a guide to understanding Hepatitis C

HCV

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Introduction

HCV *is a blood-borne virus that was previously referred to as non-A/non-B hepatitis. HCV has six major genotypes (subtypes): 1a, 1b, 2a, 2b, 3, 4, 5, and 6. Genotypes 1a and 1b, which are the most common in the U.S., are more difficult to treat. HCV enters the body through direct blood exposure. The virus attacks cells in the liver, where it multiplies (replicates). HCV causes liver inflammation and kills liver cells. Up to 80% of people initially infected with HCV may become chronically infected—that is, the infection does not clear up within six months. Most people with chronic HCV do not have symptoms and lead normal lives. However, in 10–25% of people with chronic HCV, the disease progresses over a period of 10–40 years, and may lead to serious liver damage, cirrhosis (scarring), and liver cancer. Today, HCV is the leading reason for liver transplants in the U.S. There is currently no vaccine or cure for HCV, but various treatments can eradicate the virus and/or help slow or stop disease progression for some people.*

Your Liver and Hepatitis

The liver is the largest internal organ, located behind the ribcage on the right side of the abdomen. It weighs approximately three pounds and is about the size of a football. The liver is responsible for some 500 vital functions. It processes virtually everything you eat, breathe, or absorb through the skin. The liver converts substances you eat and drink into energy and the building blocks for muscles, hormones, clotting factors, and immune factors. It stores many vitamins, minerals, and sugars for later use. Liver cells produce bile, which helps the body digest food and absorb nutrients. The liver detoxifies substances that are harmful to the body. It can regenerate its own tissue—as much as 3/4 of the liver can regenerate within a few weeks.

Hepatitis simply means inflammation of the liver. It may be caused by viruses, toxic chemicals, drugs, or other factors. The most common forms of viral hepatitis include hepatitis A virus (HAV), hepatitis B virus (HBV), and HCV. These three viruses are related only in that they affect the liver.

HCV Transmission and Prevention

HCV Transmission

HCV is transmitted by direct blood-to-blood contact. Transmission routes include sharing drug paraphernalia for both injection and noninjection drugs (needles, cookers, tourniquets, straws, pipes, etc.). Needles used for tattooing, body piercing, and acupuncture may also spread HCV. Sharing personal items such as razors, toothbrushes, or nail files is a less likely, but still possible, transmission route.

DO NOT SHARE NEEDLES OR ANY OTHER DRUG PARAPHERNALIA, RAZORS, TOOTHBRUSHES, CLIPPERS, NAIL FILES, OR ANY ITEMS THAT MIGHT CONTAIN BLOOD.

Before 1992, many people contracted HCV through blood or blood product transfusions. In 1992, a reliable blood test to identify HCV antibodies became available. Since then, the blood supply has been screened. Today the likelihood of contracting HCV through infected blood is less than 0.01%. A small percentage of people (estimated at 1–3% for monogamous heterosexuals) may contract HCV through unprotected sexual activity. Among people in so-called "high risk" groups (gay men, prostitutes, people with multiple sex partners, people with STDs), sexual transmission appears to be more common.

Healthcare workers are at risk for HCV infection because needlestick accidents and unavoidable situations may result in direct contact with blood from an infected individual.

Perinatal transmission from mothers with HCV to their infants before or during birth occurs less than 5% of the time. Whether or not transmission occurs may depend on the presence of high levels of HCV in the mother's blood; mothers coinfected with HBV or HIV are more likely to transmit HCV to their babies. Some studies have shown that HCV is present in breast milk, but transmission through breastfeeding is believed to be extremely rare.

The transmission route for up to 10% of individuals infected with HCV cannot be identified. HCV is not transmitted by casual contact such as sneezing, coughing, hugging, or sharing eating utensils and drinking glasses.

HCV Prevention

Do not share needles or any other drug paraphernalia, razors, toothbrushes, clippers, nail files, or any items that may come in contact with blood. Make sure that instruments used for tattooing, body piercing, and acupuncture are properly sterilized; most practitioners today use disposable needles. All cuts and wounds should be covered.

Although sexual transmission appears to be rare, you can reduce the risk by practicing safer sex, including the use of condoms and barriers. According to the Centers for Disease Control and Prevention (CDC), if you are in a monogamous relationship you do not need to change your current sexual practices, although partners should discuss safer sex options if either partner is concerned about transmission. If a woman has HCV, avoid sex during monthly periods. Proper dental hygiene can prevent bleeding gums, another possible transmission route.

Notify your doctor, dentist, and other healthcare professionals if you have HCV. Healthcare workers should observe standard universal precautions when dealing with blood. If you are a woman with HCV, talk to your doctor if you are thinking about becoming pregnant.

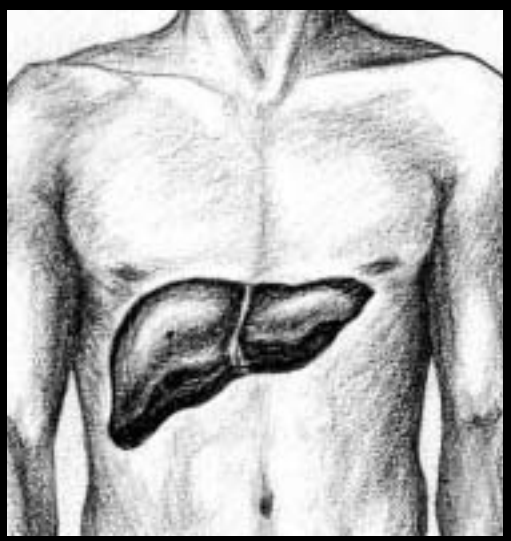
HCV Disease Progression

After exposure to HCV, the incubation period usually lasts 2–26 weeks. The initial phase of hepatitis C is called acute infection. Acute HCV usually resolves after 2–12 weeks. However, up to 80% of people initially infected with HCV do not clear the virus from their bodies, and become chronically infected. Most people with chronic HCV do not have symptoms and lead relatively normal lives. But in 10–25% of people, the disease progresses over the course of 10–40 years. Chronic HCV infection can lead to liver damage, the development of fibrous tissue in the liver (fibrosis), fat deposits in the liver (steatosis), liver scarring (cirrhosis), and liver cancer. In severe cases, a person may require a liver transplant.

