VIRAL HEPATITIS

# Viral hepatitis, caused by the hepatitis viruses A, B, C, D, E, G, TT, have an universal spreading, being known since antiquity: they are now occupying the first place among the transmissible diseases by morbidity, complications, deaths and economical damage.

- The viral hepatitis A named for a long time "epidemic hepatitis" seems to open the "hepatitis era".
- In 1945-1946, the Romanian scientist St. Nicolau and N. Cajal have been emitted the hypothesis, confirmed today, of the existence of many types of viral hepatitis.

# The viral hepatitis A (VHA) is caused by a virus with a predominant enteral transmission that is endemic-epidemic in the countries in the course of development and in the poor population from the industrialized countries. It affects especially children in that it is generally benign but when it appears in adults it could be severe. In the last years, venereal transmitted VHA cases have been seen and also by drugging, transfusions and frequently, nosocomial and as a travelers’ disease.

# The viral hepatitis B (VHB) is caused by a virus with a predominant parenteral transmission with a universal spreading. It affects every age group and it has a risk for getting chronically and for primary hepatic carcinogenesis. The hepatitis B virus (HBV) can produce 5-15% of the post-transfusional hepatitis (PTH) and frequent nososcomial infections in-patients and the medical-sanitary staff. It can being intensely transmitted by sexual relations of different types. The healthy and the after-ill carriers can make a chronic form, constituting epidemiological and clinic risk.

Yearly in the world, over 2 millions of people are dying by HBV and almost 400 millions are VHB carriers. In Romania the medium proportion is 7-9% from the general population of the country.

One of four chronic carriers can develop in time chronic hepatitis with an evolution to cirrhosis and possibly primary hepatic carcinoma (PHC).
The viral hepatitis C (VHC) has a universal spreading and an epidemiological process that has a lot of common elements with VHB and VHG. VHC is responsible for the producing of over 90% of the post-transfusional hepatitis (PTH) cases. From here derives the characteristic of being the disease that is getting chronically most frequently among the viral hepatitis. VHC is less venereal, it produces the chronic carrier status that is difficult to prove and it contributes to the production of PHC. The nosocomial and occupational risks is lower than in VHB.

The viral hepatitis D (VHD) has a universal spreading with great regional differences and is caused by the hepatitis D virus (HVD) which needs for that to associate with HBV resulting a co-infection or an over-infection. HDV is seen in different proportions, associated with the markers for the other hepatitis viruses (VH). The epidemiological process as well as the prevention of the HVD overlaps to the HVB ones.

The viral hepatitis E (VHE) has a universal spreading but it is endemic-epidemic in South Eastern Asia; in the other geographical areas it is predominantly sporadic. The VHE epidemiological process has a lot of common elements with the VHA one, but it has a particularity: the hepatitis virus E (HVE) is transmitted predominantly by contaminated water, it affects the population over 15-16 years old, it is very aggressive for the pregnant women and it can produce serious diseases in adults, especially those with immunosuppression, but also in little children.

The viral hepatitis F (VHF) is under study; the dates until now are placing it in the B, C, D, G group. It gets chronically less than HVC and more than HVB; it rarely produces PTH (Post-Transfusional Hepatitis).

The viral hepatitis G (VHG), although pointed out epidemiological more than a decade ago, when some hepatitis appeared especially PTH-like, that were non-A, B, C, D, E, is known now that it is seen i.v. doped, in poli-transfused, including sick men with hemophilia, thalassemia, hemodialysis and the blood donors. Besides acute HVG, it can evolve chronically even to PHC. VHG can be seen in the chronic carriers, alone or associated with VHB, VHC, and VHD. Generally, VHG is less severe than HVC.

