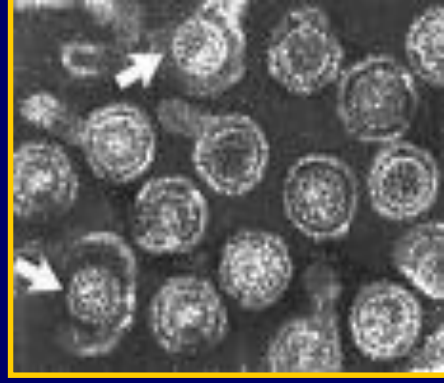
Features of the pathogens



Hepatitis A virus

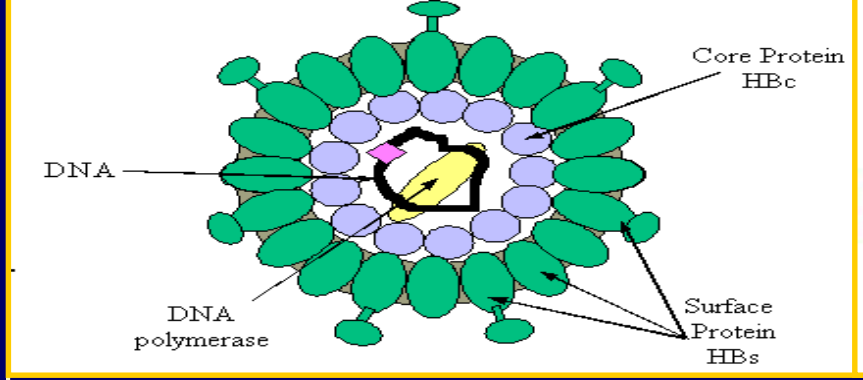
- is sensitive to the effects of chlorine in regular doses:
  - 2 mg/l free chlorine in 5 minutes;
  - 0.25 ml/l formaldehyde at 37°C;
- It is inactivated within one hour at 60°C and
- within one minute at 100 °C;
- It can last for months in residual waters, in sea water.

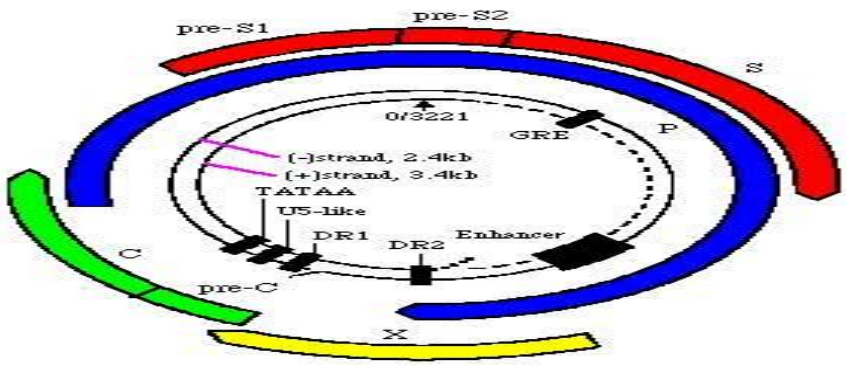
Features of the pathogens



Hepatitis B virus

- **In 1965, Blumberg noticed the emergence of a line of precipitation between an Australian Aborigine's serum and serums coming from polytransfused patients;**
- **The antigen was named Australia Ag;**
- **Subsequent research established the causal relation between Australia Ag and hepatitis B, which led to the name of HBAg's.**