Cirrhosis is a process in which liver cells are damaged or killed and replaced with scar tissue. Extensive scar tissue formation impairs the flow of blood through the liver, causing more liver cell death and a loss of liver function.

Liver cancer usually develops at later stages of HCV infection, typically after 25–30 years. The type of liver cancer associated with HCV is called primary hepatocellular carcinoma (HCC).

THE LIVER
The liver converts substances you eat and drink into energy and the building blocks for muscles, hormones, clotting factors, and immune factors.



LEANA ROSETTI

COMPENSATED CIRRHOSIS

means that the liver is heavily scarred but can still perform most functions; people with compensated cirrhosis exhibit few or no symptoms.

DECOMPENSATED CIRRHOSIS

means that the liver is extensively scarred and unable to function. People with decompensated cirrhosis often develop complications such as varices (stretched and weakened blood vessels) in the esophagus (swallowing tube) and stomach, internal bleeding, ascites (fluid accumulation), and other potentially life-threatening conditions. They may also experience reversible mental confusion.

Symptoms of HCV

Many people report few or no symptoms during the acute phase of HCV infection. Most people with chronic HCV also do not have symptoms and lead relatively normal lives. However, others experience mild flu-like symptoms including nausea, fatigue, fever, headaches, loss of appetite, abdominal pain, and muscle or joint pain. Some individuals report more severe flu-like symptoms, as well as jaundice (yellowing of the skin and whites of the eyes) and dark urine. Over time (often years or even decades) people with chronic HCV may develop various symptoms related to liver damage. Chronic HCV is also associated with a wide variety of possibly related conditions.

Symptoms Reported by People with HCV

Acute Hepatitis C

- Flu-like illness
- Fatigue (mild to severe)
- Fever
- Night sweats
- Loss of appetite (anorexia)
- Nausea
- Vomiting
- Diarrhea
- Jaundice
- Indigestion
- Headaches
- Muscle or joint pain
- Abdominal pain
- Abdominal bloating

Chronic Hepatitis C

- Fatigue (mild to severe)
- Fever
- Loss of appetite (anorexia)
- Nausea
- Indigestion
- Headaches
- Muscle or joint pain
- Abdominal pain
- Depression
- Mood swings
- "Brain fog"

Late-Stage Hepatitis C with Cirrhosis

- Fatigue (mild to severe)
- Fever
- Loss of appetite (anorexia)
- Nausea
- Vomiting
- Frequent urination
- Jaundice
- Indigestion
- Headaches
- Muscle or joint pain
- Abdominal pain
- Abdominal bloating
- Depression
- Mood swings
- Cognitive dysfunction
- Lack of concentration
- Mental confusion
- Dizziness
- Peripheral vision problems
- Fluid retention

HCV FACTS

- *The National Institutes of Health (NIH) estimates that some four million Americans are infected with HCV.*
- *An estimated 8,000–10,000 Americans die annually of complications related to HCV. This figure is expected to triple in the next 10–20 years.*
- *HCV is the leading reason for liver transplants in the U.S.*
- *Individuals with HCV should avoid drinking alcohol and using recreational drugs.*
- *Individuals with HCV should be vaccinated against hepatitis A and hepatitis B.*

Conditions Linked to HCV

A number of different conditions have been associated with HCV. Some of these are autoimmune conditions, in which the immune system attacks the body's own tissues. Conditions sometimes seen in people with chronic HCV include Sjögren's syndrome (characterized by dry eyes and dry mouth), kidney conditions such as glomerulonephritis, heart and circulatory problems such as thrombosis (blood clots), and skin conditions such as lichen planus (characterized by white lesions or bumps) and porphyria cutanea tarda (characterized by a sun-sensitive rash). Other related conditions include certain types of arthritis (joint inflammation), arthralgia (joint pain), thyroid disease, vasculitis (blood vessel damage), and cryoglobulinemia (high levels of a blood protein that settles in the kidneys, skin, and nerve endings). Most serious conditions are associated with late-stage HCV disease, when the liver is damaged and not able to function properly. Many people with HCV never experience any of these conditions. Check with your doctor if you experience any unusual symptoms.

Diagnosing HCV

Testing for HCV is not routinely done, so you may have to request a test from your physician. It is recommended that you use the same laboratory for all of your tests, since result ranges and accuracy can vary from lab to lab. Keep copies of your lab and biopsy results for future reference. The tests below can help determine whether you are infected with HCV and the state of disease progression.

HCV Antibody Tests

HCV ELISA

is a simple blood test that can detect HCV antibodies.

RIBA HCV

is a second antibody test that may be performed after an ELISA test to confirm the presence of HCV antibodies.

Viral Load Tests

Viral load tests measure the amount of HCV circulating in the blood. HCV viral load is expressed as either copies per milliliter of blood or as a standard unit of measurement called International Units. There are three different types of viral load test: HCV RNA PCR, branched-chain DNA (bDNA), and transcription mediated amplification, or TMA. The bDNA assay is the least expensive, but also the least sensitive. Viral load tests are used to confirm active HCV infection, to predict medical treatment response, and to measure how well the medications are working against the virus during treatment. An association between viral load and disease progression has not been established.

Genotype Tests

Genotype tests are used to determine what type(s) of HCV you have. This information is useful for making treatment decisions, such as which medications to use and how long treatment should last.

