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Hepatitis C

Hepatitis C is an infectious disease affecting the liver, caused by the hepatitis C virus (HCV).[1] The infection is often asymptomatic, but once established, chronic infection can progress to scarring of the liver (fibrosis), and advanced scarring (cirrhosis) which is generally apparent after many years. In some cases, those with cirrhosis will go on to develop liver failure or other complications of cirrhosis, including liver cancer[1] or life threatening esophageal varices and gastric varices.

The hepatitis C virus (HCV) is spread by blood-to-blood contact. Most people have few, if any symptoms after the initial infection, yet the virus persists in the liver in about 85% of those infected. Persistent infection can be treated with medication, peginterferon and ribavirin being the standard-of-care therapy. 51% are cured overall. Those who develop cirrhosis or liver cancer may require a liver transplant, and the virus universally recurs after transplantation.

An estimated 270-300 million people worldwide are infected with hepatitis C. Hepatitis C is a strictly human disease. It cannot be contracted from or given to any other animal. Chimpanzees can be infected with the virus in the laboratory, but do not develop the disease, which has made research more difficult. No vaccine against hepatitis C is available. The existence of hepatitis C (originally "non-A non-B hepatitis") was postulated in the 1970s and proved conclusively in 1989. It is one of five known hepatitis viruses: A, B, C, D, and E.

Signs and symptoms

Acute

Acute hepatitis C refers to the first 6 months after infection with HCV. Between 60% to 70% of people infected develop no symptoms during the acute phase. In the minority of patients who experience acute phase symptoms, they are generally mild and nonspecific, and rarely lead to a specific diagnosis of hepatitis C. Symptoms of acute hepatitis C infection include decreased appetite, fatigue, abdominal pain, jaundice, itching, and flu-like symptoms. Hep C genotypes 2A & 3A have the highest cure rates at 81% and 74% respectively.

The hepatitis C virus is usually detectable in the blood within one to three weeks after infection by PCR, and antibodies to the virus are generally detectable within 3 to 15 weeks. Spontaneous viral clearance rates are highly variable and between 10–60%[2] of persons infected with HCV clear the virus from their bodies during the acute phase as shown by normalization in liver enzymes (alanine transaminase (ALT) & aspartate transaminase (AST)), and plasma HCV-RNA clearance (this is known as *spontaneous viral clearance*). However, persistent infections are common[3] and most patients develop chronic hepatitis C, i.e., infection lasting more than 6 months.[4][5][6]

Previous practice was to not treat acute infections to see if the person would spontaneously clear; recent studies have shown that treatment during the acute phase of genotype 1 infections has a greater than 90% success rate with half the treatment time required for chronic infections.[7]

Chronic

Chronic hepatitis C is defined as infection with the hepatitis C virus persisting for more than six months. Clinically, it is often asymptomatic (without symptoms) and it is mostly discovered accidentally (eg. usual checkup).

The natural course of chronic hepatitis C varies considerably from one person to another. Although almost all people infected with HCV have evidence of inflammation on liver biopsy, the rate of progression of liver scarring (fibrosis) shows significant variability among individuals. Accurate estimates of the risk over time are difficult to establish because of the limited time that tests for this virus have been available.

Recent data suggest that among untreated patients, roughly one-third progress to liver cirrhosis in less than 20 years. Another third progress to cirrhosis within 30 years. The remainder of patients appear to progress so slowly that they are unlikely to develop cirrhosis within their lifetimes. In contrast the NIH consensus guidelines state that the risk of progression to cirrhosis over a 20-year period is 3-20 percent.[8]

Factors that have been reported to influence the rate of HCV disease progression include age (increasing age associated with more rapid progression), gender (males have more rapid disease progression than females), alcohol consumption (associated with an increased rate of disease progression), HIV coinfection (associated with a markedly increased rate of disease progression), and fatty liver (the presence of fat in liver cells has been associated with an increased rate of disease progression).

Symptoms specifically suggestive of liver disease are typically absent until substantial scarring of the liver has occurred. However, hepatitis C is a systemic disease and patients may experience a wide spectrum of clinical manifestations ranging from an absence of symptoms to a more symptomatic illness prior to the development of advanced liver disease. Generalized signs and symptoms associated with chronic hepatitis C include fatigue, flu-like symptoms, joint pains, itching, sleep disturbances, appetite changes, nausea, and depression.

