

Record for an Individual DISORDER

Record Data

Record Name:	Viral Hepatitis
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Properties

Introduction:	<p>Hepatitis are well known diseases since the antiquities. It is only in the 19th century however that a connection was made between jaundice and diseases affecting the hepatocytes. The term Hepatitis is a Greek word, meaning inflammatory disease of the liver. The causes may be numerous and several types of hepatitis exist, like viral (specific or non-specific), bacterial, toxic (e.g. drugs, herbals, alcohol consumption, food), immunologic (autoimmune), metabolic (Wilson's disease) and vascular compromise of hepatic perfusion.</p> <p>Viral hepatitis affects hundreds of millions of individuals worldwide mostly in developing countries. Industrialized countries are however severely taxed as well. The aim of this review is to focus on hepatitis caused by viral infections.</p> <p>Within thirty years (1965-1995) seven hepatitis viruses were identified. The recent discovery of the hepatitis G virus suggests that the list may not be terminated yet. A terminology that differentiates alphabetically the Hepatitis in A, B, C, D (or delta), E, F and G has been established. The viruses causing hepatitis can be classified into two groups depending on the route of transmission.</p> <p>Oro-fecal transmission: The A, E, and F (still poorly characterised) viruses have an oro-faecal transmission. These viruses can be transmitted via food, shellfish, dirty water, dirty hands, or contaminated stools. They cause epidemics and are characterised by the absence of the risk for chronic infections.</p> <p>Parenteral transmission: The second group comprises of the hepatitis type B, C, D, and G viruses transmitted parenterally (through biological fluids like blood and sperm), and characterised by the risk of chronicity that evolves to cirrhosis and primary cancer of the liver. Contaminated syringes among drug abusers, blood or blood product transfusion, transplantation of organs and hemodialysis, are the most common ways for the viruses to be passed on. Regarding the type B virus, sexual intercourse is also an important route of transmission. HBV and less commonly, HCV may also be transmitted vertically from mother to child during labour. Hepatitis G virus remains to be demonstrated if it is sexually transmitted.</p> <p>Viral Hepatitis constitutes an important public health problem often underestimated. Primary prevention is therefore mandatory, if and where it can be applied. Vaccines exist only for Hepatitis A and B and a combined vaccine for both A and B. It is important that at least young people are protected against both viruses, especially when travelling to countries with high incidence of these viruses. Application of universal high hygiene standards, meticulous disinfection of instruments in the hospital environment and non-exchange of syringes between drug addicts are necessary practices that could lower significantly the transmission rate of these viruses. Alcohol consumption, even of moderate quantities, is a risk factor aggravating the evolution of hepatic lesions.</p>
Definition:	<p>The term Hepatitis is a Greek word, meaning inflammatory lesion of the liver.</p> <p>Viral hepatitis has been alphabetically classified from type A to G. This classification is important for evaluating the clinical course of the disease, treatment and final prognosis.</p> <p>Hepatitis A virus (HAV) is a small picornavirus that belongs to the family of Polioviruses. http://www.tulane.edu/~dmsander/WWW/335/HAV.html</p> <p>Hepatitis B virus (HBV) is the only DNA virus member of the family of Hepadna viruses. It consists of spherical, enveloped particles 42-47nm diameter containing partially d/s DNA plus an RNA-dependent DNA polymerase (i.e. reverse</p>

