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Hepatitis C: Current State and Prospects

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Abstract: Among viral hepatitis with parenteral transmission, hepatitis C is the most significant health problem. First of all, this is due to the global spread of infection, a high incidence rate, a tendency to form chronic forms of infection leading to cirrhosis, primary liver cancer; hepatitis C virus is capable of affecting many human organs and tissues. At the same time, there is still no vaccine against this infection in practical healthcare, and the medications used today are still ineffective, expensive and not harmless to human health. There is an urgent need to monitor infection, to develop new methods of diagnosis, treatment and prevention of hepatitis C. This review presents data on the characteristics of the causative agent of hepatitis C, presents the features of the spread of the virus and its genotypes in the world, including in Uzbekistan, the results of clinical studies, recent data on the epidemiology of infection.

Keywords: hepatitis C, spread, clinic, morbidity, clinic.

The results of recent studies on experimental modeling of infection caused by the hepatitis C virus in vivo and in vitro, on the creation of a collection of hepatitis C virus strains suitable for the development of new diagnostic, therapeutic and preventive drugs are presented. The analysis of data on the prospects for the development and implementation of a vaccine against hepatitis C, as well as new means of treating infection, was carried out. Viral hepatitis is the cause of death of more than one million people a year. The European Association for the Study of the Liver (EASL – European Association for the study of the liver) calls on various UN agencies to take measures to combat viral hepatitis, potentially fatal infections that infect 500 million people around the globe. Even more alarming is the fact that most people only find out that they are infected when the first signs of infection appear, which may be the development of liver cancer or liver failure. That is why academician D.K. Lviv calls hepatitis C (HS) a "gentle killer" [12]. Unfortunately, of the main directions of long-term development formulated in the Millennium Declaration, the main emphasis is placed exclusively on the problems of "HIV infection", "Tuberculosis" and "Malaria". Professor Mark Thursz, General Secretary of EASL, believes that viral hepatitis should be recognized as a serious threat to humanity, and urgent measures should be taken to protect uninfected people from infection, and the infected should be provided with affordable effective treatment. Ignoring the problem of viral hepatitis is discriminatory, therefore, the Joint National Development Program (UNDP – United Nations Development Program) under the auspices of the UN should give the problem « Viral hepatitis" has the same priority as the problems of "HIV infection", "Tuberculosis" and "Malaria". And in this regard, EASL management considers it important that WHO plays a more active role in the implementation of standards for the effective control of transmission of infection through medical interventions and blood products. It will be difficult to talk about the effectiveness of anti-epidemic measures against viral hepatitis until WHO organizes screening and epidemiological surveillance in each region.

Hepatitis C virus (HCV – hepatitis C virus) is one of the main causes of acute and chronic liver disease and has been gaining increasing socio-economic importance in recent years. HCV is ubiquitous [1, 2, 8, 10].

According to WHO, 130-170 million people in the world are chronically infected with HCV, and 3-4 million are infected annually, and more than 350 thousand people die. HCV is spread by direct contact with the blood of an infected person and is transmitted mainly parenterally, as well as vertically (from mother to child). One of the main reasons for the widespread spread of HCV in the world is the use of unsafe blood transfusion methods and the reuse of needles and syringes that have not been properly sterilized. The sharing of needles, syringes and other paraphernalia used for drug use is an equally serious danger [6].

The natural reservoir of the virus is still unknown. Experimentally, it is possible to infect HCV only in chimpanzees with the development of acute and chronic infection.

Viral HS is about 20% of cases of acute hepatitis, 70% of chronic hepatitis, 40% of decompensated cirrhosis of the liver, 60% of hepatocellular carcinoma. It is known that 30% of liver transplantation cases are associated with HCV liver damage. Hepatitis C is often complicated by extrahepatic manifestations of infection, such as membranoproliferative glomerulonephritis, Behcet's disease, premature graying, cerebral vasculitis, cryoglobulinemia, diabetes, fibromyalgia, hypertrophic cardiomyopathy (HCM), lichen planus, corneal ulcer, multiple myeloma, non-Hodgkin's lymphoma, peripheral neuropathy, hepatic porphyria, pruritis, Raynaud's syndrome, HCV-induced arthritis, sialoadenitis, Shengren syndrome, Spider Nevi, systemic lupus erythematosus (SLE), thyroid diseases, vasculitis, vitiligo [6, 13]. A good reason to prove the etiological role of HCV for most of the mentioned diseases is the detection of replicative forms of HCV RNA in affected human organs and tissues.