Once chronic hepatitis C has progressed to cirrhosis, signs and symptoms may appear that are generally caused by either decreased liver function or increased pressure in the liver circulation, a condition known as portal hypertension. Possible signs and symptoms of liver cirrhosis include ascites (accumulation of fluid in the abdomen), bruising and bleeding tendency, varices (enlarged veins, especially in the stomach and esophagus), jaundice, and a syndrome of cognitive impairment known as hepatic encephalopathy. Hepatic encephalopathy is due to the accumulation of ammonia and other substances normally cleared by a healthy liver.

Liver enzyme tests show variable elevation of ALT and AST. Periodically they might show normal results. Usually prothrombin and albumin results are normal, but may become abnormal, once cirrhosis has developed. The level of elevation of liver tests do not correlate well with the amount of liver injury on biopsy. Viral genotype and viral load also do not correlate with the amount of liver injury. Liver biopsy is the best test to determine the amount of scarring and inflammation. Radiographic studies such as ultrasound or CT scan do not always show liver injury until it is fairly advanced. However, non-invasive tests (blood sample) are coming, with FibroTest[9] and ActiTest, respectively estimating liver fibrosis and necrotico-inflammatory. These tests are validated[10] and recommended in Europe (FDA procedures initiated in USA)

Chronic hepatitis C, more than other forms of hepatitis, can be associated with extrahepatic manifestations associated with the presence of HCV such as porphyria cutanea tarda, cryoglobulinemia (a form of small-vessel vasculitis)[11] and glomerulonephritis (inflammation of the kidney), specifically membranoproliferative glomerulonephritis (MPGN).[12] Hepatitis C is also rarely associated with sicca syndrome (an autoimmune disorder), thrombocytopenia, lichen planus, diabetes mellitus and with B-cell lymphoproliferative disorders.[13]

Virology

Main article: Hepatitis C virus

The Hepatitis C virus (HCV) is a small (50 nm in size), enveloped, single-stranded, positive sense RNA virus. It is the only known member of the *hepacivirus* genus in the family *Flaviviridae*. There are six major genotypes of the hepatitis C virus, which are indicated numerically (e.g., genotype 1, genotype 2, etc.).

The hepatitis C virus (HCV) is transmitted by blood-to-blood contact. In developed countries, it is estimated that 90% of persons with chronic HCV infection were infected through transfusion of unscreened blood or blood products or via injecting drug use or sexual exposure. In developing countries, the primary sources of HCV infection are unsterilized injection equipment and infusion of inadequately screened blood and blood products. There has not been a documented transfusion-related case of hepatitis C in the United States for over a decade as the blood supply is vigorously screened with both EIA and PCR technologies.

Although injection drug use is the most common routes of HCV infection, *any* practice, activity, or situation that involves blood-to-blood exposure can potentially be a source of HCV infection. The virus may be sexually transmitted, although this is rare, and usually only occurs when an STD that causes open sores and bleeding is also present and makes blood contact more likely.[14].

Transmission

Sexual activities and practices were initially identified as potential sources of exposure to the hepatitis C virus. More recent studies question this route of transmission. Currently it is felt to be a means of rare transmission of hepatitis C infection. These are simply the current known modes of transmission and due to the nature of hepatitis there may be more ways that it is transmitted than the current known methods.

Injection drug use

Those who currently use or have used drug injection as their delivery route for drugs are at increased risk for getting hepatitis C because they may be sharing needles or other drug paraphernalia (includes cookers, cotton, spoons, water, etc.), which may be contaminated with HCV-infected blood. An estimated 60% to 80% of intravenous recreational drug users in the United States have been infected with HCV.[15] Harm reduction strategies are encouraged in many countries to reduce the spread of hepatitis C, through education, provision of clean needles and syringes, and safer injecting techniques. For reasons that are not clear transmission by this route currently appears to be declining in the USA.

The VA Testimony before the Subcommittee on Benefits Committee on Veterans' Affairs, U.S. House of Representatives, April 13, 2000, Gary A. Roselle, M. D., Program Director for Infectious Diseases, Veterans Health Administration, Department of Veterans Affairs, state, "One in 10 US Veterans are infected with HCV", a rate 5 times greater than the 1.8% infection rate of the general population."

