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# Viral Hepatitis

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## Introduction

While **hepatitis** has been described for centuries, it was only in the 19<sup>th</sup> century that a connection was made between jaundice and diseases affecting the hepatocytes. The term hepatitis is Greek, meaning inflammatory disease of the liver. The causes may be numerous, with several types of hepatitis being identified, such as 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. Viral hepatitis affects hundreds of millions of individuals worldwide, particularly in developing countries. However, the incidence can be high in industrialized countries as well.

Seven hepatitis **viruses** were identified during a thirty year period (1965-1995). The recent discovery of the hepatitis G virus suggests that the list may not be complete as yet. Accepted terminology differentiates hepatitis alphabetically into A, B, C, D (or delta), E, F and G. The viruses causing hepatitis are classified into two groups depending on the route of transmission. Thus, the A, E, and F (still poorly characterized) viruses have an oro-fecal transmission. These viruses can be transmitted by food, shellfish, dirty water, dirty hands, or contaminated stools. They cause epidemics and are characterized by the absence of the risk for chronic infections. The second group is comprised of type B, C, D, and G viruses that are transmitted parenterally by way of contaminated biological fluids like blood and semen. These infections are characterized by the risk of chronicity that evolves to **cirrhosis** and primary **cancer of the liver**. Use of contaminated syringes by drug abusers, blood or blood product transfusion, and transplantation of organs and hemodialysis are the most common ways for these viruses to be acquired. Sexual intercourse is a particularly important route of transmission for the type B virus. HBV and, less commonly, HCV may also be transmitted vertically from mother to child during labor. It remains to be determined whether hepatitis G virus is sexually transmitted.

Viral hepatitis is an important public health problem. Primary prevention is, therefore, mandatory, if possible. Vaccines exist only for hepatitis A and B, both alone and combined. Young people in particular should be protected against both viruses, especially when traveling to countries with a high incidence of these viruses. High standards of hygiene, meticulous disinfection of instruments in the hospital environment, and non-exchange of syringes between drug addicts are practices that can lower significantly the transmission rate of these viruses. Alcohol consumption, even of moderate quantities, is a risk factor for aggravating the evolution of hepatic lesions.

## Definition

Viral hepatitis is classified alphabetically from A to G. This classification is used for predicting the course of the disease, its treatment and the final prognosis.

Hepatitis A virus (HAV) is a small picornavirus that belongs to the family of Polio-viruses: <http://www.tulane.edu/~dmsander/WWW/335/HAV.html>

Hepatitis B virus (HBV) is the only DNA virus member of the family of Hepadna viruses. It consists of spherical, enveloped particles 42–47 nm diameter containing partially ds DNA plus an RNA-dependent DNA polymerase (i.e., reverse transcriptase): <http://www.tulane.edu/~dmsander/WWW/335/HBV.html>

Hepatitis C virus (HCV) is a small RNA virus that belongs to the Flaviviridae family. Like all RNA viruses it is subjected to a high frequency of mutations. It resists immune defenses and can induce chronic infections: <http://www.tulane.edu/~dmsander/WWW/335/HCV.html>

Hepatitis D virus is a viroid. Similar to plant virus satellite RNAs, it is a defective transmissible pathogen dependent on HBV for replication. Its genome is a circular RNA molecule that can replicate autonomously. However, HDV cannot be secreted from hepatic cells in the absence of HBV: <http://www.tulane.edu/~dmsander/WWW/335/HDV.html>

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>

Hepatitis F virus was first identified by Deka and Coll in 1994 in patients with non-A and non-B hepatitis. While their findings have not been confirmed, the existence of this virus is probable since there has been at least one epidemic of non-A, non-B hepatitis that was not due to HEV. Infections due to the F virus appear to be very rare.

Hepatitis G virus (HGV), like the Hepatitis C virus, belongs to the family of Flaviviruses: <http://www.tulane.edu/~dmsander/WWW/335/HGV.html>

## Classification

Hepatitis A belongs to the family of Polio viruses.