The viral hepatitis TT. A new “hepatitis” DNA virus has been reported from Japan. The TT virus is member of the family Circoviridae. It was discovered in the serum of patients who had transfusion-associated hepatitis. Subsequent studies have shown TTV to be very prevalent in Japan and to be distributed throughout the world. The TT has a high prevalence in the donor population and almost all persons who receive multiple transfusions.
The characteristics with epidemiological importance of hepatitis viruses are:

- besides VHB, all the others are ARN viruses;
- the hepatitis viruses (VH) have been isolated in: 1961 (B), 1973 (A), 1977 (D), 1989 (C), 1990 (E), 1995 (G);
- the hepatitis viruses are producing epidemiological processes with common elements but also particular ones for HVA and HVE and respectively HVB, HVC, HVD, HVF, HVG;
- VH have a universal spreading but with great geographical differences;
- VH are producing human specific diseases;
- the epidemiological and clinic manifestations for all the VH and for each one have a great polymorphism;
- the etiologic plurality of the HV has been suggested since 1945-1946 by St. Nicolau and N. Cajal;
- VH have a remarkable resistance in the environment and for the usual decontaminates, excepting the oxidant substances, especially the chlorigenic ones;
- VH have complex antigenic structure but this is more evident in VHB, C, G;
- the VH transmission and the production of the hepatitis infection is promoted by the low infecting doses;
- the resistance and the low infecting doses are promoting the VH transmission through many ways;
- the detecting of the specific antibodies for sero-epidemiological estimations is practice with accessible methods for all the VH;
- the detecting of the antigen VH, excepting VHB, requires expensive techniques generally based on the genomic amplification (of the nucleic acid sequences);
- VHB an VHC are involved in the producing of some immunological abnormalities;
- VHB and, in a reduced proportion, VHC and VHG can produce chronic liver lesions, a risk substrate for the primary hepatic carcinogenesis;
- VHB, C, G are presenting mutants and genotypes that are creating difficulties in diagnosis, therapy and vaccine-preparation;
- VH are determining types and genotypes specific immunity for the VHB, C, G;
- VHD can penetrate the hepatocytes only associated with VHB.
Epidemiological process in VHA and E

I. Sources of pathogenic agents

- **The sick man** - especially children until 15 years old for HVA and the population over 15 years old for HVE; they can present typical or atypical forms, sub-clinical ones, unapparent ones (their proportion can be 60-80%). In case of epidemics, HVE can evolve seriously, with a high lethality, in pregnant women and in immunosuppressed persons.

HVA can evolve with a risk for all the ages, but especially in adults, in the populations with a hygienic-sanitary standard extremely high, where natural immunization of the children is not producing.

- **The virus carrier man**:
  - *pre-infectious* is very infectious by faeces for 8-10 days before the beginning of the disease in HVA and respectively for 10-15 days in HVE;
  - *healthy* that are eliminating VH in low amounts and for days or weeks; these carriers are seen among the persons being in close contact with the sick man or with the pre-infectious carrier;
  - *after-ill* that is spreading low doses of VH for a few days in convalescence.

In some epidemiological circumstances, sources of VHA and less of VHE can be, some non-human primates and “the sea fruits” (oysters, mussels, shells, fish etc.)

The pathological products by which the sources are spreading VH are especially the faeces and the blood during the viremia period.
II. Modes and ways of transmission

- The direct mode is implicating in the VHA and VHE transmission because the both are producing hepatitis that can be included in the group of "the dirty hands diseases", "the poor man diseases" etc. These hepatitis are interesting especially groups, collectivities, families with an "unhygienic life style" of affected by natural or social disasters. VHA can be involved in the sexual transmission or in the producing of PTH.

- The indirect mode is often involved because both the viruses are resistant, are eliminated from the sources especially by faeces and can contaminate water (especially VHE in S-E Asia), food (especially VHA), air, ground, hands, objects and domestic flies. The simultaneous associations of more transmission ways can transmit both viruses.
Epidemiological process in HVB, C, D, F, G, TT

I. Sources of pathogenic agents

- **The sick man** with acute hepatitis, typical (almost 30%) and atypical, sub-clinic, non-jaundiced, oligosymptomatic, constitutes a great risk source for the VH populational spreading. A particular place has the sick man with PTH that is spreading especially VHC (90-95%) and that can also present typical or atypical forms. Virus sources are also the sick man with chronic hepatitis, cirrhosis or PHC (Primary Hepatic Carcinoma).