Liver Biochemical/Function Tests

There are various blood tests used to assess how well your liver is working. The liver (hepatic) panel includes measurements that indicate liver function. The most common measurements are alanine aminotransferase (ALT, formerly known as SGPT)

Viral load tests are used to confirm active infection, as a predictor of medical treatment response, and during medical treatment to measure how well the medications are working against the virus. An association between viral load and disease progression has not been established.

and aspartate aminotransferase (AST, formerly known as SGOT). ALT and AST are enzymes that are released into the blood when the liver is damaged. They are often elevated in people with HCV infection. Many people with HCV have mild to moderate elevations of these two enzymes, which are often the first indication that they are infected. Other measurements include alkaline phosphatase (ALK) and gamma-glutamyl transpeptidase (GGT). Abnormal levels may indicate cirrhosis or bile duct blockage, as well as other abnormalities. In addition, your doctor may measure prothrombin time (an indication of blood clotting speed) and bilirubin levels. Bilirubin is a pigment that is often present in the blood of people with liver inflammation; high bilirubin levels result in jaundice. Many factors such as use of medications and alcohol may cause abnormal lab results. Before drawing your own conclusions, check with a healthcare provider.

Liver Biopsies

Biopsies are done to measure the severity of inflammation, the amount of scarring, and the general health of the liver. They may also be used to help determine appropriate treatment. The most common procedure is to numb the skin and muscle and then quickly insert a long, thin needle into the liver to draw out a specimen. Many people fear this procedure, but complications are rare. If you are anxious, ask your physician for a mild tranquilizer prior to your biopsy and for pain medication afterwards.

HCV Treatment Options

Until 1998, interferon alone (monotherapy) was the only approved treatment for HCV infection. Today, the standard of care for treating HCV is the combination of pegylated interferon plus ribavirin. Research is ongoing to develop new and better medications, including helicase inhibitors, protease inhibitors, and antifibrotic medications.

There are also several alternative and complementary treatments that people have used to treat HCV infection, for example, milk thistle (silymarin) and licorice root (glycyrrhizin). Herbal and other alternative therapies are discussed in a fact sheet from the Hepatitis C Support Project.

Approved Pharmaceutical Treatments

Standard interferon, pegylated interferon, and ***ribavirin*** are the only FDA-approved medications to treat hepatitis C. Interferon, given by injection, is a genetically engineered product based on a set of natural immune system proteins found in the body. Pegylated interferon (PEG) is a long-acting form of interferon that can be injected once a week. PEG maintains a more constant level of interferon in the blood and better reduces the ability of HCV to replicate. Ribavirin is an oral antiviral medication used in combination with interferon to treat HCV infection. Ribavirin alone is not effective against HCV.

Ribavirin Warning

Ribavirin has been shown to cause birth defects and miscarriages. Women of childbearing age, their partners, and female partners of male patients taking ribavirin must use at least two effective forms of contraception during treatment and during the six-month post-treatment follow-up period.

Standard Interferon Monotherapy

Currently marketed brands include Intron A (Schering-Plough), Roferon A (Roche), Infergen (InterMune, Inc.), and Alferon N (ISI Pharmaceuticals). The standard protocol for interferon administration is injection three times per week for at least one year. It is estimated that only 10–20% of individuals treated with standard interferon alone are able to permanently clear HCV to undetectable levels.

Interferon plus Ribavirin

Rebetron (Schering-Plough) is a combination of Intron A brand standard interferon plus ribavirin. Studies have shown that the combination works better than interferon alone. The protocol for Rebetron administration is three million units of interferon injected three times per week plus ribavirin taken daily. Studies

suggest that the length of treatment depends upon genotype: 48 weeks for genotype 1, and 24 weeks for genotypes 2 or 3. In clinical trials, the average **sustained virological response (SVR) rates** are approximately 28% for genotype 1 and 66% for genotypes 2 and 3.

Virological Response

how a person's viral load level responds to treatment. When a person's HCV RNA (viral load) becomes undetectable after HCV therapy has been initiated, this is considered a virological response. If the HCV RNA remains undetectable beyond six months, the term sustained virological response (SVR) is used.

Pegylated Interferon Monotherapy

Peg-Intron

Peg-Intron (peginterferon alpha 2b) is Schering's brand of pegylated interferon. It comes in a powdered form that requires mixing with a liquid (reconstituting) before injection. It is dosed by body weight. The SVR for Peg-Intron monotherapy is 14% for genotype 1 and 47% for genotypes 2 and 3.

Pegasys

Pegasys (peginterferon alpha 2a) is Roche's brand of pegylated interferon. The standard dose is 180 µg for all patients. It comes in a ready-made solution that does not require reconstitution. The SVR for Pegasys monotherapy is 28% for genotype 1 and 56% for genotypes 2 and 3. Pegasys is also indicated for treatment of people with compensated cirrhosis.

Pegylated Interferon plus Ribavirin

The combination of pegylated interferon plus ribavirin is now considered the standard of care for treating HCV. There are currently two different pegylated interferon/ribavirin combinations that have been approved by the FDA: Schering's Peg-Intron plus Rebetol brand ribavirin, and Roche's Pegasys plus Copegus brand ribavirin.

Schering's Peg-Intron plus Rebetol

SVR for Peg-Intron plus Rebetol combination therapy is 42% for genotype 1 (30% for high viral load) and 82% for genotypes 2 and 3. Treatment duration for all genotypes is 12 months.

Roche's Pegasys plus Copegus

SVR for Pegasys plus Copegus combination therapy is 46–51% for genotype 1 (41–46% for high viral load) and 76–78% for genotypes 2 and 3. Treatment duration is 12 months for genotype 1, and 6 months for genotypes 2 and 3.

Measuring Treatment Response

People receiving HCV treatment should be tested on a regular basis to monitor side effects and to make sure that they are responding to therapy. If someone has not responded after three months of treatment, further therapy is unlikely to clear the virus. Many physicians recommend stopping the medications at this time. However, some evidence suggests that interferon can decrease scarring and inflammation and improve liver health even if it does not clear the virus.