Hepatitis B belongs to the family of Hepadna viruses. It is the prototype member of the family Hepadna viridae. Although it contains reverse transcriptase activity, HBV being a DNA virus is not classified as a retrovirus: <http://www.tulane.edu/~dmsander/WWW/335/Retroviruses.html>

Hepatitis C, hepaC virus genus, member of the Flaviviridae family.

Hepatitis D. The HDV genome is a unique chimeric molecule with some of the properties of a satellite virus and some of a viroid.

Hepatitis E is classified in the family of *Calici viridae*. Studies suggest that E virus is very similar to the rubella virus.

Hepatitis G (GBCV), like hepatitis C virus, belongs to the family of Flaviviridae.

Hepatitis can be present in various forms:

Subclinical hepatitis 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 discolored.

Acute hepatitis presents as a flu, with **fever**, digestive trouble, and abdominal pain followed by jaundice, a significant increase in serum transaminases, urine darkening, and stool discoloration. There is a complete recovery in about 90% of the cases.

Fulminant hepatitis is characterized by a very rapid evolution resulting in a disastrous hepatic failure associated with encephalopathy and coma. Mortality approaches 80%. Fulminant hepatitis requires liver transplantation.

Three viruses, B (HBV), C (HCV) and D (HDV), are responsible for chronic hepatitis. Patients with chronic infections are often asymptomatic and may display 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. Some of these patients may also be co-infected with the HDV virus. HCV infected individuals may only present positive antibodies against parts of the viral genome (anti-HCV). Chronic hepatitis will lead to cirrhosis in 15-40% of HBV patients [McMahon \(1997\)](#), in 30-50% of HCV patients [Maddrey \(2000\)](#), and in 50-70% of those with chronic HBV+HDV co-infections. In the long term, primary hepatocarcinoma in the liver develops in cirrhotic HBV and HCV patients.

## Consequences

Hepatitis caused by HAV infection is a benign condition in about 99% of the cases and often goes unnoticed. It usually affects children, adolescents and young adults in developing countries. The disease is more severe in those over 30 years of age. The incubation period is 15-40 days, with a mean of 20 days. The convalescence period is prolonged. In children, the disease is subclinical and is rarely (10%) manifested by jaundice. Most often it is associated with simple flu-like symptoms. In adults, jaundice appears in 50% of the cases. The elderly become symptomatic in 70-80 % of the cases. Recovery takes between 6-8 weeks. Hepatitis A does not evolve to chronicity. Fulminant Hepatitis A rare, one case for every 100,000 infections, and the prognosis is good.

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 adults present with typical flu-like symptoms 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 unfavorable sequel is due to a hyper-reaction of the host immune system against HB V. The only therapy is an urgent liver transplantation. Up to 5-10% of the infected adults exposed to HBV develop a persistent infection, while 80% of childhood 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 half the cases it will induce cirrhosis, portal hypertension and, finally, primary liver cancer.

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 high among drug abusers and **HIV** patients. In about 30-50% of the those with chronic infection, and especially in those who consume **alcohol**, hepatitis C progresses to cirrhosis. Its complications include end-stage liver disease, portal hypertension, and hepatocellular carcinoma. HCV has also been linked to a spectrum of other extrahepatic diseases. Thus, roughly 20% of patients manifest jaundice, while 10-20% complain of malaise, **anorexia**, abdominal pain, or non-specific flu-like symptoms. Fulminant hepatic failure is rarely reported. Hepatitis C is often discovered 10-20 years after the initial contact with the virus. The mean time of appearance of cirrhosis varies between 2-30 years, with a mean of approximately 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.

Infection with the Hepatitis D virus always leads to hepatic lesions. Co-infection with HBV and HDV entails a 10-20 times higher risk of fulminant hepatitis, compared to acute

hepatitis due only to HBV infection. Co-infection with HBV and HDV leads increases the risk for chronicity.