	<p>transcriptase) http://www.tulane.edu/~dmsander/WWW/335/HBV.html</p> <p>Hepatitis C virus (HCV) is a small RNA virus that belongs to the Flaviviridae family. Like all RNA viruses it is subjected to high frequency of mutations. It resists immune defences and can induce chronic infections. http://www.tulane.edu/~dmsander/WWW/335/HCV.html</p> <p>Hepatitis D virus is a viroid. A defective transmissible pathogen dependent on HBV for replication - similar to plant virus satellite RNAs. Its genome is a circular RNA molecule that can replicate autonomously. However , HDV cannot be secreted out of the hepatic cell in the absence of HBV. http://www.tulane.edu/~dmsander/WWW/335/HDV.html</p> <p>Hepatitis E virus is an RNA single strand, non-enveloped virus. It is spherical and of larger volume than the HAV. http://www.tulane.edu/~dmsander/WWW/335/HEV.html</p> <p>Hepatitis F virus was first identified by Deka and Coll in India in 1994, in patients with non-A and non-B hepatitis. Nevertheless those data have not been confirmed ever since. Its existence is probable, since there has been at least one epidemic of non-A, non-B hepatitis that was not due to HEV. The infections due to the F virus seem to be very rare.</p> <p>Hepatitis G virus (HGV) like the Hepatitis C virus belongs to the family of Flaviviruses. http://www.tulane.edu/~dmsander/WWW/335/HGV.html</p>
<p>Classification:</p>	<p>Classification of the viruses</p> <p>Hepatitis A belongs to the family of Polio viruses</p> <p>Hepatitis B belongs to the family of Hepadna viruses. It is the prototype member of the family Hepadna viridae. Although It contains a reverse transcriptase activity HBV being a DNA virus is not classified as a retrovirus on the basis of the classical definition for retroviruses (s/s, (+)sense RNA genome). http://www.tulane.edu/~dmsander/WWW/335/Retroviruses.html</p> <p>Hepatitis C, hepaC virus genus, member of the Flaviviridae family</p> <p>Hepatitis D .The HDV genome is a unique chimeric molecule with some of the properties of a satellite virus and some of a viroid</p> <p>Hepatitis E is classified in the family of Calici viridae. Studies exist that show E virus to be very close to the rubella virus.</p> <p>Hepatitis G (GBCV) belongs to the family of Flaviviridae like the Hepatitis C virus.</p> <p>Classification of the disease</p> <p>Hepatitis can be presented in various clinical forms:</p> <p>Subclinical form. It usually affects children or young adults. It is associated with minor or non-specific symptoms like fatigue, abdominal discomfort, and loss of appetite. Infected individuals may rarely notice that their urine becomes darker and their stools discoloured. Overall, patients usually feel rather well.</p> <p>Acute hepatitis. Patients clinically feel unwell. Symptoms are presented as a flu, with fever, digestive trouble and abdominal pain followed by jaundice, a significant increase in serum transaminases, urine darkening and stool discoloration. Complete healing is observed in about 90% of the cases.</p> <p>Fulminant hepatitis. It has a very rapid evolution resulting in a disastrous hepatic failure associated with encephalopathy and coma. The mortality reaches 80% of the cases. Treatment should take place in intensive care units (ICU) and relies on urgent liver transplantation.</p> <p>Chronic Hepatitis. Three viruses are responsible for chronic hepatitis. The Hepatitis B (HBV), C (HCV) and D (HDV) viruses. Patients with chronic infections are often asymptomatic and may reveal a moderate increase in serum transaminases. Patients infected with HBV are usually carriers of the surface antigen of the virus (Hbs ag) that persists in the serum over six months and they therefore need to be surveyed. Some of these patients may also be coinfectd with the HDV virus. HCV infected patients</p>