Investigational Pharmaceutical Therapies

HCV therapy has seen impressive advances, given that the virus was identified only just over a decade ago. However, current treatment options can have many undesired side effects and treatment success may not always be achieved. There is much research underway to develop new and better HCV treatment options without the serious side effects of current HCV medications. It appears that combination therapy with two or more agents is more effective than monotherapy for treating HCV.

Researchers are studying new forms of ribavirin that may be more effective and less toxic. ***Levovirin*** and ***viramidine*** are two ribavirin-like drugs in development. In animal studies, they appear to have fewer side effects and have less detrimental effects on red blood cells.

Amantadine (Symmetrel), an antiviral medication used to treat influenza, has been studied in combination with interferon and ribavirin. Unfortunately, studies conducted to date have been disappointing, with little benefit seen when adding amantadine.

More promising medications in clinical trials include ***Ceplene*** and a synthetic version of thymosin alpha 1 (**Zadaxin**), a hormone that stimulates T-cells and natural killer (NK) cells.

HCV helicase inhibitors, HCV protease inhibitors, and ***HCV polymerase inhibitors,*** which could potentially block HCV viral replication, are currently under study and look promising.

HCV Vaccines

There is currently no vaccine for HCV, as there is for HAV and HBV. HCV vaccines will be difficult to develop due to the virus' different genotypes and its ability to change, or mutate, during infection. Some progress is being made, but an effective HCV vaccine is not expected for 5–10 years.

Clinical Trials

The process of testing a new drug involves establishing its safety and tolerability (Phase I trials), measuring its effectiveness (Phase II trials), and comparing the new drug to current standard treatments (Phase III trials). After the FDA has granted approval and the new drug is marketed, ongoing studies are done to refine the treatment for maximum safety and effectiveness (Phase IV, or postmarketing trials).

CLINICAL TRIALS CAN BE AN EXCELLENT WAY TO OBTAIN FREE MEDICATION. SOME TRIALS MAY ALSO PICK UP SOME OR ALL OF THE COSTS OF PHYSICIAN VISITS AND LAB TESTS.

Clinical trials can be an excellent way to obtain free medication; some trials may also pick up some or all of the costs of physician visits and lab tests. However, if you enroll in a clinical trial you may not be chosen to receive the new drug or the most effective dosage. You should read all clinical trial information and make sure that you fully understand the terms and conditions of the study, such as the withholding of viral load information from the participant.

Predicting Response to Treatment

Adherence to HCV therapy is an important factor in achieving the highest possible treatment response rates. Currently, it is believed that people on HCV therapy who take at least 80% of their prescribed doses of both interferon and ribavirin for at least 80% of the expected duration of therapy are more likely to have a successful treatment outcome. Treatment with interferon or interferon plus ribavirin is more likely to clear HCV if a person has a genotype other than 1, a low HCV viral load, infection with HCV for a shorter time, mild to moderate disease, is female, and is of a younger age.

After 12 weeks of antiviral treatment, a 2-log drop in viral load or elimination of HCV predicts a successful response at the end of treatment. These guidelines may be used to help tailor treatment or to stop treatment that is not working. However, some doctors believe that therapy should be continued, because some people still respond to therapy or experience improved liver health even if their viral load does not become undetectable or decrease by the suggested amount.

Managing Drug Side Effects

The most prevalent side effects of interferon and ribavirin include flu-like symptoms, muscle and joint pain, nausea, headaches, fatigue, loss of appetite, dry skin, anxiety, depression, and insomnia. Some physical symptoms may be reduced with ibuprofen or acetaminophen in low doses (2 grams per day or less). High doses of acetaminophen can be toxic to the liver. People experiencing anxiety, irritability, or depression may be helped with mild tranquilizers or anti-depressants. Check with your doctor before taking any of these medications.

Drinking as much water as possible may help reduce the severity of side effects. Eating small, frequent meals instead of large, infrequent ones may lessen gastrointestinal problems. Regular exercise may also help alleviate some side effects, such as fatigue, associated with interferon therapy. Daily moisturizing will help prevent dry skin. Vary where you inject to prevent skin inflammation or a rash at injection sites. For some people, physical side effects are worse when the drug is started and may diminish over time.

Regular exercise may help alleviate some side effects, such as fatigue, associated with interferon therapy.

The most common reason for stopping HCV therapy is anemia (low red blood cell count), thrombocytopenia (low platelet count), and neutropenia (low white blood cell count). Medications used to control these conditions include erythropoietin (for anemia), GM-CSF (granulocyte macrophage colony-stimulating factor, for low white blood cells), and IL-2 (interleukin 2, for low platelets). A low platelet count may indicate cirrhosis, and care should be taken during treatment.

Some people may develop thyroid dysfunction while on treatment with interferon. Thyroid function should be closely monitored prior to starting treatment and then every three months during therapy. In many people, thyroid function returns to normal once therapy is discontinued, but some people may develop irreversible thyroid problems that will require continuous medication.

HCV can be a difficult disease to manage. Lifestyle plays an integral part in HCV disease management and treatment. Proper diet, exercise, and stress management are all critical to maintaining good health. Many physicians are not fully educated about HCV, and you may have to educate both conventional and alternative practitioners. If you have a family doctor, you may want to quiz him or her about HCV. It is important to find a doctor who is both knowledgeable about and sympathetic to people with HCV. If you are not comfortable with your doctor, look for a new one; ask family or friends for recommendations. Once your HCV diagnosis has been confirmed, your family doctor or general practitioner should send you to a specialist. Generally, you will be referred to a gastroenterologist (a digestive disease specialist) or a hepatologist (a liver disease specialist).

Nutrition

Since the liver processes and detoxifies everything you eat and drink, a healthy, well-balanced diet is essential. A diet that follows the general guidelines for nutritional health based on the Food Guide Pyramid is generally recommended. Such a diet is low in fat and sodium, high in complex carbohydrates, and has adequate protein.