A study conducted in 1999, by the Veterans Health Administration (VHA), and involving 26,000 veterans shows that up to 10% of all veterans in the VHA system tested positive for hepatitis C.

Of the total number of persons who were hepatitis C antibody positive, and reported an era of service, 62.7% were noted to be from the Vietnam. The second most frequent group is listed as post-Vietnam at 18.2%, followed by 4.8% Korean conflict, 4.3% post-Korean conflict, 4.2% from WWII, and 2.7% Persian Gulf era veterans.

Blood products

Blood transfusion, blood products, or organ transplantation prior to implementation of HCV screening (in the U.S., this would refer to procedures prior to 1992) is a decreasing risk factor for hepatitis C.

The virus was first isolated in 1989 and reliable tests to screen for the virus were not available until 1992. Therefore, those who received blood or blood products prior to the implementation of screening the blood supply for HCV may have been exposed to the virus. Blood products include clotting factors (taken by hemophiliacs), immunoglobulin, Rhogam, platelets, and plasma. In 2001, the Centers for Disease Control and Prevention reported that the risk of HCV infection from a unit of transfused blood in the United States is less than one per million transfused units.

Iatrogenic medical or dental exposure

People can be exposed to HCV via inadequately or improperly sterilized medical or dental equipment. Equipment that may harbor contaminated blood if improperly sterilized includes needles or syringes, hemodialysis equipment, oral hygiene instruments, and jet air guns, etc. Scrupulous use of appropriate sterilization techniques and proper disposal of used equipment can reduce the risk of iatrogenic exposure to HCV to virtually zero.

Occupational exposure to blood

Medical and dental personnel, first responders (e.g., firefighters, paramedics, emergency medical technicians, law enforcement officers), and military combat personnel can be exposed to HCV through accidental exposure to blood through accidental needlesticks or blood spatter to the eyes or open wounds. Universal precautions to protect against such accidental exposures significantly reduce the risk of exposure to HCV.

Recreational exposure to blood

Contact sports and other activities, such as "slam dancing" that may result in accidental blood-to-blood exposure are potential sources of exposure to HCV.[16]

Sexual exposure

Sexual transmission of HCV is considered to be rare. Studies show the risk of sexual transmission in heterosexual, monogamous relationships is extremely rare or even null.[17][18] The CDC does not recommend the use of condoms between long-term monogamous discordant couples (where one partner is positive and the other is negative).[19] However, because of the high prevalence of hepatitis C, this small risk may translate into a non-trivial number of cases transmitted by sexual routes. Vaginal penetrative sex is believed to have a lower risk of transmission than sexual practices that involve higher levels of trauma to anogenital mucosa (anal penetrative sex, fisting, use of sex toys).[20]

Body piercings and tattoos

Tattooing dyes, ink pots, stylets and piercing implements can transmit HCV-infected blood from one person to another if proper sterilization techniques are not followed. Tattoos or piercings performed before the mid 1980s, "underground," or non-professionally are of particular concern since sterile techniques in such settings may have been insufficient to prevent disease. Despite these risks, it is rare for tattoos to be directly associated with HCV infection and the U.S. Centers for Disease Control and Prevention's position on this subject states that, "no data exist in the United States indicating that persons with exposures to tattooing alone are at increased risk for HCV infection."[21]

Shared personal care items

Personal care items such as razors, toothbrushes, cuticle scissors, and other manicuring or pedicuring equipment can easily be contaminated with blood. Sharing such items can potentially lead to exposure to HCV. Appropriate caution should be taken regarding any medical condition which results in bleeding such as canker sores, cold sores, and immediately after flossing.

HCV is *not* spread through casual contact such as hugging, kissing, or sharing eating or cooking utensils. [22]

Vertical transmission

Vertical transmission refers to the transmission of a communicable disease from an infected mother to her child during the birth process. Mother-to-child transmission of hepatitis C has been well described, but occurs relatively infrequently. Transmission occurs only among women who are HCV RNA positive at the time of delivery; the risk of transmission in this setting is approximately 6 out of 100. Among women who are both HCV and HIV positive at the time of delivery, the risk of transmitting HCV is increased to approximately 25 out of 100.