	<p>may only present positive antibodies against parts of the viral genome (anti-HCV).</p> <p>Chronic hepatitis may ultimately lead to cirrhosis in 15% to 40% of chronic HBV patients (<i>McMahon BJ, 1997</i>), in 30% to 50% of chronic HCV patients (<i>Maddrey WC, 2000</i>) and in 50% to 70% of the patients with chronic HBV+HDV coinfections. In the long term, primary hepatocarcinoma in the liver develops in cirrhotic HBV and HCV patients.</p>
<p>Consequences:</p>	<p>Hepatitis caused by HAV infection is a benign disease in about 99% of the cases and it often runs unnoticed. It usually affects children, adolescents and young adults in developing countries. The disease is more severe in adults aged 30-40 years or older. The incubation period is short and silent, 15-40 days, with a mean of 20 days. The convalescence is long. In children, the disease is subclinical and is rarely (10%) manifested by jaundice. Most often it is manifested by simple flu-like symptoms. In adults, jaundice appears in 50% of the cases. Elders become symptomatic in 70-80 % of the cases. Recovery is rapid and takes between 6-8 weeks. Hepatitis A does not evolve to chronicity. Fulminant Hepatitis A is rare, one case for every 100,000 infections. Fortunately, when it happens, the prognosis is good.</p> <p>Hepatitis B virus is responsible for about 80% of the primary liver cancer cases. Hepatitis B is a very contagious disease that essentially affects the liver. Two thirds of the infected adult individuals present typical flu-like symptoms at the beginning and soon become jaundiced. In the remaining cases, patients are anicteric but with elevated serum transaminases; in 1 out of 1000 cases, hepatitis will evolve into the fulminant form with a mortality of 90% within 1-3 weeks from the beginning of jaundice. This unfavourable sequel is due to a hyper-reaction of the host immune system against HBV. The only therapy is an urgent liver transplantation. 5-10% of the infected adults exposed to HBV develop a persistent infection, while 80% of children cases become chronic. The natural history of chronic hepatitis evolves in four stages: 1) active multiplication of the virus; 2) Immunologic effort of the host to eliminate HBV, which is usually unsuccessful; 3) HBV integration into the hepatic genome, stop of replication of the virus and lowering of viral DNA in the serum. HbsAg remains present, although in some patients it is not expressed. Hepatic pathology is consistent either with a pattern of chronic hepatitis or even cirrhosis; 4) Reactivation -during which HBV (usually the mutant type) is multiplied aggressively leading to terminal disease. In one out of two cases it will induce cirrhosis, portal hypertension and will finally evolve towards a primary liver cancer.</p> <p>Hepatitis C is a chronic condition in about 85% of infected individuals due to a weak natural host immune response against the virus. It is usually the result of blood transfusion in previous decades. HCV incidence is currently high among drug abusers and HIV patients. In about 30-50% of the patients with chronic infection, and especially in those who consume alcohol, hepatitis C progresses to cirrhosis and its complications include end-stage liver disease, portal hypertension and hepatocellular carcinoma. HCV has also been linked to a spectrum of other extrahepatic diseases. Roughly 20% of patients manifest jaundice clinically while 10%-20% complain about malaise, anorexia, abdominal pain or non-specific flu-like symptoms. Fulminant hepatic failure is rarely reported. Hepatitis C is often discovered with a delay or by chance, in average 10-20 years after the initial contact with the virus. The mean time of appearance of cirrhosis varies between 2-30 years or more with a mean around 18 years from the initial contamination. Approximately 4 million people in the United States and about 170 million people world-wide are infected with HCV.</p> <p>Infection with the Hepatitis D virus always leads to hepatic lesions. Coinfection with HBV and HDV entails a 10-20 times higher risk of fulminant hepatitis, compared to acute hepatitis due only to HBV infection. Coinfection with HBV and HDV leads to an increased risk for chronicity (80% of the cases).</p> <p>Hepatitis E frequently appears in the form of epidemics that are often massive and long lasting. It mainly affects adolescents and young adults (age range 15-40 years). The incubation period is estimated in 36 days in average. The disease is clinically similar to hepatitis A. The duration of symptoms lasts approximately two weeks. Half of the infections are asymptomatic and they often run a benign course without evolution to chronicity or cirrhosis. HEV is responsible for more than 50% of acute cases of non-A non-B hepatitis in the developing countries. Pregnant women are at higher risk of a fulminant course, with a percentage of mortality that can reach 15-20%. Transmission of the virus from mother to child can lead either to a benign</p>