In the past, diet modification was seen as an important part of HCV management. This is less true today. However, avoiding certain foods may reduce the processing and detoxification work the liver must do, and may improve the overall health of your liver. Processed foods often contain chemical additives, so reduce your consumption of canned, frozen, and other preserved foods. Eating organic fruits and vegetables can help you avoid the pesticides and fertilizers used to grow nonorganic produce. *Read all labels* to acquaint yourself with ingredients.

Protein derived from poultry, fish, and vegetable sources may be most beneficial. Some doctors recommend that people with any type of liver disease should not eat raw or undercooked shellfish (even if they are immune to hepatitis A). It is often recommended that people with HCV should avoid foods high in fat, salt, or sugar. Caffeine is a chemical that must be processed by the liver, and it is recommended that you limit your caffeine intake by reducing your consumption of coffee,

tea, and soda. Because chocolate has a high fat (and in some types, caffeine) content, eat it in moderation. Some people with HCV cannot tolerate dairy products. If this is the case for you, you may wish to use nondairy substitutes such as soy milk or rice milk.

A well-balanced diet should contain all the essential vitamins and minerals you need, but some people also take vitamin supplements. Taking megavitamin supplements may be harmful. Avoid taking high doses of vitamins A and D; vitamin A can be very toxic to the liver. If you need extra vitamins and/or minerals, choose a low-dose supplement without iron.

People with HCV should consult a licensed nutritionist or dietitian for specific dietary recommendations. Do not undertake any unconventional diet without consulting a medical practitioner. In addition, be sure to inform your doctor about any vitamins and minerals you are taking.

HAV AND HBV VACCINATION

It is strongly recommended that people with HCV get vaccinated against hepatitis A and B if they are not already immune. Severe HAV and HBV infections have been reported in people coinfected with HCV. The hepatitis A vaccine consists of two doses within a six-month period, and the hepatitis B vaccine requires three doses within a six-month period. Both vaccines are made from killed viruses and are considered safe and effective. A combination HAV/HBV vaccine was approved by the FDA in May 2001.

Alcohol and Drugs

Many studies have shown that heavy consumption of alcohol can severely accelerate HCV disease progression. In fact, one recent study showed that 58% of a group of heavy drinkers (more than five drinks per day) with HCV progressed to cirrhosis, compared with only 10% of a nondrinking group with HCV. It is not yet known if light or moderate alcohol consumption is harmful to the liver, but most experts recommend that people with HCV should avoid alcohol. Many drugs (whether prescription, over-the-counter, or recreational) must be processed by the liver. People with HCV should avoid recreational drugs and tobacco. Check with your doctor before taking over-the-counter or prescription medications. Certain herbal remedies have also been shown to damage the liver.

General Wellness

➥ *Stress management*

Controlling stress is a major factor in managing HCV disease. Living with a chronic disease is stressful. Many people report "flare-ups" (periods of increased symptoms) following episodes of stress. Exercise, meditation, and time management can all help reduce stress. Try to maintain a realistic picture of your health and a positive attitude. Understanding the severity of your liver disease is an important part of having a realistic picture of your condition.

➥ ***Managing fatigue***

Fatigue and low energy levels are common in people with HCV. Learn your limits and do not overextend yourself. When you plan activities, allow time in between for relaxation or naps. Remember that your health is important—learn to say "no" to friends and family who have unrealistic expectations of your energy level.

➥ ***Time management***

Plan activities well in advance and try to make realistic work and play schedules. Use a daily planner to help with organizing and remembering activities. Consult your planner regularly when making appointments and scheduling daily tasks. Don't forget to include restful activities.

➥ ***Meditation***

Meditation can be a useful tool in managing and living with HCV or any chronic illness. It is simple and easy to learn. Meditation can reduce stress and help you maintain a healthy outlook on life.

➥ ***Exercise***

Moderate exercise is highly recommended for all individuals who are not in an acute phase of HCV. Exercise can help reduce stress and is important for maintaining good health. However, too much exercise can lead to flare-ups. Select low impact types of exercise such as walking and swimming. Slowly increase your workouts until the desired level is achieved. Always check with your doctor before starting any exercise program.

Support Groups

Many people with HCV feel isolated and find it difficult to cope with the effects of living with a chronic illness. A support group can offer a safe space to discuss the emotional issues surrounding HCV. Furthermore, the information shared by peer members can be helpful in making decisions about a wide variety of issues facing people with HCV. It is highly recommended that you join a support group while undergoing HCV treatment. Support group information can be obtained by contacting the organizations listed at the end of this booklet.

The Internet

The Internet contains a wealth of information, both good and bad. Always check the sources of the information you find. Look for dates and references. Challenge any information you believe is in error. Be skeptical of Web sites that contain the word "cure" or other misleading information. Remember that not all the information you find on the Internet is correct. Talk to your doctor about any information you are concerned about. Common sense can take you a long way! Visit our Web site at www.hcvadvocate.org for recommended sites.

ENVIRONMENTAL TOXINS

Everything you breathe or absorb through the skin must be filtered by the liver. Fumes from paint thinners, pesticides, and aerosol sprays can damage your liver and should be avoided.

Coinfection ***refers to infection with two or more different disease-causing organisms. HCV, HBV, and HIV are transmitted in similar ways, and some people are infected with two or even all three viruses.***

HIV/HCV Coinfection

HIV/HCV coinfection is a growing public health concern. Up to one-third of Americans with HIV may also have HCV (although coinfection rates among some populations, such as injection drug users, are much higher), and about 10% of people with HCV also have HIV. The U.S. Public Health Service recommends that all people with HIV should be screened for HCV.

Most studies show that HIV infection leads to more aggressive hepatitis C and a higher risk of liver damage. It is less clear how HCV affects HIV disease. HCV does not appear to accelerate HIV disease progression, but may impair immune system recovery after starting anti-HIV therapy. Most people coinfected with HCV and HIV can be successfully treated for both diseases. The most recent NIH Hepatitis C Consensus Statement recommends that all people with both HCV and HIV should be considered for HCV treatment.