The source of infection is a sick person. Transmission paths: a) transfusion – after blood transfusion; b) from the mother to the fetus and newborn; c) the genital tract, d) during manipulations with damage to the integrity of the skin and mucous membranes [11]. The response to the appearance of virus antigens in the body is the production of specific total antibodies to HCV. The dynamics of the appearance of HCV antibodies in the blood of infected individuals is variable, the average interval from the onset of the disease to the appearance of antibodies is about 15 weeks. (4-32 weeks), antibodies against HCV in patients with chronic hepatitis are detected for a long time, more than 7 years.

Morphology and physico-chemical properties. The pathogen of HS is a small (30-38 nm in diameter) RNA-containing, enveloped virus. The floating density of HCV virions in the CsCl density gradient is 1.24 g/cm3, in the sucrose gradient – 1.08-1.11 g/cm3; the sedimentation coefficient is 200 S. A lighter fraction equal to 1.04–1.06 g/cm3 is also detected, which is probably a consequence of the association of HCV with serum beta-lipoprotein. The heavier fraction (1.17 g/cm3) in the sucrose density gradient is most likely associated with non-infectious immune complexes of the virus and antibodies. The HCV nucleocapsid has a buoyant density in the sucrose gradient equal to 1.25 g/cm3 [20]

HCV stability. The infectious activity of HCV is inactivated under the influence of lipid solvents or detergents, by heating to 60 ° C for 10 hours, or at 100 ° C for 2 minutes in an aqueous solution. Formaldehyde in a dilution of 1:2,000 inactivates HCV for 72 hours at 37 °C [2]. The virus is inactivated by beta-propiolactone and ultraviolet irradiation. HCV is relatively unstable at room temperature under long-term storage conditions, unstable to repeated freezing/thawing.

The HCV genome is represented by a single-stranded linear RNA molecule of positive polarity with a length of about 9,400 nm, one extended open reading frame encoding a large polyprotein containing up to 3,000 au, which is cleaved by host and viral proteases into separate viral proteins [21, 22]. The HCV genome was cloned in 1989, and the results of cloning and complete sequencing of HCV RNA, as well as the physicochemical characteristics of the virus allowed HCV to be attributed to the Flaviviridae family, separating it into a separate genus Hepacivirus, which occupies an intermediate position between the genera Flavivirus and Pestivirus of this family. Comparative

analysis of HCV RNA with genomes of other viruses belonging to this family revealed similarity of HCV RNA structure with fragments of genomes of dengue hemorrhagic fever 2 viruses (Flaviviridae, Flavivirus) and carnation mottling virus (Tombusviridae, Carmovirus). In addition, so-called "local" homologies (no more than 16 n.o.) with viruses of classical swine fever and cattle diarrhea (Flaviviridae, Pestivirus) have been registered [1]. The presence of HCV RNA homology with plant virus genomes suggested that, in evolutionary terms, HCV occupies an intermediate position between animal and plant viruses.

It has been shown that HCV RNA contains a highly conserved 5'-untranslated region up to 340 BP containing a site necessary for HCV genome translation. This RNA element binds the ribosomal subunit 40 S in the absence of other translation initiation factors. The untranslated site at the 3'-end is terminated by polyuridine ribonucleotides. They are followed by another highly conserved sequence consisting of 98-100 BP, which is called the X-tail and plays an important role in virus replication. The open reading frame encodes a polyprotein consisting of 3,010-3,033 a.o.. When this polyprotein is translated, at least 10 mature proteins are formed in the endoplasmic reticulum of an infected cell. Structural proteins include the nucleocapsid protein and two shell glycoproteins E1 and E2, as well as a small protein p7.