Hepatitis E, which mainly affects adolescents and young adults, frequently appears in the form of epidemics that are often massive and long lasting. The incubation period is estimated to average 36 days. The disease is similar to hepatitis A. The duration of symptoms lasts approximately two weeks. Half of the infections are asymptomatic and run a benign course without evolving to chronic hepatitis 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 mortality rate that can reach 15-20%. Transmission of the virus from mother to child can lead either to a benign infection of the fetus or to its death in the uterus.

When it is only due to HGV, hepatitis G appears as a benign disease. The virus can be present in children for up to 9 years and can evolve to a persistent infection [Terrault and Wright \(1998\)](#). HGV has yet to be demonstrated as a cause of liver disease. It can be associated with hepatitis due to infections by HBV or HCV.

## Associated Disorders

Extrahepatic manifestations of acute HAV infection are less frequent than with HBV. They appear frequently in patients with more protracted disease [Schiff \(1992\)](#). An evanescent rash (14%) or arthralgias (11%) most commonly appear with hepatitis A. Less commonly there is vasculitis, glomerulonephritis, and true arthritis. Myocarditis, optic neuritis, neuropathies as well as thrombocytopenia and aplastic anemia have also been reported with this infection. A post-hepatitic syndrome characterized by prolonged malaise, abnormal liver enzymes, and persistent IgM anti-HAV antibodies has been described.

Extrahepatic findings are common with HBV infection, with arthralgias and rashes occurring in 25% of the patients. A more severe form of vasculitis (polyarteritis nodosa) may evolve with either acute or chronic HBV infection. This syndrome typically presents with fever, abdominal pain, and renal failure. Other manifestations, which are secondary to the vasculitis, are neuropathies (Guillain-Barre and polyneuropathies), renal disease, arthritis, and Raynaud's phenomenon. Chronic and, to a lesser degree, acute HBV infection 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. Chronic HBV leads to cirrhosis and hepatocellular carcinoma.

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, moorens's corneal ulcer are other conditions associated with hepatitis C infection. Moreover, the incidence of **diabetes mellitus** appears to be higher among HCV patients.

## Etiology

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 throughout the intestine from where it is excreted (fecal excretion). 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. Three types of viral particles, the virion, the spheres and the filaments, can be identified in the serum of infected humans. The virion, or 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 synthesized 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 of the biological fluids of the infected individual, including blood, sexual secretions, saliva, urine, and milk. However, data regarding infectivity are consistent with viral concentrations in serum and semen. Moreover, because the virus is relatively resistant in the environment it survives for days in an external medium or for up to 10 hours at 60°C and for 5 min at 100° C. It is very resistant in ether, 90% alcohol, and to extremely cold temperatures. 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 \(2000\)](#). 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 defined, it is believed that they may follow a similar pattern. The greatest hindrances to understanding HCV infection is the low level of HCV particles in plasma and the lack of an efficient cell culture system for the virus. To date it has not been possible to grow HCV reliably and efficiently in a laboratory cell culture of cells. This has decelerated critical studies on the biochemical and functional properties of the viral proteins, as well as on understanding the steps of the **viral life cycle** and its interactions with the host cell. HCV resists immune defenses and can induce chronic infections. It is known that HCV blocks the interferon-induced antiviral host response, which is thought to be responsible for the failure of interferon-based treatment of this disorder. Hepatitis D (HDV) is a viroid, which is a defective or incomplete virus that can multiply only in the presence of HBV virus. HDV borrows the envelope from HBV, which makes it capable of attaching to and entering 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 from the hepatic cell. 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 a larger volume than HAV. Unlike HAV, it is a very fragile virus, with its conservation requiring storage at -80° C. Its life in the environment is probably very short. Hepatitis appears in the form of epidemics that are often long. Geographically, E virus can be found in India, the former Soviet Union, Southeast Asia, and Mexico. The disease manifests similar to very hepatitis A, with symptoms that can last approximately two weeks. HGV, like the hepatitis C virus, is a Flavivirus. The three types of HGV are GBV.A, a virus of the tamarin monkeys transmissible to humans and vice-versa, GBV.B and GBV.C, human viruses isolated from the virus of an African patient. It was discovered in 1995. The HGV virus or viruses are single stranded RNA viruses. HGV has no little clinical significance as the disease caused by this virus appears to be mild and self-limiting. HGV can, however, be associated with HBV and HCV infections. HGV alone, or in association with HCV, has been implicated in fulminant hepatitis.