The risk of vertical transmission of HCV does *not* appear to be associated with method of delivery or breastfeeding.

Diagnosis

The diagnosis of "hepatitis C" is rarely made during the acute phase of the disease because the majority of people infected experience no symptoms during this phase of the disease. Those who *do* experience acute phase symptoms are rarely ill enough to seek medical attention. The diagnosis of chronic phase hepatitis C is also challenging due to the absence or lack of specificity of symptoms until advanced liver disease develops, which may not occur until decades into the disease.

Chronic hepatitis C may be suspected on the basis of the medical history (particularly if there is any history of IV drug abuse or inhaled substance usage such as cocaine), a history of piercings or tattoos, unexplained symptoms, or abnormal liver enzymes or liver function tests found during routine blood testing. Occasionally, hepatitis C is diagnosed as a result of targeted screening such as blood donation (blood donors are screened for numerous blood-borne diseases including hepatitis C) or contact tracing.

Hepatitis C testing begins with serological blood tests used to detect antibodies to HCV. Anti-HCV antibodies can be detected in 80% of patients within 15 weeks after exposure, in >90% within 5 months after exposure, and in >97% by 6 months after exposure. Overall, HCV antibody tests have a strong positive predictive value for exposure to the hepatitis C virus, but may miss patients who have not yet developed antibodies (seroconversion), or have an insufficient level of antibodies to detect. Rarely, people infected with HCV never develop antibodies to the virus and therefore, never test positive using HCV antibody screening. Because of this possibility, RNA testing (see nucleic acid testing methods below) should be considered when antibody testing is negative but suspicion of hepatitis C is high (e.g. because of elevated transaminases in someone with risk factors for hepatitis C).

Serum alanine aminotransferase levels may not be helpful to diagnose severity of pathologic liver histology among patients with positive hepatitis c antibodies according to a narrative review that pooled multiple cohorts. Among patients with hepatitis C, the negative predictive value of a normal serum alanine aminotransferase for pathologic liver changes is only 24%. [23]

Anti-HCV antibodies indicate exposure to the virus, but *cannot* determine if ongoing infection is present. All persons with positive anti-HCV antibody tests must undergo additional testing for the presence of the hepatitis C virus itself to determine whether current infection is present. The presence of the virus is tested for using molecular nucleic acid testing methods such as polymerase chain reaction (PCR), transcription mediated amplification (TMA), or branched DNA (b-DNA). All HCV nucleic acid molecular tests have the

capacity to detect not only whether the virus is present, but also to measure the amount of virus present in the blood (the HCV viral load). The HCV viral load is an important factor in determining the probability of response to interferon-based therapy, but does *not* indicate disease severity nor the likelihood of disease progression.

In people with confirmed HCV infection, genotype testing is generally recommended. HCV genotype testing is used to determine the required length and potential response to interferon-based therapy.

Prevention

According to Centers for Disease Control, hepatitis C virus is spread by exposure to large quantities of blood, either through the skin or by injection: [24]

Injection drug use (currently the most common means of HCV transmission in the United States)

Receipt of donated blood, blood products, and organs (once a common means of transmission but now rare in the United States since blood screening became available in 1992)

Needlestick injuries in healthcare settings

Birth to an HCV-infected mother

HCV can also be spread infrequently through

Sex with an HCV-infected person (an inefficient means of transmission)

Sharing personal items contaminated with infectious blood, such as razors or toothbrushes (also inefficient vectors of transmission)

Other healthcare procedures that involve invasive procedures, such as injections (usually recognized in the context of outbreaks)

Strategies such as the provision of new needles and syringes, and education about safer drug injection procedures, greatly decrease the risk of hepatitis C spreading between injecting drug users.

No vaccine protects against contracting hepatitis C, or helps to treat it. Vaccines are under development and some have shown encouraging results. [25]

Treatment

The hepatitis C virus (HCV) induces chronic infection in 50%-80% of infected persons. Approximately 50% of these do not respond to therapy. There is a very small chance of clearing the virus spontaneously in chronic HCV carriers (0.5% to 0.74% per year). [26][27]

However, the majority of patients with chronic hepatitis C will not clear it without treatment.