HIV Basics

HIV (human immunodeficiency virus) is a retrovirus associated with AIDS (acquired immunodeficiency syndrome). It primarily infects immune system white blood cells called CD4 T-cells. As CD4 cells die, immune function is impaired and the body is less able to fight infections and cancers. HIV is a blood-borne virus transmitted through infected blood, semen, and vaginal secretions. HIV is much more likely than HCV to be transmitted sexually or from mother to child during pregnancy, birth, or breastfeeding; in addition, having HIV increases the risk of sexual or perinatal transmission of HCV.

Two antibody tests—ELISA and Western blot—are used to detect HIV antibodies. Viral load tests—PCR and bDNA—measure HIV RNA (genetic material) in the blood. The CD4 cell count is measured to assess the health of the immune system. If the CD4 cell count falls below 200 cells/mm^3, a person is considered to have AIDS and is more likely to develop opportunistic illnesses.

Approved Anti-HIV Drugs

Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs):

- AZT (Retrovir)
- 3TC (Epivir)
- ddI (Videx)
- ddC (Hivid)
- d4T (Zerit)
- abacavir (Ziagen)
- tenofovir DF (Viread)
- emtricitabine (Emtriva)

Non-nucleoside reverse transcriptase inhibitors (NNRTIs):

- delavirdine (Rescriptor)
- efavirenz (Sustiva)
- nevirapine (Viramune)

Protease inhibitors (PIs):

- amprenavir (Agenerase)
- indinavir (Crixivan)
- lopinavir/ritonavir (Kaletra)
- nelfinavir (Viracept)
- ritonavir (Norvir)
- saquinavir (Fortovase or Invirase)
- atazanavir (Reyataz)

Entry inhibitors:

- enfuvirtide (Fuzeon, T-20)

When to start anti-HIV treatment is controversial. The latest U.S. guidelines suggest starting treatment when the CD4 cell count falls below 350 cells/mm^3 and viral load is above 55,000 copies/mL. Standard therapy for HIV is a combination regimen of at least three antiretroviral drugs (see sidebar on page 16); using multiple medications helps prevent drug resistance. Anti-HIV medications are associated with many side effects including diarrhea, low blood cell counts, lipodystrophy (body fat abnormalities), and high blood fat levels.

Treating HIV in People with HCV

Although coinfection can complicate treatment, most people with HCV can be successfully treated for HIV. Many anti-HIV medications are metabolized by the liver and can cause hepatotoxicity (liver-related side effects); ritonavir and nevirapine appear to be the worst offenders. People with existing liver damage due to chronic hepatitis are more likely to experience hepatotoxicity, and should have their liver enzyme levels monitored regularly. In many cases liver enzyme levels stabilize over time, but some people may need to substitute drugs that are easier on the liver.

Treating HCV in People with HIV

Many people with hepatitis C—coinfected or not—do not need HCV treatment. The usual guidelines for treating HCV generally can be applied to coinfected people. However, HIV positive people with fewer than 200 CD4 cells/mm^3 or a concurrent opportunistic illness are not considered good candidates for HCV treatment. Doctors usually recommend that HIV should be brought under control first, before a person starts HCV treatment. However, in some cases HCV can be treated first in people with early-stage HIV disease so that they can better tolerate anti-HIV drugs later.

Most coinfected people should be treated with interferon plus ribavirin. Sustained response rates tend to be lower in coinfected people, but recent research suggests that coinfected people with well-controlled HIV disease may do nearly as well as those with HCV alone. HCV medications and some anti-HIV drugs can interact and cause worse side effects—including low blood cell counts and mitochondrial toxicity—when used together. People being treated for both HIV and HCV should be closely monitored during therapy.

HBV/HCV Coinfection

Hepatitis B, like hepatitis C, can cause serious liver damage including liver cirrhosis and cancer. HBV/HCV coinfection is poorly understood, and research is just beginning on how these two viruses interact. Studies to date indicate that HBV/HCV coinfection can lead to more serious liver damage than infection with either HBV or HCV alone. HBV/HCV-coinfected people are at higher risk for liver cancer and for fulminant hepatitis, a serious acute liver inflammation that can result in rapid liver damage and death. Some studies suggest that even people who have recovered from hepatitis B may be at higher risk of developing cirrhosis and liver cancer if they later become infected with HCV. Because coinfection may lead to more severe liver disease, people with HCV should ask their doctor about getting vaccinated against hepatitis A and hepatitis B.

Conclusion

Chronic hepatitis C is a liver disease that can have serious consequences. It is important to remember that many people do not experience symptoms or disease progression. Those who do eventually experience disease progression may remain symptom-free for decades. However, some people develop serious liver disease that can result in liver failure or death. New treatments for HCV are currently being tested, and it is believed that better treatment options will be available within five years. Additionally, lifestyle changes such as good nutrition, exercise, and stress management can help alleviate side effects and may slow disease progression.

We hope this information has helped you to understand the hepatitis C virus and how it can affect your physical and emotional health. We welcome any suggestions or ideas for improving this booklet.

Resources

For more information about HCV, contact the following organizations

- ***Hepatitis Foundation International***
  800-891-0707, www.hepfi.org
- ***American Liver Foundation***
  800-465-4837, www.liverfoundation.org
- ***Hep C Connection***
  800-522-4372, www.hepc-connection.org
- ***L.O.L.A. (Latino Organization for Liver Awareness)***
  888-367-5652, www.lola-national.org

Suggested reading

The Hepatitis C Help Book, by Misha Cohen, OMD, LAc, and Robert Gish, MD. St. Martin's Press.

Living with Hepatitis C: A Survivor's Guide, by Gregory T. Everson, MD, and Hedy Weinberg. Hatherleigh Press. 800-367-2550.