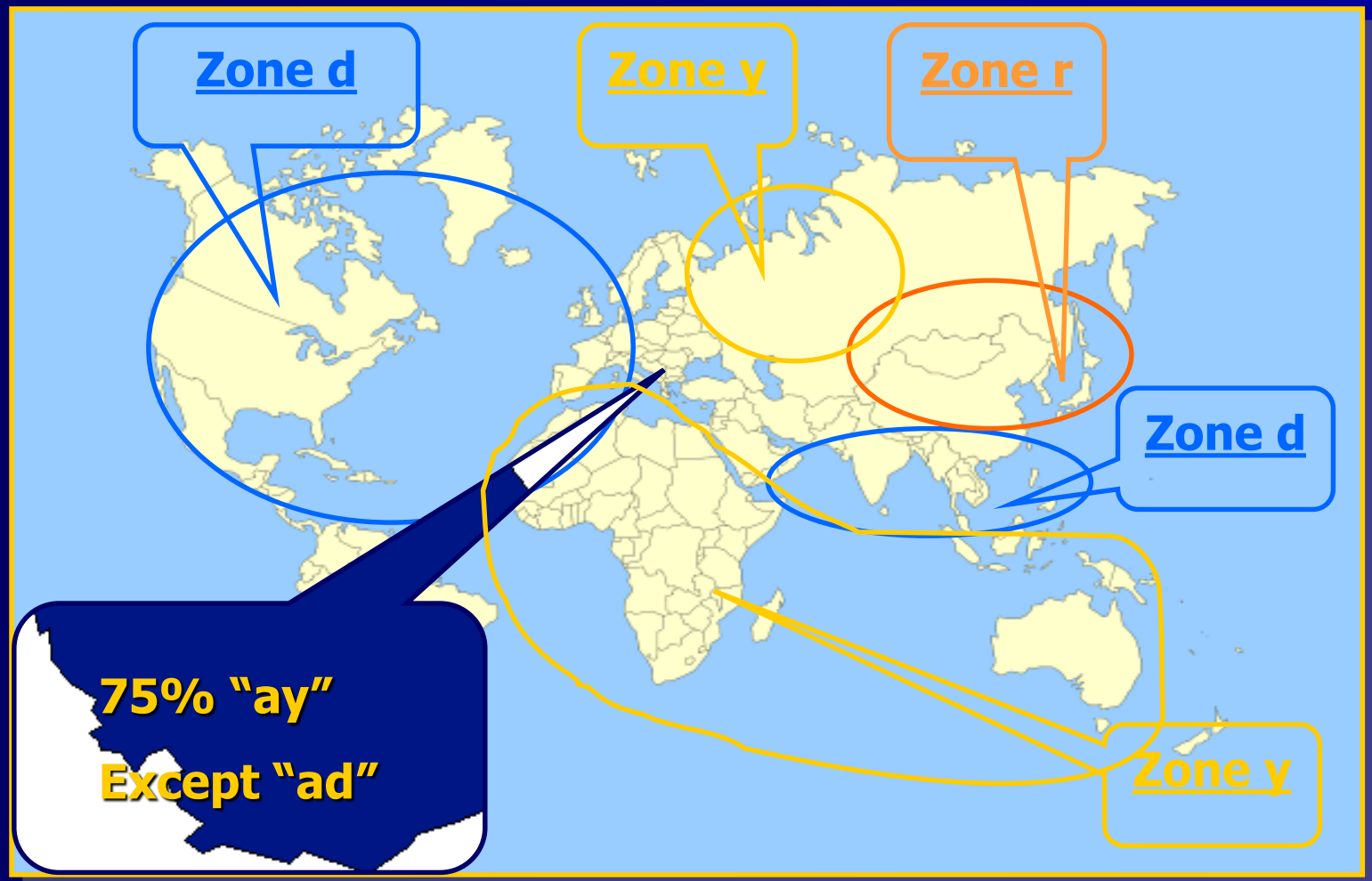




Hepatitis B virus

- In 1970, Dane described a double-contour particle, with a similar structure to a virus – the hepatitis B virus;
- This is a member of the *Hepadnavirus* family;
- It can last 7 days at room temperature under treatment with 0.2% phenol or ethyl alcohol;
- It is inactivated by β-propiolactone in a concentration of 4g/l and by glutaraldehyde in an alkaline water solution.

HB-antigen subdeterminants



Features of the pathogens

Hepatitis D virus

- The first discoveries connected with Delta Atc/Ag were made by Rizetto in 1977. He described them as a new antigenic system in B-virus infections;
- Subsequent reconsiderations have led to the individualization of a new hepatitic agent called the delta hepatitis virus;
- It is a rudimentary virus also known as a defective virus, which cannot multiply on its own, but needs HBV as a virus helper.

Features of the pathogens

Hepatitis D virus

- **When D-virus contamination occurs simultaneously with HBV, we are dealing with a coinfection, which generally has a benign manifestation (the replication and survival potential of HDV is limited by the the short-term HB antigenemia);**
- **If HDV contamination occurs after the HBV contamination, we are dealing with a superinfection, which can evolve towards a fulminating hepatitis or an aggressive chronic hepatitis (HDV finds large quantities of HBAg's, which are needed for its synthesis).**

Features of the pathogens

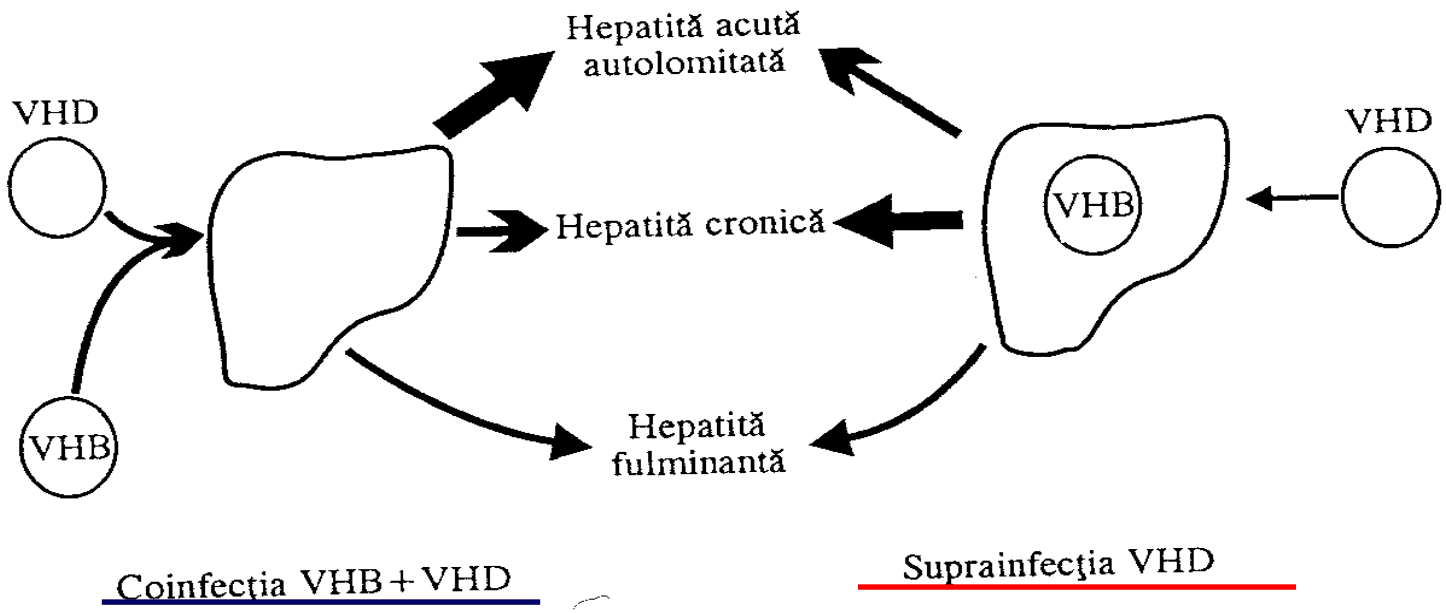
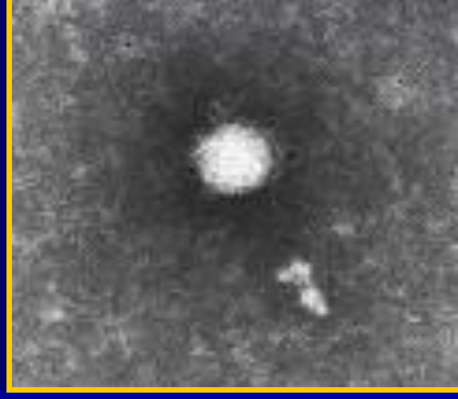