The protein of the inner part of HCV (nuclear protein) is the main protein that binds to the RNA of the virus and forms a nucleocapsid. In addition, it has been shown that the nuclear protein participates in the modulation of transcription and translation of some cellular genes and has an oncogenic effect on cell culture and transgenic mice. Proteins E1 and E2 are part of the HCV shell. Two hypervariable sites HVR1 and HVR2 were identified in E2. Under the influence of the immune system ("immune press"), the HVR1 site easily mutates. The E2 protein may play a role in the formation of virus-neutralizing antibodies, and HVR1 mutations determine the synthesis of antibodies to the most immunogenic antigenic determinants [7]. In addition, the role of E2 in the binding of HCV to the host cell has also been shown. The significance of the p7 protein is not entirely clear, but it seems to be necessary for HCV replication and acts like viroporin. The NS2 protein has protease activity. Together with the NS3 N-terminus, it forms NS2/NS3-npoTea3y, which undergoes cleavage at the NS2/NS3 bond level. The NS3 protein has both protease and helicase activity. The NS4a protein essentially plays the role of a cofactor of the NS3 protein. In addition, HCV NS3/4a serine protease has been shown to block the action of regulatory factor 3 IFN, a key cellular antiviral factor. The function of the NS4b protein is unclear, and the NS5a protein modulates the effect of IFN on the virus. An area has been identified in the NS5a protein that determines sensitivity to IFN. Mutations in this area significantly reduce the effectiveness of IFN treatment. NS5a protein has also been shown to be a potent inhibitor of IFN-induced PKR protein kinase, which belongs to antiviral factors. The NS5a protein has RNA-dependent RNA polymerase activity and plays an essential role in RNA synthesis and replication. The mechanism of initiation of RNA synthesis by viral RNA-dependent RNA polymerase has not been definitively studied.

HCV genotypes and subtypes, their distribution. For HCV RNA circulating in various regions of the world and persisting in the patient's body, the main feature was revealed – high heterogeneity of certain parts of the genome [7, 10]. Two hypervariable sections of HCV RNA are isolated. The first of them (HVR1) is 90 nm long, located at the 5' end of the E2 gene. The second is hypervariable the section (HVR2) with a length of 21 n.o. is adjacent to the 3'-end. The presence of hypervariable sections of the HCV genome ensured the appearance of various HCV genovariants. Analysis of the RNA of numerous HCV variants circulating in various regions of the world revealed the existence of the main groups of the virus, designated by types or genotypes (with homology of nucleotide sequences between them less than 72%). At least six major HCV genotypes have been identified. Comparative analysis of HCV RNA homology of different genotypes allowed us to establish the presence of more than 100 subtypes (the level of homology between different subtypes within the genotype is 72-86%). In addition, the presence of differences in sequences of 1-14% determines the existence of multiple variants of the virus or its quasi-individuals that appear as a result of the long-term persistence of the virus in the human body. An HCV-infected patient may have many millions of HCV quasi-individuals at the same time. Their existence explains the appearance of constantly

changing antigenic structures of the virus circulating in the human body and providing the phenomenon of HCV "escaping" from the neutralizing action of antibodies induced by HCV in the human body. There is a constant competition between the formation of new antigenic variants and the production of virus neutralizing antibodies. And the winner is always the virus, not the immune system. The rapid change in the HCV genome underlies the long-term, often lifelong, HCV carrier. Phylogenetic analysis of HCV RNA suggested that the division of HCV into genotypes could have occurred from 500 to 2,000 years ago, and the division of genotype 1 into subtypes 1a and 1b – more than 300 years ago [32]. The high variability of HCV RNA is associated with the appearance of point mutations, insertions and deletions that occur during virus replication.

Another mechanism that ensures the variability of the genome of viruses is recombination, which is characteristic of many RNA–containing viruses: influenza virus, HIV, poliovirus and dengue virus. The study of recombination between different HCV genotypes is at the initial stage [7].

HCV circulation is found everywhere. According to WHO, the countries with the highest percentage of chronically infected patients are Egypt (22%), Pakistan (4.8%) and China (3.2%). The main route of transmission of the virus in these countries is associated with the use of unprotected parenteral injection methods and contaminated equipment.

Analysis of the distribution of HCV and its genotypes and subtypes of HCV in the world has shown that subtypes 1a, 1b, 2a, 2b and 3a have the greatest distribution [37]. They dominate Europe, North America, Asia and Oceania. In European countries, subtype 1b is 50-91% (Germany – 59%, Belgium – 65%, Hungary – 84%, Italy (Sicily) – 91%), and subtype 1a — no more than 40% (Germany - 32%, Denmark - 40%, France - 35%). Subtype 1a prevails in the USA, which even received the designation "American genotype". The detection rate of subtypes 1a and 1b in the United States averages 37% and 30%, respectively. All other genotyped HCV variants are represented in no more than 10%. In Japan, Taiwan, China (especially in the southern provinces), Singapore, Indonesia and South Korea, subtype 1b, the "Japanese genotype", is most often detected (with the exception of the Philippines, where the frequency of subtype 1b reaches 54.5%). Subtypes 2a and 2b have a more limited distribution in the world than subtypes 1a and 1b and a smaller proportion among the genotypes represented in this territory. Genotype 2 is most often represented in Asian countries. Genotype 3 is most common in Thailand (up to 50%), northern Europe (up to 25% in the UK) and Australia. Genotype 4 is widely represented in the countries of Central Asia, North and Central Africa. Thus, among HCV carrier donors in Egypt, genotype 4 occurs in 30-40% of HCV detection cases. Genotype 5 is often detected among patients with chronic hepatitis in South Africa, and genotype 6 has been identified in Southeast Asian countries.