- **The carrier man:**
  - *pre-infectious* carrier that is spreading VH for 30-40 days before the beginning of the disease (that is typical or atypical); these carriers can be detected among the persons from the patient’s company or the chronic carriers, only after their detecting;
  - *healthy carrier* that is seen in general population, in different proportions, depending on the geographical area and on the hepatitis virus type; the healthy carriers situation is better known for VHB – they can get rid of the virus spontaneously, after a period of weeks or months; different proportions of these carriers continue to spread VH all the life (“chronic healthy carriers”) and other category, depending on the factors in relation to VH and the human organism, can be activated, passing to viral chronic hepatitis, cirrhosis and PHC;
  - *after-ill carrier*, in different proportions, can spread VH during convalescence for weeks and months or they are outrunning this period and are becoming *chronic after-ill carriers*; a part of these ones can “auto-sterilize” themselves, others remain chronic carriers for years or all the life and, finally, some of them will get into chronic hepatitis, with a risk for cirrhosis and PHC;
  - other sources with particular roles are represented by the VH carrier mothers and some monkey species;
  - all the sources can house and spread one VH or simultaneously many VH types;
  - the mentioned VH sources can spread VHB, C, D, G for different periods and with different intensities by blood and derivatives, saliva, cervical-vaginal secretions, sperm, and every organic product (secretions of serosis, tears, transpiration etc.).
II. Modes and ways of transmission

- **The direct mode** of transmission for the VHB, C, D, G includes: the transplacental transfer, sexual relations (especially for VHB), the suckling (by the mamelonary area fissures), saliva, food masticated by the mother and transferred to the children, contamination of the preexistent lesions with organic products from the VH sources, blood and derivative transfusions (especially for VHC) etc.

- **The indirect mode** assures the VH transmission in a different way depending on its type and the epidemiological circumstances. The air, the hands, objects contaminated are involved in VHB, C, D, G vheculation but a special place have the objects and instruments used for realizing invasive interventions or for the organic products manipulation and investigations (laboratories, dialysis, surgery, obstetrics, gynecology, endoscopies, catheterisms, acupuncture etc.)

The complex character of these VH spreading by the direct mode results also for the many risk activities at the populational level: injections, i.v. doping, tattooing, circumcision, the nose and lips perforation, manicure, pedicure, shaving, the teeth washing with a "common" toothbrush etc.
hepatitis virus

ions without type specific antibodies, and re. and genotype specific ones, at protective levels. 
estimated only in relation with every VH type, its tain populational category and a certain geographical munity following the antibodies transfer from mother to it in all the VH infections but is extremely evident in HVA, tically all women at the fertility age have high amounts of for VHA.

as where HVA and HVE are endemic-epidemic, almost the who nation is immunized and re-immunized periodically by passing through with VHA or by its ingestion “in the conditions of a unhy style”.

If the strongly developed countries where sporadicity doesn’t a natural immunization, vaccinoprevention has to be done.
The quality of the natural immunization for VHB, C, and G de strain, subtypes and genotypes

• The presence of antibodies for VHB, C, and G estim especially for an epidemiological marker and less for a indicator. The presence of the specific antibody in differently from a HV type to another.

• The VHB sick persons or carriers are susceptible for other VH but compulsory for VHD.

• Receptivity and non-receptivity are difficult to ne person, of the markers for two or mar
Manifestation forms of the epidemiological process

Depending on the populational particularities of the VH circulating strain and on the geographical area, in every HV, the epidemiological process can manifest: sporadically, endemically, epidemically, and pandemically. These forms are often evolving mixed, intricated (endemic-epidemic, endemic-spordadic etc.).