	<p>infection of the fetus or to its death in the uterus of the mother.</p> <p>Hepatitis G appears as a benign disease, when it is only due to HGV. The virus can be present in children for long time that can be up to 9 years and it can evolve to a persistent infection..(Terrault, N. & Wright N. 1998). HGV has yet to be demonstrated to be a cause for liver disease. It can be associated with hepatitis due to infections by HBV or HCV.</p>
<p>Associated Disorders:</p>	<p>Hepatitis A: Extrahepatic manifestations of acute HAV infection are less frequent than with HBV infections. They appear frequently in patients with more protracted disease (Shiff E. 1992). An evanescent rash (14%) or arthralgias (11%) most commonly appear. Less commonly a vasculitis, glomerulonephritis and true arthritis can ensue. Myocarditis, optic neuritis, neuropathies as well as thrombocytopenia and aplastic anaemia have also been reported. A post-hepatitic syndrome characterized by prolonged malaise, abnormal liver enzymes and persistent IgM anti-HAV antibodies has been described.</p> <p>Hepatitis B: Extrahepatic findings are common with HBV infection. Arthralgias and rashes occur in 25% of the patients. A more severe form of vasculitis (polyarteritis nodosa) may occur with either acute or chronic HBV infection. This syndrome typically presents with fever, abdominal pain and renal failure. Other manifestations, due to vasculitis effect are neuropathies (Guillain-Barre and polyneuropathies), renal disease, arthritis and Raynaud's phenomenon. Chronic HBV infection and to a lesser degree acute, is associated with an immune- type glomerulonephritis that leads to end stage renal failure. Sometimes chronic HBV infection may be associated with autoimmune hepatitis. Rarely, HBV has been associated with pancreatitis and pericarditis. Finally we should always bear in mind that chronic HBV leads to cirrhosis and hepatocellular carcinoma.</p> <p>Hepatitis C: Mixed type cryoglobulinemia, proliferative glomerulonephritis, polyarteritis nodosa and sicca syndrome, comprise a group of diseases strongly associated with HCV infection. On the other hand autoimmune thyroid disease, skin lesions like porphyria cutanea tarda and lichen planus, aplastic anemia, lymphoma, idiopathic pulmonary fibrosis, neuropathies, mooren's corneal ulcer are other diseases that can also be associated with HCV infection. Finally, diabetes mellitus incidence seems to be higher among HCV patients.</p>
<p>Etiology:</p>	<p>HAV is a small picornavirus and resembles the polioviruses. The viral capsid, that contains the RNA has an icosahedral structure and lacks a membrane envelope. HAV is very resistant to the external environment. It penetrates the organism by the oral route and multiplies in the hepatocytes before spreading in the intestine from where it is excreted (faecal excretion).</p> <p>HBV is an enveloped DNA virus of the family of Hepadna viruses. Its genes can be integrated in the human hepatocellular genome and be responsible for chronic infections that may progress to cirrhosis and ultimately to hepatic cancer. We can identify three types of viral particles in the serum of infected humans. The virion, the spheres and the filaments. The virion or the viral particle is composed of an envelope with surface proteins and a nucleocapsid carrying the proteins of the capsid and the viral DNA. The spheres and the filaments are empty envelopes that consist of proteins and are synthesised in excess during viral replication. These empty envelopes are not infectious but highly antigenic and activate host immune mechanisms against the virus. Hepatitis B is a very contagious disease because HBV is present in most biological fluids of the infected individual (blood, sexual secretions, saliva, urine, maternal milk etc). However, clear data with regard to infectivity are consistent with viral concentrations in serum and semen. Additionally the virus is relatively resistant in the environment. It survives several days in an external medium, in habitual temperatures, for 10 hours in 60°C and 5 min in 100°C. It is in parallel very resistant in ether, 90% alcohol treatment or in freezing conditions for several years.</p> <p>HCV is a small RNA virus that belongs to the Flaviviridae family, other members of which are the flaviviruses. Like all RNA viruses it is subject to a high frequency of mutations and exists in the form of 'quasi' species in the infected individuals (Maddrey, W.C., 2000). For many of the single-stranded positive-sense RNA viruses, most of the viral non-structural proteins and some cellular proteins form a multi-protein complex to direct the replication of the viral RNA genome. Although the mechanisms of HCV template RNA replication are not well understood, it is believed that they may follow a similar pattern. The most severe barrier in the understanding of</p>