In recent years, there has been a further decrease in acute HS diseases (OGS) (up to 1.7 per 100 thousand population in 2011) with an increase in chronic forms of HS (HCV) [11].

The overwhelming number of deaths from HS in Russia falls on patients with chronic forms of hepatitis B (HBV) and HS. In 2010, 25 patients with acute HBV and 2 OHS died, while from chronic forms of HBV – 84, and HCV - 70. It should be noted that in 71 deceased, the etiology of chronic viral hepatitis has not been deciphered [6].

According to D.K. Lvov et al., subtype 1b dominates in Russia [7, 8, 10, 12,]. The share of subtype 1b is 64.7% in various regions of Northern Eurasia, 80-83% in the Far East, and 50-56% in the Central Chernozem and Volga-Vyatka regions of Russia. Subtype 1a was most often detected in the Central, Northwestern, Volga-Vyatka regions - 11.2–21.9%, while in Eastern Siberia, the Central Chernozem region and the Urals it can be detected extremely rarely (up to 5%). Subtypes 2a and 2b among people with HCV in Russia are also classified as rarely detected (2a and 2b – 4.7–0.5%). Recently, the proportion of subtype 3a in HCV circulation in some regions of the Russian Federation has been significantly increasing and reaches 40% (long-term data from the D.I. Ivanovsky Research Institute of Virology in Moscow and the Moscow region).

HCV replication. Information about HCV replication is still extremely limited and in most cases contradictory. This situation can be explained by the absence, until recently, of an available experimental HCV model. However, studies conducted in Russia [3, 4, 5, 6] and in other countries

[26, 29] have allowed the development of experimental HCV models in vitro and in vivo. HCV reproduction in primary brain cell cultures of newborn white mice led to the selection of infectious cytopathogenic HCV variants characterized by a wide range of cell cultures sensitive to virus replication. This made it possible to isolate highly productive HCV variants. Another model of HCV infection in vivo, created in Canada, is based on implantation of the human hepatoma cell line Huh-7 into the liver of bestimus mice. After infection of Huh-7 HCV cells, it was possible to find HCV RNA sequences in liver cells and blood sera of mice.

Features of the clinical course of HS. The course of the disease varies from moderate severity, lasting for several weeks, to a severe form of chronic infection, lasting throughout life, and leading to cirrhosis and liver cancer [6, 9, 13, 15, 16, 17, 20]. The incubation period for HCV is from 2 weeks to 6 months.. After initial infection, approximately 80% of people have asymptomatic infection. The acute phase of HS is traditionally limited to a 6-month period. It can occur both imperceptibly for a person (doctors call this stage subclinical or inaparant), and in the form of obvious external manifestations. In acute infection, patients have fever, weakness, decreased appetite, runny nose, nausea, abdominal pain, dark urine, gray face, joint pain, jaundice (yellowness of the skin and sclera of the eyes). Approximately 75-80% of newly infected people develop a chronic infection, and 60-70% of chronically infected people develop chronic hepatitis, which in 5-20% ends with cirrhosis of the liver, and 1-5% of chronically infected HCV people die from cirrhosis or liver cancer. The cause of 25% of all cases of human liver cancer is HS.

Most patients with HCV suffer in the latent form of the acute phase. In this case, it is possible to establish a diagnosis only with a mass examination of persons belonging to high-risk groups of infection

In a small percentage, patients with HS recover. Data were obtained that predictors of convalescence of patients with OGS during the 1st month. from the onset of the disease are: 1) absence or low activity (optical density in ELISA

< 0.1) antibodies to NS5A protein; 2) low concentration of nucleocapsid protein in blood serum (< 40 pg/ml); 3) low concentration of soluble form of sCD38 differentiation antigen in blood serum (< 20 IU/ml). Absence of HCV RNA in blood serum and normalization of ALT after 3 months. from the onset of the disease, they also indicate the recovery of patients with HS [14].