The First Year—Hepatitis C: An Essential Guide for the Newly Diagnosed, by Cara Bruce and Lisa Montanartelli. Marlow and Co.

Pharmaceutical resources

- ***Roche Patient Assistance Program—Pegassist***
  877-PEGASYS (734-2797)
- ***Schering-Plough Commitment to Care***
  800-521-7157

HIV resources

- ***Project Inform***
  www.projectinform.org
  hotline: 800-822-7422
- ***San Francisco AIDS Foundation***
  www.sfaf.org
  hotline: 800-367-2437
- ***HIV and Hepatitis.com***
  www.hivandhepatitis.com
- ***National AIDS Treatment Advocacy Project***
  www.natap.org

Glossary

ACUTE
the rapid-onset, short-term initial stage of a disease. Contrast with *chronic.*

ACUTE HEPATITIS
the initial stage of viral hepatitis following infection. In HCV, acute hepatitis refers to the first six months of infection.

ADVERSE EVENT
an undesired reaction or side effect of treatment.

ALOPECIA
hair loss.

ALT (*formerly* SGPT)
abbreviation for alanine aminotransferase. ALT is an enzyme produced inside liver cells. It is frequently elevated in people with chronic HCV infection because of a breakdown of the membranes of liver cells due to inflammation. Serum ALT levels are measured using a common blood test.

ANEMIA
reduced number of red blood cells or reduced ability of blood to carry oxygen. There are several types of anemia, all with different causes. Symptoms may include fatigue, weakness, pale skin, and difficulty breathing.

ANTIBODY
a protein produced by the immune system when a foreign substance enters the body. The presence of antibodies is an indicator of a past or possibly current infection. HCV antibodies are written as "anti-HCV." The test for anti-HCV is often the first step in diagnosing chronic HCV infection. A positive anti-HCV test must be followed by other laboratory tests to confirm the diagnosis. The antibody test alone is not sufficient to make a diagnosis of chronic HCV infection.

ARTHRALGIA
joint pain.

AST (*formerly* SGOT)
abbreviation for aspartate aminotransferase. AST is an enzyme produced in the liver. When liver cells are damaged, AST is released. Elevated levels may indicate liver disease, but are also seen in people with muscle damage.

AUTOIMMUNE RESPONSE (AUTOIMMUNITY)
a condition in which a person's immune system produces antibodies that attack the body's own tissues. Several conditions associated with hepatitis C appear to have an autoimmune aspect.

BID
taken twice a day.

BILIRUBIN
a yellowish pigment released when red blood cells are broken down. Normally bilirubin is processed and excreted by the liver. Hyperbilirubinemia (an excess level of bilirubin in the blood) indicates liver damage, and can lead to jaundice (yellowing of the skin and whites of the eyes), pale-colored stools, and dark urine.

BIOCHEMICAL RESPONSE
how a person's serum ALT responds to treatment. When a person's elevated serum ALT level becomes normal after HCV therapy has been initiated, this is considered a biochemical response.

BIOPSY
a procedure in which a sample of cells or tissue is taken to examine in a laboratory. In HCV, liver biopsies are used to monitor the health of the liver.

BLOOD-BORNE
transmitted through direct blood-to-blood contact, for example, through sharing needles or through a blood transfusion.

BRAIN FOG
mental confusion, memory loss, and/or lack of alertness. Not to be confused with encephalopathy.

BREAKTHROUGH
the return of detectable viral load in a person who had previously achieved a virological response during treatment.

CHRONIC
long-term or persistent disease. Contrast with *acute.*

Glossary

CHRONIC ACTIVE HEPATITIS
a condition in which HCV continues to replicate and infect new cells beyond the first six months after acquiring HCV.

CIRRHOSIS
liver damage in which normal liver cells are replaced with scar tissue. In **compensated cirrhosis,** the liver is damaged but can still function. In **decompensated cirrhosis,** liver function is severely impaired and scar tissue interferes with normal blood flow through the liver, potentially leading to bleeding varices, ascites, mental confusion, and other symptoms.

COINFECTION
concurrent infection with more than one disease-causing organism (e.g., HCV and HIV).

COMBINATION THERAPY
two or more drugs used in combination to improve the effectiveness of treatment. When applied to HCV treatment, this term most often refers to the use of interferon plus ribavirin.

CYTOPENIA
low levels of blood cells.

EDEMA
swelling caused by the accumulation of fluid in body tissues.

EFFICACY
effectiveness; the ability to achieve a desired effect.

ENCEPHALOPATHY
disease of the brain. Hepatic encephalopathy, associated with advanced cirrhosis, is characterized by reduced cognitive function, confusion, and memory loss.

END OF TREATMENT (EOT) RESPONSE
the disappearance of detectable HCV RNA from the blood at the end of a course of treatment.

EXTRAHEPATIC
outside the liver.

FDA
abbreviation for the Food and Drug Administration. This U.S. federal government agency has many functions, including the responsibility for granting or denying approval for drugs to be sold to the public.

FIBROSIS (*adjective* FIBROTIC)
liver damage that involves the development of fibrous scar tissue.

FLARE-UP
a sudden worsening of disease symptoms.

FULMINANT HEPATITIS
a severe, life-threatening form of hepatitis.

GENOTYPE
genetic variation in the structure of HCV. There are six major genotypes, designated by the numbers 1 through 6. There are also many subtypes, e.g., 1a, 1b, 2a, etc. In the U.S., genotype 1 is predominant (approximately 70–75% of those infected).

HCV RNA
the genetic material of the hepatitis C virus. HCV is a single-stranded ribonucleic acid (RNA) virus.

HEPATIC
relating to the liver.

HEPATITIS
inflammation of the liver. Hepatitis may have various causes, including viruses, toxins, and heavy alcohol consumption.

HEPATOCELLULAR CARCINOMA (HCC)
a type of primary liver cancer seen in some people with long-term liver damage due to chronic hepatitis C or hepatitis B.