	<p>the HCV infection is the low level of HCV particles found in the patient plasma and the lack of an efficient cell culture system for HCV. Up to date no one has been able to grow HCV reliably and efficiently in a laboratory culture of cells; a lack that has decelerated critical studies on the biochemical and functional properties of the viral structural or non-structural proteins, as well as the understanding of the steps of viral life cycle and its interactions with the host cell.</p> <p>HCV resists immune defences and can induce chronic infections. It is known that HCV blocks the interferon induced antiviral host response and this is considered to be a cause for failure of the INF-α based treatment.</p> <p>Hepatitis D (HDV) is a viroid. A "defective" or incomplete virus that can multiply only in the presence of HBV virus. HDV necessarily borrows the envelope from HBV, being thereby able to attach to and enter hepatocytes. Its genome is a circular RNA molecule that can replicate autonomously. However, in the absence of HBV that acts as a helper, Delta virus cannot be secreted out of the hepatic cell.</p> <p>Hepatitis E is an RNA single stranded, non-enveloped virus. It shares similarities with the Calciviridae/Alpha super group family, like Norwalk, rubella and plant furoviruses. It is spherical and has larger volume than HAV. Unlike HAV, it is a very fragile virus and its conservation requires freezing to -80°C. Its life in the environment is probably very short. Hepatitis appears in the form of epidemics that often last long. Geographically, E virus can be found in India, the former Soviet Union, South East Asia and Mexico. The disease has a clinical manifestation very close to the one of Hepatitis A, with symptoms that can last approximately two weeks.</p> <p>HGV like the Hepatitis C virus is a Flavivirus. Three types of this virus exist: GBV.A: a virus of the tamarin monkeys transmissible to humans and vice-versa; GBV.B and GBV.C, a human virus isolated from the virus of an African patient. It was discovered in 1995 by two American labs (Abbot and Genelab). The HGV virus or viruses are single stranded RNA viruses.</p> <p>HGV has no clinical significance as the disease caused by this virus, appears to be very rare, mild and self-limiting when it is only due to the HGV infection. It can however be associated with HBV and HCV infections. HGV alone or associated with HCV could be implicated in the fulminant hepatitis but this has not been confirmed.</p>
<p>Epidemiology:</p>	<p>Hepatitis A is found throughout the world. The disease is very closely related to the socio-economic level of each country. In general, it is found in intertropical countries with poor hygiene conditions in which it mostly affects children. The majority of adults have antibodies against the virus. Age is a very important factor regarding the clinical course of the disease. The majority of cases are observed in Africa and South America, in the middle East countries and in Asia. However, HAV infection does not constitute a major problem in these countries, as it is usually subclinical or mild and can only be serologically diagnosed. Regions with intermediate endemicity are North America, Spain, Greece, countries of East Europe and some countries of South America and Southeast Asia. Improvement in hygiene conditions has lowered the incidence of infections in many Western countries.</p> <p>Hepatitis B is present worldwide. However endemicity varies a lot. Areas of high endemicity (Hbsag prevalence $>8\%$ of the population) are Southeast Asia, China, Africa, Alaska, South America and Middle East. In these areas transmission takes place vertically from pregnant mothers to infants or within the family, between parents and children, during the first five years of life. Areas with intermediate endemicity (Hbsag prevalence 2-7% of population) are East Europe, Russia, Mediterranean basin, and parts of Middle East and Japan. Areas with low endemicity (Hbsag prevalence $<2\%$ of population) are North America and Western Europe. Transmission occurs during sexual intercourse and in specific high-risk population groups, like homosexuals and drug addicts.</p> <p>Hepatitis C. It is estimated that more than 170 million persons are infected with HCV worldwide (<i>WHO, 1997</i>). Precise estimate of HCV prevalence is not available in the general population of most countries. In developed nations general population HCV prevalence rate is generally less than 3%, while among volunteer blood donors is less than 1%. In a few nations and distinct regions within nations HCV prevalence in the general population exceeds 10%. After the introduction of blood screening with anti-HCV in 1991, transfusion related cases declined in USA and injection drug use is the most common risk factor identified. In Egypt HCV prevalence varies from, 10% to 30%. In most highly endemic areas, HCV infection is prevalent among persons over</p>

	<p>40 years of age, but uncommon in those less than 20 years of age. This cohort effect suggests a time-restricted exposure, which in many instances appears to have been receipt of a medical procedure. While not yet confirmed, in Egypt it is suspected that a national campaign to treat schistosomiasis was responsible.</p> <p>Hepatitis D. Fifteen million individuals are infected world wide with HDV (<i>Alter M. & Mast E, 1994</i>). Although the epidemiological pattern of HDV is similar to HBV pattern, the geographic distribution is not always similar to HBV. Thus, there are three types of endemicity. High endemicity is found in areas with high HBV prevalence with the exception of <i>Alaska (Alter and Mast, 1994)</i>. Intermediate HDV prevalence is found in areas with intermediate or high HBV prevalence. Low HDV prevalence is found in areas with low, intermediate or high HBV prevalence. Transmission modes are similar to those of HBV infection. Drug abusers, haemophiliacs and people receiving large blood amounts are at increased risk. Sexual transmission of HDV is not that common compared to HBV.</p> <p>Hepatitis E virus can be found in India, former Soviet Union, China, South East Asia and Mexico. In these countries occur either epidemic or sporadic infections. In endemic countries outbreaks of E virus present a periodicity of approximately 5-10 years. In non-endemic areas, only sporadic infections occur affecting travellers formerly been in endemic areas. The reservoir for HEV during interepidemic period is unknown. The overall case-fatality rate for the general endemic population is 0.5%-4% (<i>Mast et al., 1996</i>). Pregnant women have higher fatality rates (20%) and fetal deaths are higher especially in the third trimester (<i>Tsega, et al., 1992</i>).</p> <p>Hepatitis G virus infection is present in a significant proportion of volunteer blood donors especially with normal serum aminotransferases (<i>Linnen et al., 1996</i>). When HGV is associated with HCV, it is more frequently found in patient groups with parenteral risk factors.</p>
<p>Pathophysiology:</p>	<p>Over the last few years, new data have contributed to our knowledge about the mechanisms by which different viruses cause liver injury (<i>Terrault et al., 1998</i>).</p> <p>Hepatitis A: The precise pathogenetic mechanism of cell injury is unknown. HAV seems to be directly cytotoxic in tissue culture. However, most evidence indicates that hepatocyte injury is secondary to host immune response. Immuno-histochemical analysis has revealed immunoglobulins and HAV antigens in various hepatic cells.</p> <p>Hepatitis B: It was recently discovered that immune response of the host is more important than viral factors in the pathogenesis of liver injury. In other words, the virus might be harmless and hepatocytes are destroyed due to an intensive reaction of the host against HBV (e.g. fulminant hepatitis). HBV mutants especially at a specific precore genomic region affect natural history of the disease as well as treatment outcomes.</p> <p>Hepatitis C: Mechanisms of viral persistence and hepatocellular injury are poorly understood in chronic HCV infection. In general, viral infection can produce cellular injury by direct cytopathicity and indirect immune-mediated injury.</p> <p>Hepatitis D: There is some evidence that HDV antigen and HDV RNA may be directly cytotoxic to hepatocytes. However, other studies have failed to demonstrate the above findings. Autoimmunity may be one possible mechanism by which liver disease is propagated. This may partly explain the differences in severity seen in patients with HDV plus HBV versus HBV alone.</p> <p>Hepatitis E: There is a mixed mechanism of HEV action. Direct hepatocellular injury includes interference with the production of cellular macromolecules, alteration of cellular membranes and lysosomal permeability. Immune-mediated injury includes lysis of virally infected hepatocytes either by direct lymphocyte cytotoxicity or antibody-mediated cytotoxicity.</p> <p>Hepatitis G: No data are available regarding the pathogenesis of HGV.</p>
<p>Signs and Symptoms:</p>	<p>Most common clinical manifestations of hepatitis are listed below. The majority of them characterise both acute or/and chronic hepatitis (<i>Shiff, E 1992</i>). Features marked with asterisk denote chronicity. These are quite helpful guides in the diagnostic procedure.</p> <p>Systemic Anorexia, malaise, fatigue, fever</p>