*The sporadic manifestation* can be seen in every HV but with some differences determined by the geographical area and the structure of some populational groups.

In HVA and HVE, the sporadic manifestation can be recorded in the inter-epidemic periods, in the collectivities for medical-social assistance, areas with poor social-economical population and in some proportion in “rich” population. HVA can be sporadically among the tourists from the industrialized countries and HVE among the adults from the zones where is not epidemic.

HVB, C, D, and G are frequently recording sporadic cases in all the populational categories and in many geographical areas.

*The endemic manifestation* is characteristic for HVA and only in Asia for the HVE; HVB, C, and G may be epidemic in the collectivities for medical-social assistance and in the case of nosocomial infections.
The epidemic manifestation is characteristic for HVA and E; HVB, C and G can record epidemic outbreaks in the collectivities for medical-social assistance, groups with sexual transmission risk, especially for HVB, nosocomial infections.

The extensive and severe hepatitis can be seen after the contaminated water drinking, especially for VHE and after the contaminated food eating especially for HVA.

In all the hepatitis, but especially in HVA and E, many ways of transmission can associate with epidemic outbreak.

The epidemics may affect certain populational structures and age groups. Thus, HVA is especially epidemic in children and HVE in children teenagers, young adults and adults. The other VH can produce epidemic outbreaks generally in small proportions but that can interest every age group but with a certain predominance in adults because of the sexual, occupational, therapeutical risks.

The pandemic manifestation is present in HV that together realized a specific pandemization of the contemporary man.

Unlike the pandemics of cholera, variola, pest, influenza and others, that have been seen, but which are characterized by a temporal limited evolution, HV have produced a pandemic which after reaching a chaining, it maintains with little variations without inter-pandemic periods ("lasting pandemic").
Prevention of the A and E viral hepatitis

- **The general prevention** of the HVA and E are, in general, similar with those efficient in the diseases with a digestive gateway (salmonelosis, shigellosis, cholera, enterovirosis etc.)

  In these prevention measures category are included:
  - epidemiological population surveillance with particular addressability for the high risk groups: the children for HVA and the pregnant women for HVE; the adults with organic tare for the both;
  - global daily hygienization, disinsection, decontamination, human settlements sanitation etc.;
  - the avoiding of the nosocomial infections;
  - the adults protection, especially those with organic tares, including those with occupational risk;
  - the protection of the tourists from the industrialized countries that are reaching in endemic zones;
  - the avoiding of the hydric transmission and the contaminated food transmission of the VHA and E;
  - the avoiding of the VHA transmission by transfusions, sexual relations, doping etc.

- **The special prevention** has been benefited by over 4 decades of the standard Ig use for the protection of the risk groups against VHA. Now the Ig use is limited.

- **The specific prevention.** Vaccinoprevention is used in the industrialized countries for the protection of all the ages exposed to the VHA infection in the case of the virus "import" or during the travelling in endemic areas. For this purpose, from many alternatives has been imposed the killed virus vaccine, with many commercial formulas, with 2 vaccine dozes of 0,5 ml, i.m., administrated at a 30 days period and a revaccination, with a unique dose at 6-12 months. Thus, is provided a specific protection for at least 10 years with a possible re-vaccination at 5-6 years from the primary vaccination. Other types of vaccine are during experiments. For the HVE the vaccines are in the first stages of the researches.
Control of A and E viral hepatitis

The control of the epidemiological process of HVA and E supposes:

- the epidemiological inquiry;
- organizing the actions for detecting, including the atypical cases;
- the urgent and nominal report of the typical and atypical cases and of the suspects;
- hospital isolation;
- the contacts will be epidemiological, clinic and laboratory surveyed, for 30-40 days; they can get Ig or vaccine; they will be excluded from the blood donating for 6 months;
- the convalescents will be followed up over 6 months, with clinic and laboratory control; they will be educated to respect the hygiene rules and they will be excluded from donation for all their life;
- the environmental decontamination will be realized especially with chlorogenic substances;
- the hygienization and sanitation with special measures during the 30-40 days of surveying the epidemic focus, calculating the time elapsed from the date of the last detected case;
- disinsection and deratization can be useful;
- education with specific HV theme can promote the populational cooperation.
Prevention of the B, C, D, F, G and TT hepatitis

- **The general prevention** is addressed to the population, medical-sanitary staff and the staff that is working in the services for collecting, processing, conservation and transfusion of the blood and derivatives.

1. **The general population** has to be helped to know the infection risks with VHB, C, D, G and the prevention ways.

   The education will refer to: avoiding the injections without strict individualization of the needles and of the syringe; procedures of boiling sterilization; the risk of perforations for ornaments, done by uninstructed persons; the risks of VH transmission by operations of manicure, pedicure, shaving, tattooing, circumcision, cupping glasses with scarifications; the hygienization during the menstruation; the risks of unprotected sexual relations; the possibility of VH transmission through saliva; by eating “serial” food by the children; the risk of intra-familial contact with VH sources; the risk of the mother carrying VH markers for the intrauterine conception products, intrapartum and by suckling (“the peri-mamelonary fissures”) etc.

2. **The medical-sanitary staff** can be exposed to the contamination and possibly to the infection during the invasive acts done for some patients with an unknown “hepatitis status”.

   It’s possible that also the patients will be exposed to some risks when the medical-sanitary staff gets an atypical HV or is VH carrier.

   The mechanical protection will be done with care for the pre-existent lesions or those created during some services (medical-surgery acts).

   Every patient and organic product must be considerate with risk.

   The manipulation of the material for transplants can constitute a risk for the physician and for the receptor.

   The sterilization of the instruments with correct manipulation during use can eliminate risk situations for the VH transmission.
3. The collecting, processing, conservation and transfusion of the blood and derivatives must be considered risk operations that require prevention measures.

The epidemiological, clinic and laboratory sorting of the blood donors can eliminate the majority of the risks. It is added the exclusion from donation for 6 months of the contacts with sick persons or known carriers and of the persons receiving a blood or derivatives.

The exclusion for all life will be done for the after HV ill persons, the carriers of VH markers and the donors involved in PTH producing.

- The specific prevention is referring now to the VHB infection for which it can be used both specific Ig and vaccine.

Now is available the vaccine based on genetic recombinants, manufactured in Belgium, France and USA.

Beginning with 1988 the genetic recombinant vaccine Engerix B has been imposed that is used for i.m. injection, in doses of 1 ml for adults and 0,5 ml for new born and children until 10 years old.

Generally, 3 doses are administrated at an interval of 30 days between the first and the second and after 6 months the third inoculation. Other administration schemes can be used. The vaccine is extremely efficient and with no adverse reactions.

The most accepted orientation in anti-HVB vaccinoprevention is the one supposed the immunization of all the new born: a dose after birth, one at 3 months and one at 6 months.

The anti-HVB vaccination is solving also the protection against VHD and for HVC and HVG, the vaccines are in the first stages of research and experiments.
Control of the B, C, D, F, G and TT viral hepatitis

The control of the epidemiological process of HVB, C, D, F, G and TT is including the same stages as those for HVA an E. There are added laboratory investigations for the detecting among the contacts of the carriers of markers for VHB, C, D, F, G and TT to provide their exclusion from the blood, tissue organs donating, and for their including into educational programs for the protection of themselves and of their company.

All the measures mentioned at the prevention of the HVB, C, D, F, G and TT would be taken into account for control during the epidemiological surveillance period of these hepatitis that are lasting over 3 months.

The prevention and control measures against HVB are also solving the problems with HVD.