Fig. 3. *Modalităţi evolutive ale infecţiei cu VHD (după Koff – 27)*

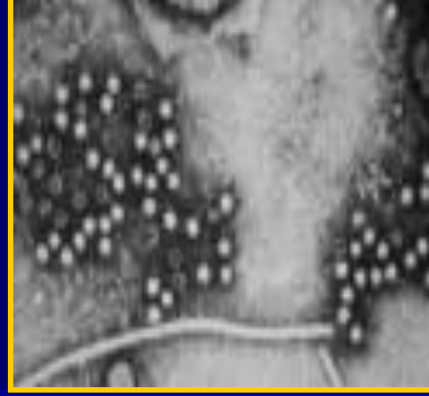
Features of the pathogens



Hepatitis C virus

- It is part of the ***Flaviviridae*** family, ***Hepacivirus*** genus;
- From certain epidemiological points of view, it resembles HBV, being responsible for most post-transfusional hepatitides (in retrospective studies);
- At least 6 genotypes with several subtypes are known.

Features of the pathogens



Hepatitis E virus

- It is an RNA virus belonging to the *Calicivirus* family, *Hepevirus* genus;
- It is responsible for hepatitides that , until recently, were called non-a, non-B hepatitides with epidemic features and digestive route transmission, especially under circumstances of lacking hygiene;
- From certain epidemiological points of view, it resembles HAV;
- In pregnant women, it can result in fulminating hepatitides, leading to death in 20-39% of cases.

Features of the pathogens

Hepatitis G virus

- HGV is an RNA virus, without coating, belonging to the *Flaviridae* family, with several genotypes;
- It is resistant to ambient conditions, but it is destroyed by chlorine-based decontaminants;
- It generates spontaneously resolutive acute hepatitides, which are supposed to be able to evolve towards chronicity;
- The high percentage of chronic HGV and HBV/HCV infections suggests the helper role of these 2 latter viruses.

The entry

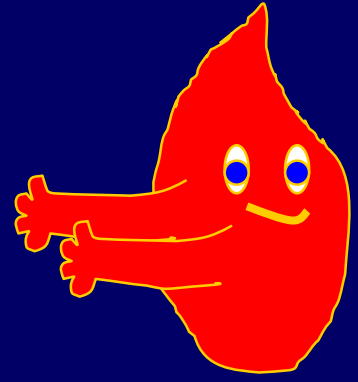
HAV and HEV

- **the digestive tract**
- **in exceptional cases, teguments or mucosas;**

HBV, HCV
HDV, HGV

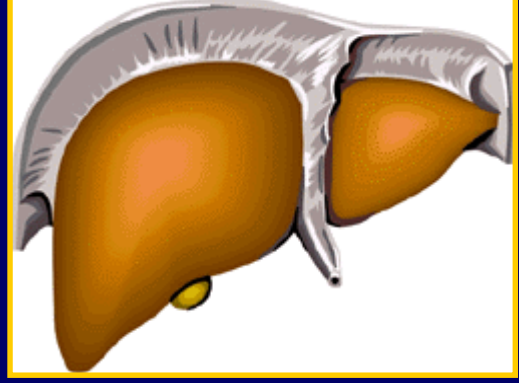
- **teguments or mucosas.**

Elimination



HAV	▪ **faeces, blood, urine;**
HEV	▪ **faeces;**
HCV and HDV	▪ **blood;**
HBV	▪ **blood** ▪ **sperm, vaginal secretions, and possibly other secretions and excretions**

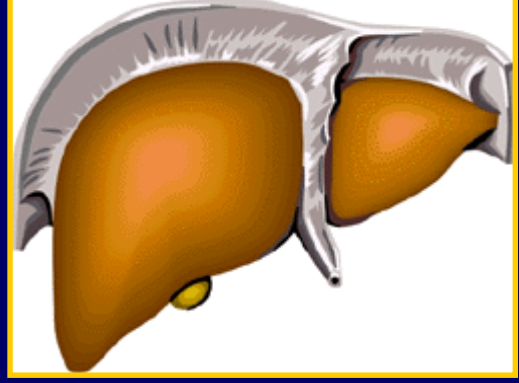
The infection source



HAV

- **The ill person with an icteric or an anicteric form of the disease;**
- **The virus is eliminated through faeces, starting with the second half of the incubation period, and disappears or is reduced to a few days following the onset of jaundice;**
- **Generally, the contagious stage of the disease lasts 10-14 days after the onset and there is no chronic carrier state.**