HEPATOLOGY (*also* HEPATOLOGIST)
the medical specialty that deals with the liver; a hepatologist treats liver disease.

HEPATOTOXICITY (*adjective* HEPATOTOXIC)
toxic or poisonous to the liver.

HISTOLOGICAL
refers to bodily tissue. In HCV, histological improvement means improvement in liver tissue, either reduced inflammation or reduced fibrosis, when comparing pretreatment biopsies with biopsies obtained typically six months after HCV therapy.

Glossary

INCUBATION PERIOD
the period of time between initial exposure to an infectious microorganism and the development of disease symptoms.

INTERFERON (IFN)
a naturally occurring protein in the human body produced by the immune system. Interferon interferes with viral replication. Genetically engineered products based on the natural protein have been developed by several pharmaceutical companies, and are approved for the treatment of chronic HCV infection.

INVESTIGATIONAL NEW DRUG (IND)
a drug that the FDA allows to be used in human clinical trials to gain information for evaluation, usually for approval of commercial marketing.

JAUNDICE
yellowing of the skin and whites of the eyes due to high bilirubin levels in the blood. Jaundice is often a sign of liver damage or gallbladder disease.

LIVER
a large organ on the upper right side of the abdomen that plays an important role in the metabolism of sugars and fats, synthesizes several proteins, and filters toxins from the blood.

LOG
a measure based on the logarithmic scale that refers to quantities in factors of ten. A log change is an exponential, or 10-fold, increase or decrease (e.g., a change from 10 to 100 is a 1-log increase; a change from 1,000,000 to 10,000 is a 2-log decrease). Viral load is sometimes expressed in logs.

MALAISE
a generalized feeling of illness and discomfort; a flu-like feeling.

MONOTHERAPY
use of a single drug for treatment. Traditionally, monotherapy for chronic HCV infection is interferon alone.

MYALGIA
muscle pain.

NEUTROPENIA
an abnormally low number of neutrophils, resulting in increased susceptibility to infection.

NEUTROPHIL
the most common type of immune system white blood cell. Neutrophils are phagocytes that engulf and destroy invading organisms such as bacteria and fungi.

NONRESPONDER
a person who does not show sufficient improvement while undergoing treatment. In HCV, a nonresponder is a person who does not experience a normalization of ALT levels or disappearance of HCV RNA.

PEGYLATED INTERFERON (PEG-INTRON, PEGASYS)
a form of interferon that has a long half-life in the body and can be injected less often (typically once per week). Pegylated interferon is approved for the treatment of HCV. See also *standard interferon.*

PERCUTANEOUS
through the skin.

PERINATAL TRANSMISSION (VERTICAL TRANSMISSION)
transmission from a mother to a fetus or newborn. Vertical transmission may occur *in utero* (in the womb), intrapartum (during birth), or postpartum (e.g., via breast-feeding).

PLATELET
see *thrombocyte.*

PRURITUS (*adjective* PRURITIC)
itchiness.

QUALITATIVE
relating to, or expressed in terms of, quality. A qualitative viral load test measures the presence of a virus.

QUANTITATIVE
relating to, or expressed in terms of, quantity. A quantitative viral load test measures the amount of viral genetic material.

Glossary

QUASISPECIES
individual genetic variants of HCV. Within a single genotype there may be multiple quasispecies.

RELAPSE
recurrence of disease symptoms following a period of improvement. In HCV, relapse can refer to an increase in viral load after it has been suppressed by antiviral treatment.

RESPONDER-RELAPSER (*or* RELAPSER)
a person who initially responds well to treatment but then experiences a relapse. In chronic HCV infection, this is someone who initially has a positive response to treatment (normal ALT and loss of HCV RNA), but does not sustain that response when therapy is stopped.

RESPONSE TO TREATMENT
how a disease responds to drug therapy. The term can refer to a biological, histological, or virological response.

RIBAVIRIN (COPEGUS, REBETOL)
an antiviral medication that is used in combination with interferon for treatment of chronic HCV infection.

STEATOSIS
buildup of fat in the liver.

SUBCUTANEOUS (SQ)
underneath the skin; usually refers to a drug injected under the skin.

SUSTAINED RESPONDER
a person who maintains a long-term response to treatment. In HCV, a sustained responder has a long-term beneficial result from HCV treatment (usual endpoints are normal ALT and undetectable HCV RNA) that persists after treatment has been stopped (six months is the generally accepted time interval).

SUSTAINED VIROLOGICAL RESPONSE (SVR)
see *virological response.*

THROMBOCYTE (PLATELET)
a type of blood cell responsible for normal blood clotting.

THROMBOCYTOPENIA
an abnormally low number of platelets, which may result in abnormal bleeding and bruising.

THYROID GLAND
an organ at the base of the neck that produces thyroxin and other hormones involved in regulating metabolism.

TREATMENT-NAIVE
a person who has not had prior treatment for a particular condition.

VIRAL LOAD
the amount of virus (e.g., the HCV RNA level) that can be measured, usually in the blood.

VIRAL REPLICATION
the ability of a virus to reproduce copies of itself.

VIROLOGICAL RESPONSE
how a person's viral load level responds to treatment. In HCV, when a person's HCV RNA becomes undetectable after HCV therapy has been initiated, this is considered a virological response. If the HCV RNA remains undetectable beyond six months, the term sustained virological response (SVR) is used.

VIRUS
a microscopic, infectious organism that invades a living host and makes copies of itself (viral replication).

WINDOW PERIOD
the time between exposure to a microorganism and the production of sufficient antibodies to be detected in a test.

Visit the HCV Advocate Web Site

- *HCV Advocate* newsletter
- *HepSquads* newsletter
- Educational materials in English and Spanish
- *Medical Writers' Circle*
- HCSP fact sheets
- HIV/HCV coinfection information
- National support group listing
- Hepatitis C news
- Hepatitis C events
- Clinical trials listing
- Links to recommended Web sites

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