In the majority of patients, the acute phase of HS is replaced by a latent one, with a long-term persistence of the virus in the body. The hidden phase can last for many years, up to 10-20 years. During this period, most infected people consider themselves healthy, remaining potential sources of infection. The only complaint may be a slight heaviness in the right hypochondrium, which manifests itself in violation of the diet and physical exertion. In patients, a slight increase and compaction of the liver and spleen are detected. Blood tests show only a slight increase in ALT levels, and HCV RNA is periodically detected.

Reactivation of HS, as a rule, occurs on average after 14 years, cirrhosis of the liver – after 18 years, hepatocellular carcinoma – 23-28 years. During this period of the disease, symptoms such as rapid fatigue, lethargy, malaise, progressive decrease in working capacity, insomnia combined with drowsiness in the daytime; a feeling of heaviness in the right hypochondrium, decreased appetite are especially characteristic. There is a tendency to lose weight, a slight rise in temperature without signs of jaundice. During the examination, an increase and compaction of the liver are noted, in later terms - enlargement of the spleen. In 20-40% of patients with HCV, irreversible changes occur in the liver during the reactivation phase, its consolidation due to the formation of new connective tissue – a transition to liver cirrhosis is observed. For many years, cirrhosis can be unnoticed, Even with 15-year follow-up, its signs are established in no more than 10% of patients. The final phase of reactivation of HCV, especially occurring with cirrhosis of the liver, may be the development of liver cancer – hepatocellular carcinoma. Markers (predictors) of the formation of chronic HCV infection have been established. In particular, a direct relationship was found between the activity of antibodies to HCV NS5A protein and the formation of persistent (chronic) infection.

The possibility of perinatal transmission of HCV infection. It is known that HCV is transmitted parenterally and, first of all, by syringes in risk groups (drug addicts, patients with hemophilia, patients with hemodialysis units and other categories of persons in contact with human blood or its products). According to WHO, the most common method is HCV transmission by infection with infected blood [11]. This may be the case:

- ✓ during transfusion of contaminated blood, its products, or during organ transplantation;
- ✓ in procedures involving injections with contaminated syringes, needles and needle injuries in medical practice.
- ✓ when using intravenous drugs;
- ✓ when HCV is transmitted to a child by an infected mother.

HCV can be transmitted sexually or by sharing blood-contaminated personal items, but these are less common ways of infection. HCV is not spread through breastfeeding, writing or water, or through casual contact such as hugging, kissing or eating or drinking together

The possibility of perinatal HCV transmission is shown [Cheshik S.G. et al.). Risk factors for intrauterine HCV transmission were the presence of HCV infection in both parents and the use of psychotropic drugs by the mother.

Diagnosis of HS. The acute form of HCV infection is often not diagnosed, since most infected people do not show symptoms of infection. Conventional methods for determining antibodies cannot differentiate the acute or chronic stage of infection. The presence of antibodies against HCV indicates that a person is either infected with a virus or has been infected before. The method of recombinant immunoblotting (RIBA – Recombinant immunoblot assay) and HCV RNA testing are used to confirm the diagnosis. Diagnosis of chronic infection is based on the detection of HCV antibodies in human serum for more than 6 months.. Just as with acute infection, the diagnosis of "chronic infection" is confirmed by additional tests. Special tests are often used to detect cirrhosis and liver cancer. Early diagnosis can prevent health problems that may result from infection and prevent transmission of infection among family members and other close contacts. Some countries recommend screening of populations at risk of HCV infection, including:

- ✓ people who were transfused with blood or its products, had organ transplants before screening;
- ✓ current or former drug addicts (including people who took drugs once, many years ago)
- ✓ people on long-term hemodialysis;
- ✓ employees of medical and preventive institutions;
- ✓ persons infected with HIV;
- ✓ persons with liver disease, or with poor test results reflecting liver function;
- ✓ newborns from infected mothers.

Studies conducted in the field of HS diagnostics have shown that HCV RNA is detected with the highest frequency (up to 95%) by RT-PCR in human blood cells (lymphocytes, mononuclears) than in human blood serum (up to 76%). These data allow us to recommend the use of HCV RNA detection in human blood cells for the diagnosis of infection [17].

Detection of HCV in peripheral blood mononuclears using monoclonal antibodies against NS5a protein: on the left – brown color in the area of formation of antigen (HCV)–antibody complexes; on the right – control (monoclonal antibodies against HIV-1).

Currently, a method has also been developed for detecting antigenically active HCV proteins in peripheral blood mononuclear cells of HS patients using monoclonal antibodies (Fig. 1). And it was found that peripheral blood mononuclears can be not only a reservoir for HCV, but also a place of active replication of the virus, which can cause immune disorders and enhance the severity of the course of HS.