The infection source



For HBV

- **the infection source consists of:**
  - **Ill people with acute, icteric or anicteric forms;**
  - **Ill people with persistent or aggressive chronic hepatitis;**
  - **Ill people with HBV-aetiology cirrhosis;**
  - **Ill people with hepatocarcinoma with positive HBAg's;**
  - **Convalescent or chronic HBAg carriers;**
- **Serologic research have indicated the existence of over 300 million carriers of HBAg's;**

For HCV, HDV, HEV, HGV

- **The infection source is represented by acutely ill people and carriers.**

Transmission routes and mechanisms



HAV

- **Complex transmission mechanism; the passage of the viral agent, eliminated through faeces, occurs through:**
  - **Dirty hands, objects, laundry, thermometers,**
  - **Contaminated water & food or vectors, especially houseflies.**

Transmission routes and mechanisms

For HBV

- **2 transmission ways are known:**
  - **Parenteral transmission – through contaminated blood transfusions, improperly sterilized medical instruments, shaving machines/ contaminated scissors, instruments used for tattoos , for manicure and pedicure !!!**
  - **Non-parenteral transmission – through direct sexual contact and perinatally, from the mother to the baby.**

Transmission routes and mechanisms

For HCV

- **The transmission is parenteral, through blood (transfusions), through coagulation factors or through improperly sterilized medical instruments;**
- **Sexual/vertical transmission is also possible;**

For HDV

- **the infection sources are similar to those of HBV:**
  - **Parenteral transmission through blood or medical instruments;**
  - **Transmission through direct contact and possibly vertical transmission (mother – infant).**

Transmission routes and mechanisms

For HEV

- **Transmission through person-person contact by faecal-oral route or through the consumption of contaminated water;**

For HGV

- **the infection sources are similar to those of HCV:**
  - **Parenteral transmission through blood (transfusions) and contaminated medical instruments;**
  - **Vertical transmission, is also possible, such as the sexual route.**

The receiving population

- **The population receptiveness is general for all forms of viral hepatitides;**
- **HAV: in our geographic area, the higher frequency of diseases is recorded among preschool and school children and young people;**
- **HBV: the incidence of morbidity is higher among adults, both sexes being equally affected;**
  - **There is a professional risk for medical and healthcare staff, especially in the haemodialysis, oncology, obstetrics-gynaecology, surgery, stomatology wards, in medical labs, transfusion centres, as well as in mental institutions.**

The receiving population

- **HCV: universally spread, the vast majority being post-transfusional;**
  - **There are certain risk groups – polytransfused patients, leukaemics, transplantation patients, a similar phenomenon to the one in HDV, HGV.**