	<p>-general deterioration * ,</p> <p>-weight loss * ,</p> <p>-cirrhotic habitus * ,</p> <p>-pruritus * ,</p> <p>-xanthomas/xanthelasma * ,</p> <p>-malabsorption *</p> <p>-Jaundice</p> <p>-hepatomegaly +/- pain</p> <p>-portal hypertension,</p> <p>-ascites *</p> <p>-cutaneous and endocrine changes *</p> <p>coagulopathy: hypoprothrombinemia, thrombocytopenia</p> <p>circulatory changes: Hyperdynamic circulation, nail clubbing.</p>
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Standard Therapies:	Agents
	<p>Vaccines are available for Hepatitis A and B prevention. Vaccination is considered to be the corner stone for the decline of HBV infection in high prevalence regions. Studies coming from Taiwan, a country with high HBV prevalence report a decline on hepatocellular carcinoma incidence, as a result of a general population vaccination strategy. Over the last years, a recombinant HBV vaccine is in use worldwide. HBV vaccination is highly effective >95%. Revaccination works in 30-50% of non-responders to primary vaccination. Revaccination is not recommended after two series. Protective titers are those over 10 mlu/ml. Vaccination is indicated for newborns of HBV positive mothers, HBV negative children in high endemic areas, family members of HBV positive patients, dialysis patients, frequently transfused and HBV negative social workers. There are no significant side effects due to vaccination.</p> <p>Three different vaccine strategies have been used in HAV vaccine development: a live attenuated virus vaccine, an inactivated virus vaccine and a recombinant vaccine. All of them are highly effective with regard to the development of protective antibodies. However, the last of them seems to be the cheapest and safest. Vaccination is found to be cost-effective when travelling to high HAV incidence countries occurs three or more times in a decade or if staying there is longer than half a year.</p>