## Epidemiology

Hepatitis A is found throughout the world, with the incidence being very closely related to the socio-economic level of the country. In general, it is found in intertropical countries with poor hygiene conditions where it mostly affects children. The majority of adults have antibodies against the virus. Age is very important with respect to the clinical course of the disease. The majority of cases are present in Africa, South America, the middle East, and 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, Eastern Europe and some countries of South America and Southeast Asia. Improvement in hygiene conditions has lowered the incidence of infections in many Western countries.

While hepatitis B is present worldwide, endemicity varies greatly. Areas of high endemicity (Hbsag prevalence  $>8\%$  of the population) are Southeast Asia, China, Africa, Alaska, South America, and the 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 Eastern Europe, Russia, the Mediterranean basin, and parts of the 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 particular high-risk groups, such as homosexuals and drug addicts.

It is estimated that more than 170 million persons are infected with HCV worldwide [World Health Organization \(1997\)](#). A precise estimate of HCV prevalence is not available for the general population in most countries. In developed nations the 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 exceeds 10%. After the introduction of blood screening with anti-HCV in 1991, transfusion related cases declined in the United States. Injection drug use is the most common risk factor today. In Egypt, HCV prevalence varies from 10-30%. In most highly endemic areas, HCV infection is prevalent among persons over 40 years of age, but is uncommon in those less than 20 years of age. This cohort effect suggests a time-restricted exposure, which in many instances was a medical procedure. While not yet confirmed, it is suspected that in Egypt a national campaign to treat schistosomiasis was responsible.

Fifteen million individuals are infected world wide with HDV [Alter and Mast \(1994\)](#). Although the epidemiological pattern of HDV is similar to HBV, the geographic distributions are not always similar. Thus, high endemicity is found in areas with high HBV prevalence, with the exception of Alaska [Alter and Mast \(1994\)](#), intermediate HDV prevalence is found in areas with intermediate or high HBV prevalence, and 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, hemophiliacs, and those receiving large quantities of blood are at increased risk. Sexual transmission of HDV is not common in comparison to HBV.

Hepatitis E virus is found in India, the former Soviet Union, China, Southeast Asia, and Mexico. Both epidemic and sporadic infections are known to occur in these countries. In endemic countries, outbreaks of E virus occur every 5-10 years. In non-endemic areas, only sporadic infections occur. The reservoir for HEV during the interepidemic period is unknown. The overall case-fatality rate for the general endemic population is 0.5-4% [Mast and Krawczynski \(1996\)](#). Pregnant women have higher fatality rates (20%), with fetal deaths being even higher, especially in the third trimester [Tsega et al \(1992\)](#).



Hepatitis G virus infection is present in a significant proportion of volunteer blood donors [Linnen et al \(1996\)](#). When HGV is associated with HCV, it is more frequently found in patient groups with parenteral risk factors.

## Pathophysiology

Over the last few years new data have contributed to our knowledge about the mechanisms by which different viruses cause liver injury [Terrault and Wright \(1998\)](#).

For 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 the host immune response. Immuno-histochemical analysis has revealed immunoglobulins and HAV antigens in various hepatic cells.

It was recently discovered for hepatitis B that the 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 mutations, especially those at a specific precore genomic region, affect the natural history of the disease, as well as treatment outcomes.

The 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.

There is some evidence that HDV antigen and HDV RNA may be directly cytotoxic to hepatocytes. Autoimmunity may be one possible mechanism by which liver disease is propagated. This may partly explain the differences in severity seen in those with HDV plus HBV versus HBV alone.

There is a mixed mechanism of HEV action. Direct hepatocellular injury includes interference with the production of cellular macromolecules, alteration of cellular membranes and of lysosomal permeability. Immune-mediated injury includes lysis of virally infected hepatocytes, either by direct lymphocyte cytotoxicity or antibody-mediated cytotoxicity.