Treatment of HS is still based on the use of interferon or interferon drugs in combination with virazole (ribavirin). It is characterized by low efficacy (not all infections caused by different HCV genotypes are equally treatable with interferon). In addition, treatment with IFN drugs is characterized by high cost and is associated with side effects associated with the toxic properties of the drug [3].

To assess the effectiveness of HCV therapy, serological indicators and indicators of different results of combined antiviral therapy in HCV were established; in particular, it was shown that: 1) if IgM to HCV is detected in the blood of people at a titer of 1:32 and higher, then this is evidence of a negative result of antiviral therapy; 2) a significant decrease in the content of anti-NS3 IgG, anti-NS4ab IgG and anti-HCV IgM by the 1st and 3rd months of therapy is an indicator of sustained virological the answer.

The influence of genetic polymorphism of HCV and some genes of infected people on the effectiveness of antiviral therapy is being studied. Among the analyzed mutations in the interleukin (IL) genes, a significant predominance of the SS allele variant in the IL-6 gene (- 174 S/T) and a tendency to a low occurrence of the TT variant in the eNO synthetase gene (+ 894 G/T) in patients with a sustained viral response. In the latter case, the involvement of ischemic disorders in the formation of a response to therapy is noted for the first time. The non-mutant HH genotype of the hemochromatosis gene (+63 N/D) was significantly more often detected in the group of patients with mild HCV and in the group of individuals characterized by a stable viral response to therapy. In the Russian population, such an association of IL-6 and HFE gene polymorphisms with the achievement of a stable viral response in the treatment of patients is shown for the first time. Based on the data obtained, it can be assumed that the probability of achieving a stable viral response is minimal in patients infected with subtype 1b virus and having allelic variants of the TT IL-6 gene and the DD variant of the HFE gene.

Research is continuing on modeling HCV infection in cell cultures of various origins in order to create experimental models of HCV infection in vitro for screening antiviral compounds [4]. A highly productive HCV variant for cell cultures was isolated from the blood serum of a patient with hepatocellular carcinoma containing 106 ME/ml of HCV subtype 1b RNA and IgG antibodies at a dilution of 1:1,000. The infectious titer of the virus for SPEV cell cultures, Vero-E6, reached 7.5 lg TCD50/ml. Thus,a unique collection of cytopathogenic HCV variants was replenished, suitable for the development of diagnostic, therapeutic and preventive drugs based on them. Conditions have been developed to significantly increase the sensitivity and specificity of RT-PCR for detecting HCV RNA in cell cultures of various origins. The data obtained made it possible to stably determine HCV RNA persisting in cell cultures.

Data on a wide range of cell cultures sensitive to replication of isolated HCV strains, as well as the collected collection of cytopathogenic HCV strains, allow them to be used for screening antiviral drugs, since the problem of HCV treatment remains highly relevant. As a result of preclinical studies conducted to study the antiviral activity of compounds on the HCV infection model in vitro, data were obtained indicating the prospects for further study of the antiviral activity of many drugs, including birch bark extract – betulin and its derivatives, as well as extracts of birch fungus (chaga) Inonotus obliquus – Stimforte® [5, 6, 19]. Data on the high antiviral effect of these drugs against HCV infection in cell cultures were obtained.

May 13, 2011 The US Federal Food and Drug Administration (USFDA – USA Food and Drug Federal Administration) has approved the use of a new protease inhibitor boceprevir (INN – boceprevir). The drug was developed by Schering-Plough Corp., and further, after the merger in 2009, the research was continued by Merck & Co., Inc. [35]. On May 23, 2011, the USFDA approved the use of a new HCV protease inhibitor (INN – telaprevir). The drug was developed by Janssen in collaboration with Vertex and Mitsubishi Tanabe Pharma [24]. According to clinical studies, new HCV protease inhibitors are promising drugs. During phase III clinical trials, patients in the study group received telaprevir and peginterferon alpha-2b/ribavirin for 12 weeks, then telaprevir was canceled and therapy continued with peginterferon alpha-2b/ribavirin, in some patients for another 12 weeks, and in another part for 36 weeks. (12 + 36 = 48 weeks is the standard duration of

HCV therapy with peginterferon alpha-2b and ribavirin). In the telaprevir group, the cure occurred in 60% within 24 weeks, i.e. twice as fast as with standard therapy.

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