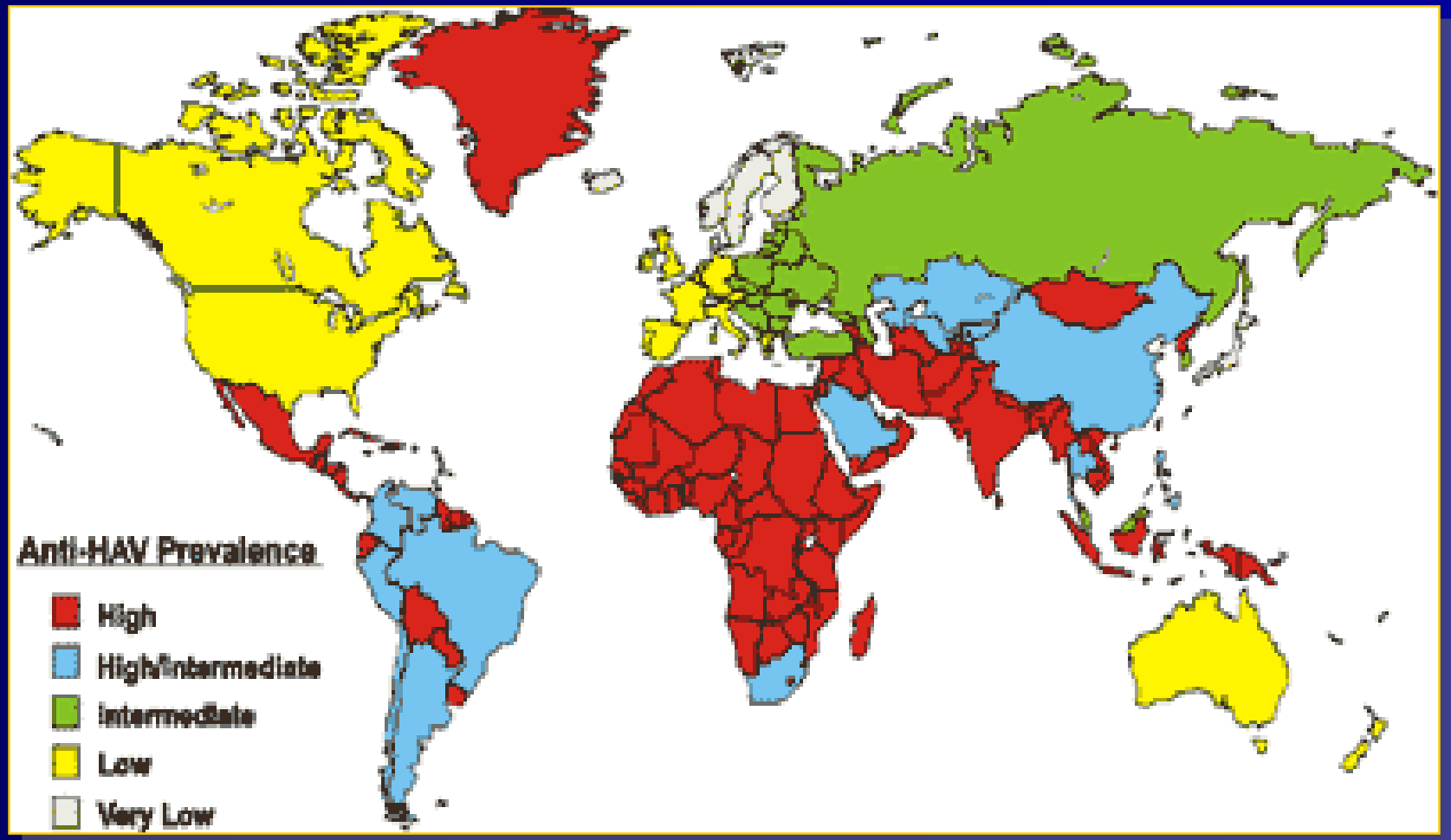
The favouring factors

- **The socio-economic factors:**
  - **Improper hygiene;**
  - **Human agglomerations;**
  - **The privacy of cohabitation;**
  - **Aberrant sexual practices, promiscuity, drug consumption;**
  - **Residency in areas that are endemic for parenterally transmitted hepatitides;**
  - **Frequent contact with blood and blood derivatives;**
  - **Poor sanitary education.**

Manifestation forms of the epidemiological process

- **Viral hepatitides evolve endemically-epidemically with variable densities, depending on the geographic area;**
- **HAV: evolves sporadically-endemically or endemically-epidemically, with a cyclical evolution tendency after the build-up of a segment of receptive population;**
  - **3-10-year periodicity;**
  - **Autumn-spring seasonal features;**
  - **Higher morbidity in rural areas;**
  - **Hydric epidemics, contact epidemics, food epidemics, with the most frequent food culprits being: milk, butter, orange juice, cakes, ice cream, seafood, raw vegetables.**

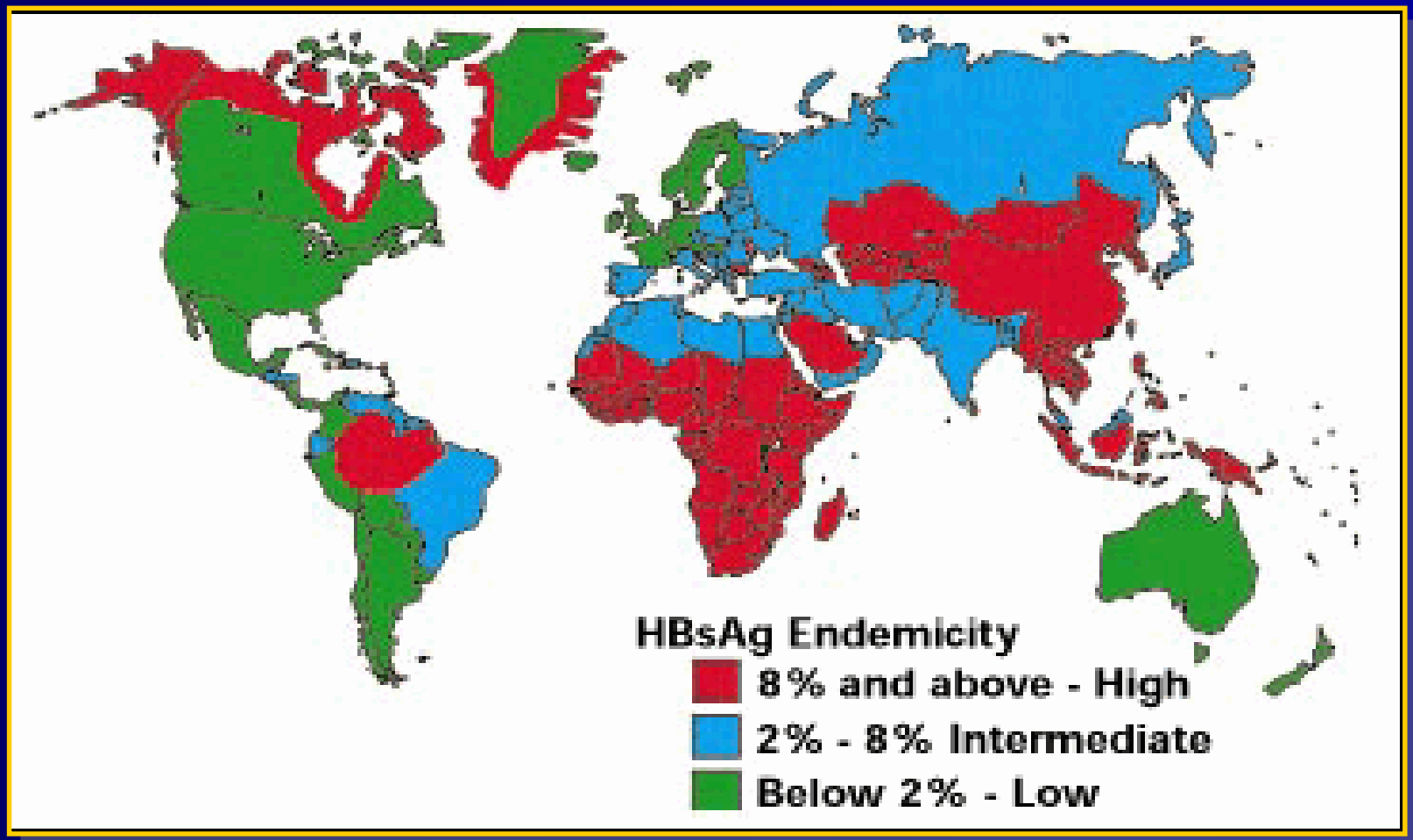
Manifestation forms of the epidemiological process