Current treatment is a combination of Pegylated interferon-alpha-2a or Pegylated interferon-alpha-2b (brand names Pegasys or PEG-Intron) and the antiviral drug ribavirin for a period of 24 or 48 weeks, depending on hepatitis C virus genotype.

Pegylated interferon-alpha-2a plus ribavirin may increase sustained virological response among patients with chronic hepatitis c as compared to pegylated interferon-alpha-2b plus ribavirin according to a systematic review of randomized controlled trials . [28] The relative benefit increase was 14.6%. For patients at similar risk to those in this study (41.0% had sustained virological response when not treated with pegylated interferon alpha 2a plus ribavirin), this leads to an absolute benefit increase of 6%. 16.7 patients must be treated for one to benefit (number needed to treat = 16.7. click here to adjust these results for patients at higher or lower risk of

sustained virological response). However, this study's results may be biased due to uncertain temporality of association, selective dose response.

Treatment is generally recommended for patients with proven hepatitis C virus infection and persistently abnormal liver function tests. Sustained cure rates (sustained viral response) of 75% or better are seen in people with HCV genotypes 2 and 3 with 24 weeks of treatment.[29] Sustained responses are rarer with other genotypes, at about 50% in patients with HCV genotype 1 given 48 weeks of treatment and 65% in those with genotype 4 given 48 weeks of treatment. Approximately 80% of hepatitis C patients in the United States have genotype 1. Genotype 4 is more common in the Middle East and Africa.

In patients with HCV genotype 1, if treatment with pegylated interferon + ribavirin does not produce a 2-log viral load reduction or complete clearance of RNA (termed "early virological response") after 12 weeks the chance of treatment success is less than 1%. Early virological response is typically not tested in non-genotype 1 patients, as the chances of attaining it are greater than 90%. The mechanism of cure is not entirely clear, because even patients who appear to have a sustained virological response still have actively replicating virus in their liver and peripheral blood mononuclear cells.[30]

The evidence for treatment in genotype 6 disease is currently sparse, and the evidence that exists is for 48 weeks of treatment at the same doses as are used for genotype 1 disease.[31] Physicians considering shorter durations of treatment (e.g., 24 weeks) should do so within the context of a clinical trial.

Treatment during the acute infection phase has much higher success rates (greater than 90%) with a shorter duration of treatment; however, this must be balanced against the 15-40% chance of spontaneous clearance without treatment (see Acute Hepatitis C section above).

Those with low initial viral loads respond much better to treatment than those with higher viral loads (greater than 400,000 IU/mL). Current combination therapy is usually supervised by physicians in the fields of gastroenterology, hepatology or infectious disease.

The treatment may be physically demanding, particularly for those with a prior history of drug or alcohol abuse. It can qualify for temporary disability in some cases. A substantial proportion of patients will experience a panoply of side effects ranging from a 'flu-like' syndrome (the most common, experienced for a few days after the weekly injection of interferon) to severe adverse events including anemia, cardiovascular events and psychiatric problems such as suicide or suicidal ideation. The latter are exacerbated by the general physiological stress experienced by the patient.

Current guidelines strongly recommend that hepatitis C patients be vaccinated for hepatitis A and B if they have not yet been exposed to these viruses, as infection with a second virus could worsen their liver disease.

Alcoholic beverage consumption accelerates HCV associated fibrosis and cirrhosis, and makes liver cancer more likely; insulin resistance and metabolic syndrome may similarly worsen the hepatic prognosis. There is also evidence that smoking increases the fibrosis (scarring) rate.

Host genetic factors

For genotype 1 hepatitis C treated with Pegylated interferon-alpha-2a or Pegylated interferon-alpha-2b (brand names Pegasys or PEG-Intron) combined with ribavirin, it has been shown that genetic polymorphisms near the human IL28B gene, encoding interferon lambda 3, are associated with significant differences in response to the treatment. This finding, originally reported in Nature [32], showed that genotype 1 hepatitis C patients carrying certain genetic variant alleles near the IL28B gene are more possibly to achieve

sustained virological response after the treatment than others. Later report from Nature [33] demonstrated that the same genetic variants are also associated with the natural clearance of the genotype 1 hepatitis C virus.