<i>Agent Name</i>	<i>Discussion</i>
Interferon-alpha2a, Interferon-alpha2b, consensus interferon, pegylated interferon alpha2a ,a2b	Hepatitis A: Due to autoremission only supportive measures Hepatitis B: Acute infection: A spontaneous recovery up to 99% ensues. No antiviral therapy is required. Chronic infection: Interferon- α 2a, Interferon- α 2b, pegylated interferon α 2a, lamivudine. Compensated cirrhosis: Interferon- α 2b, Interferon- α 2a, pegylated interferon- α 2a, a2b. Lamivudine. Uncompensated cirrhosis: Low dose interferon, lamivudine. Hepatitis, B+D: Interferon- α 2a, Interferon- α 2b, consensus interferon, pegylated interferon α 2a, a2b. Hepatitis C: Chronic infection: Interferon- α 2a, Interferon- α 2b, consensus interferon, pegylated interferon α 2a, a2b plus ribavirin. Hepatitis E: Due to autoremission only supportive measures.
Ribavirin	The nucleoside analogue, ribavirin has been recently approved for use in combination with interferon and appears to greatly improve the sustained response rates for patients with chronic Hepatitis C.
Nucleoside analogues (Lamivudine or 3TC)	It was initially used in HIV patients. Over the last years lamivudine is recommended for treatment of chronic HBV infection and HBV cirrhosis. The mechanism of action has to do with inhibition of HBV DNA polymerase. The duration of therapy is up to 5 years. High percentage of viral mutants after the first two years of treatment (40-50%).
Adefovir	A nucleoside analogue of adenosine, adefovir has been recently approved for chronic HBV treatment, especially in patients resistant to lamivudine treatment.

To enter information about a new agent, copy the row outlined in blue above, and paste at the beginning of this line.

Repeat for each new agent.

Experimental Therapies:

Agent Name	Discussion
Entecavir	Nucleoside analogue of guanoside tested for chronic HBV treatment: powerful antiretroviral drug. It is currently under phase 2 and 3 clinical trials.
Emtricitabine; Clevudine; L-deoxythymidine	Nucleoside analogues for chronic HBV treatment: powerful antiretroviral drug. They are currently under phase 2 and 3 clinical trials.

To enter information about a new agent, copy the row outlined in blue above, and paste at the beginning of this line.
Repeat for each new agent.

Animal Models:

Transgenic mouse model of fulminant Hepatitis (rev Mingfeng et al. 2001)

Two small-animal (rodent) models of virus-induced FHF have provided great insight into the molecular mechanism of virus-induced FHF. The first is a transgenic HBV model of FHF in which HBV proteins are overexpressed in mice. The second involves the RNA Coronavirus MHV-3, which produces a strain-dependent pattern of FHF in inbred strains of mice). Although the transgenic HBsAg model is an elegant means of dissecting the pathogenic mechanisms of FHF, the model has limitations in that it differs markedly from the clinical situation, in which a replicating virus exists

Animal models for immune defects caused by hepatitis C virus (rev. Myungsoo J. 2000)

The potential role of HCV infection in evasion from immune surveillance has been elucidated by studies on HCV-infected chimpanzees and an experimental murine animal model.

Development of animal models of hepatitis B and C viral infection (H. Wald:

http://english.hadassah.org.il/people/pphana_wald.htm, M. Ketzinel-Gilad:

http://english.hadassah.org.il/people/ppmali_ketzinel.htm)

The study of HBV and HCV, and the development of new therapies have been slow to evolve due to lack of a practical and convenient small animal model. HBV animal models based on non-primates provide useful information but lack many aspects of human disease. The goal of this group is to develop a new small animal model of HBV infection. This model may be valuable for the investigation of viral infections of other hepatitis viruses and will provide a convenient system for evaluating the effects of vaccines or anti-viral therapeutic agents.

Other Information

Websites:

<http://www.cdc.gov/ncidod/diseases/hepatitis/> CDC viral hepatitis site.

The Virus Hepatitis Network <http://www.hepnet.com/>.

The American Liver Foundation <http://www.liverfoundation.org/>.

The Viral Hepatitis Prevention Board <http://www.vhpb.org/>.

European Association for Study of the Liver <http://www.easl.ch/initiatives.htm>.

The American Association for the Study of Liver Disease
<http://www.aasld.org/>.

Tulane University (Information about HDV)
<http://www.tulane.edu/~dmsander/WWW/335/HDV.html>.

Tulane university (Information about HCV)
<http://www.tulane.edu/~dmsander/WWW/335/HCV.html>.

Tulane university (Information about HAV)
<http://www.tulane.edu/~dmsander/WWW/335/HAH.html>.

Tulane university (Information about HBV)
<http://www.tulane.edu/~dmsander/WWW/335/HBV.html>.

Tulane university (Information about HGV)
<http://www.tulane.edu/~dmsander/WWW/335/HGV.html>.