Manifestation forms of the epidemiological process

- **HBV – evolves endemically, even hyperendemically for certain geographic areas;**
  - **There are no seasonal variations;**
  - **Chronic carrying occurs in 20% of the cases;**
  - **Approximately 40% of the chronically infected people will die of disease complications;**
  - **It is the first human virus clearly involved in malignant process aetiology (CHP).**

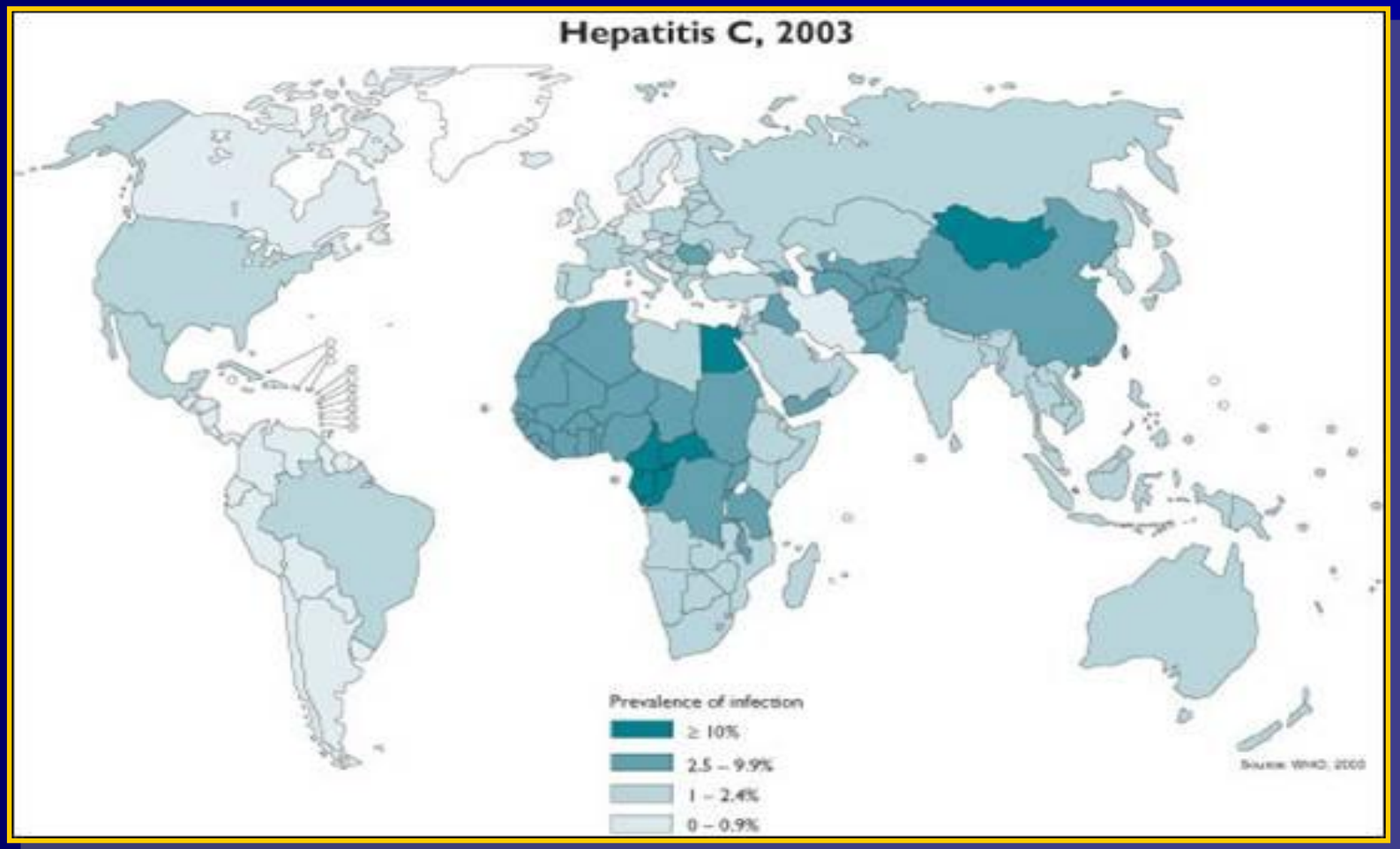
Manifestation forms of the epidemiological process