Viral factors

The basis for the differential response to treatment between viral genotypes is still being worked out. Mutations in the core arginine70glutamine (R70Q) and in the non structral protein 5A within its interferon sensitivity determining region have been associated with responsiveness at weeks 12 and 4 respectively.[34]

Pregnancy and breastfeeding

If a woman who is pregnant has risk factors for hepatitis C, she should be tested for antibodies against HCV. About 4% infants born to HCV infected women become infected. There is no treatment that can prevent this from happening. There is a high chance of the baby ridding the HCV in the first 12 months.

In a mother who also has HIV, the rate of transmission can be as high as 19%. There are currently no data to determine whether antiviral therapy reduces perinatal transmission. Ribavirin and interferons are contraindicated during pregnancy. However, avoiding fetal scalp monitoring and prolonged labor after rupture of membranes may reduce the risk of transmission to the infant.

HCV antibodies from the mother may persist in infants until 15 months of age. If an early diagnosis is desired, testing for HCV RNA can be performed between the ages of 2 and 6 months, with a repeat test done independent of the first test result. If a later diagnosis is preferred, an anti-HCV test can performed after 15 months of age. Most infants infected with HCV at the time of birth have no symptoms and do well during childhood. There is no evidence that breast-feeding spreads HCV. To be cautious, an infected mother should avoid breastfeeding if her nipples are cracked and bleeding.[35]

Alternative therapies

Several alternative therapies aim to maintain liver functionality, rather than treat the virus itself, thereby slowing the course of the disease to retain quality of life. As an example, extract of *Silybum marianum* and Sho-saiko-to are sold for their HCV related effects; the first is said to provide some generic help to hepatic functions, and the second claims to aid in liver health and provide some antiviral effects.[36]. There has never been any verifiable histologic or virologic benefit demonstrated with any of the alternative therapies.

Epidemiology

It is estimated that Hepatitis C has infected nearly 200 million people worldwide, and infects 3-4 million more people per year.[37][38]

There are about 35,000 to 185,000 new cases a year in the United States. It is currently a leading cause of cirrhosis, a common cause of hepatocellular carcinoma, and as a result of these conditions it is the leading reason for liver transplantation in the United States. Co-infection with HIV is common and rates among HIV positive populations are higher. 10,000-20,000 deaths a year in the United States are from HCV; expectations are that this mortality rate will increase, as those who were infected by transfusion before HCV testing become apparent. A survey conducted in California showed prevalence of up to 34% among prison inmates;[39] 82% of subjects diagnosed with hepatitis C have previously been in jail,[40] and transmission while in prison is well described.[41] Prevalence is higher in some countries in Africa and Asia.[42] Egypt has the highest seroprevalence for HCV, up to 20% in some areas. There is a hypothesis that the high prevalence is linked to a now-discontinued mass-treatment campaign for schistosomiasis, which is endemic in that country.[43] Regardless of how the epidemic started, a high rate of HCV transmission continues in Egypt, both iatrogenically and within the community and household.

Co-infection with HIV

Approximately 350,000, or 35% of patients in the USA infected with HIV are also infected with the hepatitis C virus, mainly because both viruses are blood-borne and present in similar populations. HCV is the leading cause of chronic liver disease in the USA. It has been demonstrated in clinical studies that HIV infection causes a more rapid progression of chronic hepatitis C to cirrhosis and liver failure. This is not to say treatment is not an option for those living with co-infection.

History

In the mid 1970s, Harvey J. Alter, Chief of the Infectious Disease Section in the Department of Transfusion Medicine at the National Institutes of Health, and his research team demonstrated that most post-transfusion hepatitis cases were not due to hepatitis A or B viruses. Despite this discovery, international research efforts to identify the virus, initially called *non-A, non-B hepatitis* (NANBH), failed for the next decade. In 1987, Michael Houghton, Qui-Lim Choo, and George Kuo at Chiron Corporation, collaborating with Dr. D.W. Bradley from CDC, utilized a novel molecular cloning approach to identify the unknown organism. [44] In 1988, the virus was confirmed by Alter by verifying its presence in a panel of NANBH specimens. In April of 1989, the discovery of the virus, re-named hepatitis C virus (HCV), was published in two articles in the journal *Science*. [45][46]