	<p>Hepatitis virus database http://s2as02.genes.nig.ac.jp/.</p> <p>HepC AB: Diseases and Symptoms Associated with HCV http://www.geocities.com/HotSprings/Spa/7563/diseasesindex.html.</p> <p>American hepato-pancreato-biliary Association http://www.ahpba.org.</p> <p>International Liver Transplantation Society http://www.its.org.</p> <p>Hepatitis Foundation International http://www.hepfi.org/.</p> <p>SIGN (Safe injection Global network) http://www.injectionsafety.org.</p> <p>Hepatitis Doctor Home http://www.hepatitisdoctor.com/.</p> <p>HIV and Hepatitis.com http://www.hivandhepatitis.com/</p> <p>Deutsches Hepatitis C http://www.hepatitis-c.de.com/.</p>
Further Reading:	

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Bibliographic References

<i>Author(s)</i>	<i>Article Title</i>	<i>Journal</i>	<i>Year</i>	<i>Vol (Issue)</i>	<i>Page(s)</i>
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Maddrey, W.C.	Hepatitis C: a work in progress	In: Gastroenterology and hepatology at the millennium and beyond. 2000 American Gastroenterological Association Spring Post graduation Course	2000		49-61
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End of Record for an Individual DISORDER

Reviewer's Comments

Assistant Editor comments:

This is an excellent review of viral hepatitis and very clearly takes each aspect of all types of viral hepatitis in to consideration. I would like to thank the authors for this well-written contribution. There are few stylistic corrections already incorporated into the document. Few comments are made in the text in sections "Pathophysiology" and "Web sites", in RED for author's consideration. I request the authors to consider the following suggestions for a minor revision:

Author is requested to suggest any web-sites relevant to the topic, if possible. A google search (www.google.com) may provide relevant web sites.

Please cite either review articles or literature references in the Further Reading section for the readers. These could be some of the books or literature reviews that are already in the Bibliography section

Please mention the bibliographic references in the main text, where appropriate. At least all the bibliography should be cited once in the main text of the record.

Once again, this is an excellent record contribution by the authors to xPharm.

Associate editor's comments:

This record has much useful information and is quite well done.

I have made a number of corrections to clarify the document and to insert U.S. spelling.

Please clarify the following sentences.

In the introduction section, under parenteral transmission, what is meant by "eventually saliva"? In the definition section, under hepatitis D, please clarify the last sentence in that section.

_ In the consequences section, last sentence of the first paragraph, Fulminant hepatitis seems serious yet the prognosis is good. Should your sentence contain a word like 'yet' or 'despite' to contrast these two thoughts?

_ In the same section under Hepatitis G, next to last sentence, persistent without being chronic almost seems like a contradiction. Please clarify.

_ In the associated disorders section, please rewrite the sentence beginning with" An evanescent...

In the etiology section, under hepatitis D, should it read "with the help of the envelope it is able to burrow"? (or similar wording) Please clarify.

_ Please use complete sentences throughout including a sentence to explain the importance of each website.

_ Please follow the format for placing references in the reference section!

Is HBV a retrovirus? The question arises from the fact that antiretroviral drugs are indicated for its treatment in the agents section. The retrovirus issue should be addressed in the definition section. Does HBV have reverse transcriptase activity?

Please add any animal models that are appropriate, and reference them

Please use the checklist below to help you complete your record.

_____ Please revise this copy of your record when you respond.

_____ Use complete sentences throughout the record.

_____ Either define all abbreviations once within each section of the record, or insert a glossary item at first mention in each section, then abbreviate thereafter.

_____ Include website references and a sentence of explanation about the website. (Try google.com to search.)

_____ Perform an American spell-check of the document.

_____ In the "agents" section of your record, include a sentence or two identifying and describing each drug listed.

_____ Include all author names in the list of references, unless the number of authors exceeds 10. Thereafter insert et al.

_____ Format references in the text according to the following examples (e.g., Bylund, 1998; or Bylund and Enna, 1998; or Bylund et al., 1998), whichever is appropriate. Full reference details are required in order to link to the cited literature (i.e., at least six author names and then et al., may be added; use inclusive page numbers and issue numbers; author names-especially for book references).

_____ Please cross-check reference citations. If a reference is cited in the text, the full reference details must be provided in the bibliography. If article details are supplied in journal/book bibliography it must be cited in the text of the record.

_____ References not cited in the text should be in the section entitled "Further Reading".

_____ Do not number figures unless more than one figure is present in a section. Images and tables must be .jpeg or .gif files. Tables must be converted to images (.gif or .jpeg) and imported into record. Tables are essentially tabular data that get scrambled on conversion from word to XML and will be incomprehensible to a reader.

_____ Include a summary of relevant animal models along with references.