Manifestation forms of the epidemiological process

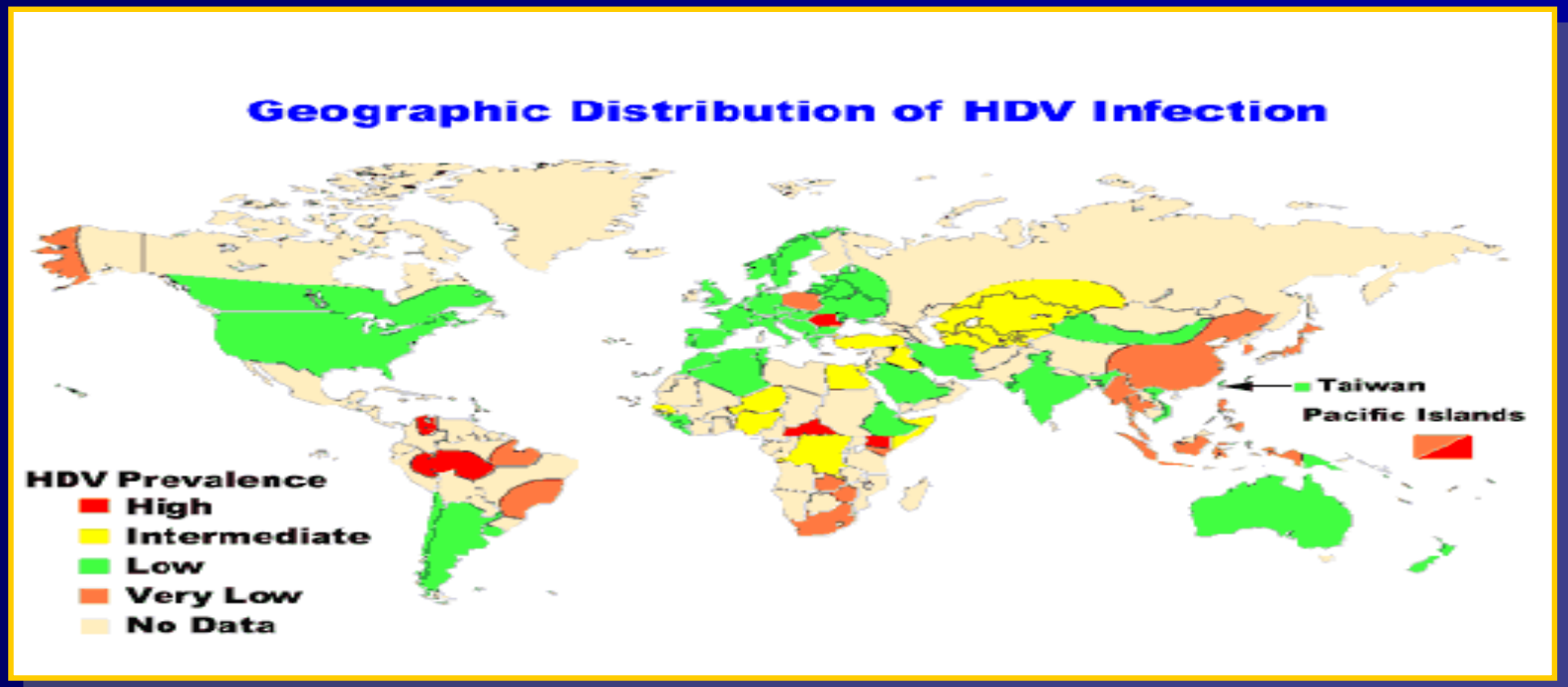
- **HCV: in the past, 90% of the cases were post-transfusional; currently, these account for just 10% of the cases;**
  - **For the rest – sporadic evolution;**
  - **It especially affects adults, especially males;**
  - **Chronic development in over 50% of the cases.**

Manifestation forms of the epidemiological process



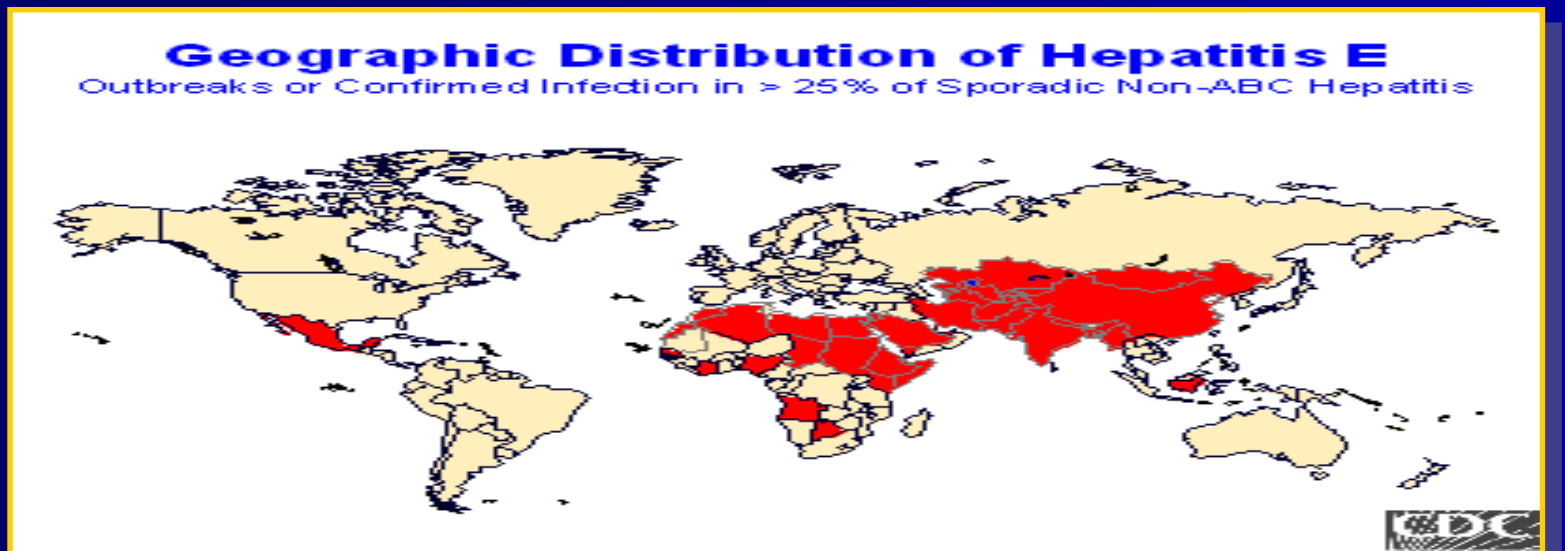
Manifestation forms of the epidemiological process

- **HDV: endemic in S-E Europe, Africa, the Middle East, and South America, with some epidemic outbreaks occurring in the same areas.**



Manifestation forms of the epidemiological process

- **HEV:** causes **epidemics** similar to HAV in some regions in Asia and Eastern Mediterranean;
  - In these cases, the main transmission route has been the consumption of contaminated water, with epidemic episodes occurring after floods.