Chiron filed for several patents on the virus and its diagnosis. [47] A competing patent application by the CDC was dropped in 1990 after Chiron paid $1.9 million to the CDC and $337,500 to Bradley. In 1994 Bradley sued Chiron, seeking to invalidate the patent, have himself included as a co-inventor, and receive damages and royalty income. He dropped the suit in 1998 after losing before an appeals court. [48][49]

In 2000, Drs. Alter and Houghton were honored with the Lasker Award for Clinical Medical Research for "pioneering work leading to the discovery of the virus that causes hepatitis C and the development of screening methods that reduced the risk of blood transfusion-associated hepatitis in the U.S. from 30% in 1970 to virtually zero in 2000." [50]

In 2004 Chiron held 100 patents in 20 countries related to hepatitis C and had successfully sued many companies for infringement. Scientists and competitors have complained that the company hinders the fight against hepatitis C by demanding too much money for its technology. [48]

Research

The drug viramidine, which is a prodrug of ribavirin that has better targeting for the liver, and therefore may be more effective against hepatitis C for a given tolerated dose, is in phase III experimental trials against hepatitis C. It will be used in conjunction with interferons, in the same manner as ribavirin. However, this drug is not expected to be active against ribavirin-resistant strains, and the use of the drug against infections which have already failed ribavirin/interferon treatment, is unproven.

There are new drugs under development like the protease inhibitors (including *VX 950*), entry inhibitors (such as *SP 30* and *ITX 5061*) [51][52][53] and polymerase inhibitors (such as *NM 283*), but development of some of these is still in the early phase. VX 950, also known as Telaprevir [54] is currently in Phase 3 Trials. [55][56] One protease inhibitor, *BILN 2061*, had to be discontinued due to safety problems early in the clinical testing. Some more modern new drugs that provide some support in treating HCV are *Albuferon*, [57] *Zadaxin*, [58]. Antisense phosphorothioate oligos have been targeted to hepatitis C. [59] Antisense Morpholino oligos have shown promise in preclinical studies [60] however, they were found to cause a limited viral load reduction.

Immunoglobulins against the hepatitis C virus exist and newer types are under development. Thus far, their roles have been unclear as they have not been shown to help in clearing chronic infection or in the prevention of infection with acute exposures (e.g. needlesticks). They do have a limited role in transplant patients.

In addition to the standard treatment with interferon and ribavirin, some studies have shown higher success rates when the antiviral drug amantadine (Symmetrel) is added to the regimen. Sometimes called "triple therapy", it involves the addition of 100 mg of amantadine twice a day. Studies indicate that this may be especially helpful for "nonresponders" - patients who have not been successful in previous treatments using interferon and ribavirin only.[61] Currently, amantadine is not approved for treatment of Hepatitis C, and studies are ongoing to determine when it is most likely to benefit the patient and when it is a risk due to their liver deterioration.

Among the more novel treatments under development is the Hemopurifier(R),[62] a first-in-class medical device that selectively removes infectious viruses and immunosuppressive proteins from the bloodstream. In HCV care, the Hemopurifier(R) inhibits viral replication through selective adsorption of circulating HCV and augments the immune response by removing toxic proteins shed from HCV to kill-off immune cells. Recent clinical data validates the mechanical removal of HCV through blood filtration in combination with SOC therapy can increase HCV cure rates by greater than 50%. Studies are ongoing at the Fortis Hospital in New Delhi, India.

See also

- List of people with hepatitis C
- World Hepatitis Day

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External links

Information and resources

CDC's Hepatitis C Fact Sheet

Hepatitis C at the Open Directory Project

"What I need to know about Hepatitis C". National Digestive Diseases Information Clearinghouse. May 2004. http://digestive.niddk.nih.gov/ddiseases/pubs/hepc_ez/.

Hepatitis C – Full Movie”

Organizations and programs

National Hepatitis C Program U.S. Department of Veterans Affairs

Hepatitis C American Liver Foundation

Hepatitis Australia Hepatitis Australia

Hepatitis C homepage of the UK National Health Service

National Canadian Research Training Program in Hepatitis C Training program funded by the Canadian Institutes of Health Research.