## Signs and Symptoms

Most common clinical manifestations of hepatitis are listed below. The majority of these characterize both acute or/and chronic hepatitis [Schiff \(1992\)](#). Features marked with asterisk denote chronicity. These are quite helpful guides in the diagnosing these infections.

- anorexia
- malaise
- fatigue
- fever
- general deterioration\*
- weight loss\*
- cirrhotic habitus\*
- pruritus\*
- xanthomas/xanthelasma\*
- malabsorption\*
- jaundice
- hepatomegaly ± pain



- portal hypertension
- ascites\*
- cutaneous and endocrine changes\*
- coagulopathy: hypoprothrombinemia, thrombocytopenia
- circulatory changes: Hyperdynamic circulation, nail clubbing

## Standard Therapies

Vaccines are available to prevent hepatitis A and B. Vaccination is considered the main reason for the decline of HBV infection in high prevalence regions. Studies coming from Taiwan, a country with a 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 has been put in use worldwide. HBV vaccination is highly effective >95% of individuals. Revaccination works in 30-50% of those who fail to respond to the primary vaccination. Revaccination is not recommended after two series. Protective titers are those over 10 mlu/ml. Vaccination is indicated for new-borns of HBV positive mothers, HBV negative children in high endemic areas, family members of HBV positive patients, dialysis patients, and frequently transfused and HBV negative social workers. There are no significant side effects associated with vaccination.

Three different strategies have been used in developing HAV vaccines: a live attenuated virus vaccine, an inactivated virus vaccine, and a recombinant vaccine. All of them are highly effective in promoting the development of protective antibodies. However, the recombinant form appears to be the least expensive and safest. Vaccination is found to be cost-effective when traveling to high HAV incidence countries occurs three or more times in a decade, or if staying there is longer than six months.

Agent Name	Discussion
Interferon-alpha2a, Interferon-alpha2b, Consensus interferon, Pegylated interferon alpha2a, Pegylated interferon a2b	These agents (Interferon-alpha2a, <b>Interferon-alpha2b</b> , Consensus interferon, Pegylated interferon alpha2a, <b>Pegylated interferon a2b</b> ) are employed for the treatment of chronic infections, and for compensated and uncompensated cirrhosis.
<b>Ribavirin</b>	This nucleoside analog is approved for use in combination with interferon and appears to greatly improve the sustained response rates for patients with chronic hepatitis C.
<b>Nucleoside analogues (Lamivudine or 3TC)</b>	Lamivudine is recommended for treatment of chronic HBV infection and HBV cirrhosis. Its mechanism of action entails inhibition of HBV DNA polymerase. The duration of therapy is up to 5 years. There is a high percentage of viral mutants after the first two years of treatment.
<b>Adefovir</b>	A nucleoside analogue of adenosine, adefovir is approved for chronic HBV treatment, especially for those resistant to <b>lamivudine</b> .

## Experimental Therapies

Agent Name	Discussion
Entecavir	Entecavir is a nucleoside analog of guanoside with antiviral activity, has been tested as a therapy for chronic HBV treatment.

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Emtricitabine	These agents are nucleoside analog antivirals that have been tested as treatment for chronic HBV.
Clevudine	These agents are nucleoside analog antivirals that have been tested as treatment for chronic HBV.
L-deoxythymidine	These agents are nucleoside analog antivirals that have been tested as treatment for chronic HBV.

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## Animal Models

**Transgenic mouse model of fulminant Hepatitis** [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. The second involves the RNA Coronavirus MHV-3 which produces a strain-dependent pattern of FHF. 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** [Myungsoo \(2000\)](#) 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** [http://english.hadassah.org.il/people/pphana\\_wald.htm](http://english.hadassah.org.il/people/pphana_wald.htm)[http://english.hadassah.org.il/people/ppmali\\_ketzinel.htm](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 antiviral therapeutic agents.

## Other Information – Web Sites

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

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

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