Prevention and control

HAV

- **Measures regarding the ill:**
  - **Identification, nominal declaration;**
  - **The patient is quarantined at the hospital for 21 days;**
- **Similar measures for suspects as well, with isolation from the other patients, up to the clarification of the diagnosis;**
- **Measures regarding contacts:**
  - **Clinical and lab check-up for 15-45 days.**

Prevention and control

For HBV

- **Measures regarding the ill:**
  - **Identification, nominal declaration;**
  - **Isolation for 30-40 days, with segregation of HBAg+ from the other patients with viral hepatitides;**
- **Similar measures for suspects as well, with separation from the other patients, up to the clarification of the diagnosis;**
- **Measures regarding carriers:**
  - **Identification, treatment at a medical facility – check-up after 1, 3, 6, 9, 12 months;**
  - **Patients are considered to have been cured after 2 successive check-ups with normal test results;**
  - **Moral isolation of the carrier state, with recommendations regarding their profession, their attitude towards others.**

Prevention and control

For HBV

- **Measures regarding carriers:**
  - **The carrier state is mentioned on all hospitalization or special investigation referral notes;**
- **Measures regarding contacts:**
  - **Clinical check-up and laboratory check-up during the maximum incubation of the disease;**
- **Compulsory epidemiological investigation;**
- **Continuous sanitary education.**

Measures regarding the transmission routes

- **Prevention of the non-percutaneous transmission:**
  - **Disinfection of the discharged matter of ill people (faeces, urine) with 2% chloramine or 20% bleaching powder (chlorinated lime);**
  - **Laundry disinfection through a 30-minute contact with 0.5% chloramine;**
  - **Dish disinfection using detergents;**
  - **Terminal disinfection in rooms with formolisation.**

Measures regarding the transmission routes

- **Prevention of percutaneous transmission:**
  - **Proper autoclaving/sterilization of the medical instruments;**
  - **Disinfection of shared objects;**
  - **Avoiding accidental professional exposure to blood or other infected biological fluids;**
  - **Sterilization of the medical instruments used for manicure, pedicure, tattoos/piercing.**

Measures regarding the receptive population

HAV:

- **Passive immunoprophylaxis through the administration of total Ig in amounts of 0.02-0.05 ml/body kg, during the first 72 hours following an infecting contact;**
  - **It is administered in the case of children's collectivities where cases of HAV have occurred or collectivities where the epidemiological investigation forecasts the possibility of epidemic outbreaks;**
  - **Mass prophylactic administration is not recommended.**

Measures regarding the receptive population

HAV:

- **Active immunoprophylaxis: through the administration of:**
  - **inactivated vaccine (Havrix) for paediatric use, 0.5 ml/dose – used up to the age of 15 – or 1 ml/dose – used for adults – with im. administration**
  - **Another commercially available substance is Avaxim.**

Measures regarding the receptive population

- **Administration:**
  - **2 doses at an interval of 6-12 months;**
  - **Adverse reactions: pain, erythema, local induration, subfebrile state, headache, asthenia, gastro-intestinal disorders.**

Measures regarding the receptive population

HBV:

- **Passive immunoprophylaxis through the administration of anti-HBV Ig:**
  - **Pre-exposure – haemodialysis patients, before an organ transplant;**
  - **Post-exposure – newborns with HBAg+ mothers, in a dose of 0.5 ml or for sexual partners of an HBAg carrier/exposure to blood, potentially contaminated biological fluids – in a dose of 5 ml for adults.**

Measures regarding the receptive population

HBV:

- **Active immunoprophylaxis:**
  - **With anti-HBV vaccines obtained through genetic recombination – HBAg is produced on yeast (*Saccharomyces cerevisiae*) or on *E.coli* cells where the S-gene, which is the HBAg synthesis gene, has been included as a plasmid – Engerix B, Euvax, Recombivax;**
  - **There are paediatric-use vials with 10µg/0.5 ml of vaccinal product, or adult-use vials, with 20µ g/1 ml.**

Measures regarding the receptive population

HBV:

- **Active immunoprophylaxis:** the vaccine is administered to newborns in maternities, to previously unvaccinated children/teenagers, adults in risk groups:
  - medical staff, prison staff/inmates, mental institutions;
  - children in close collectivities;
  - homosexuals, drug abusers;

Lab

Prevention of post-transfusion hepatitides

- **Measures regarding donors:**
  - **Life-long exclusion of ex-donors from the donation process;**
  - **Screening with the exclusion of HBAg+ people;**
  - **Exclusion for 6 months of contacts with HBAg carriers, of transfused patients;**
  - **Preference for honorific donors rather than those with an interest;**
- **Measures regarding the product:**
  - **Treatment with U.V, with β-propiolactone;**
  - **Storage for 6 months;**
  - **Checking the doses.**

Prevention of post-transfusion hepatitides

- **Measures regarding the population:**
  - **Limiting transfusions and replacing them with substitutes.**

Thank you!

Images – sources
The Internet