CONQUERING HEPATITIS C

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CONTENTS

INTRODUCTION

This book is written for people who have been diagnosed with hepatitis C and are under the care of a physician and also for individuals who want to learn more about this disease that affects so many. The book is designed to answer many of your questions so that you can be fully informed about your condition and play an active role in its treatment. Please remember, this book is *not* intended to replace the advice and expertise of your physician. Hopefully, the book will help you focus your questions and more fully understand the answers—and the options.

Also, there are many situations where hepatitis C is associated with other disorders, such as hepatitis B, human immunodeficiency virus (HIV) infection, and chronic kidney failure. These special situations are beyond the scope of this book and should be treated on the advice of a specialist.

CHAPTER ONE

HEPATITIS C: AN OVERVIEW

UNDERSTANDING YOUR LIVER

Where is the liver?

Your liver is located in the upper right portion of the abdomen underneath the lower rib cage (Fig. 1–1). Part of your liver lies across the middle of your abdomen towards the left side of your body. Many vital organs surround your liver—

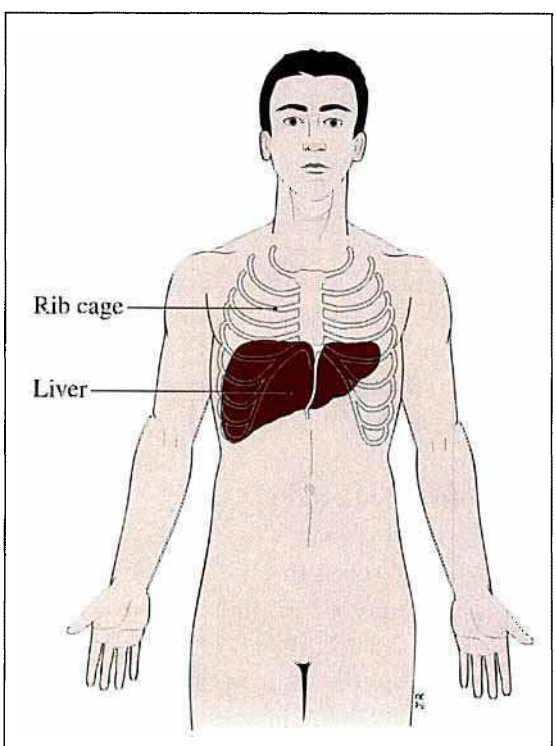

Figure 1–1 Your liver is located in the upper right portion of the abdomen underneath the lower rib cage.

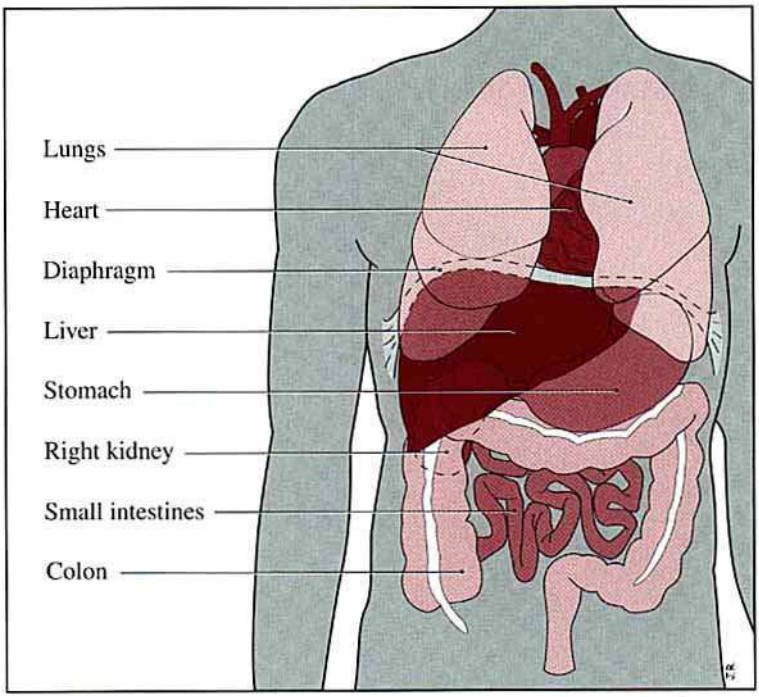

Figure 1–2 Many vital organs surround your liver.

your diaphragm and lungs above, the right kidney behind, and the small intestine and colon below (Fig. 1–2).

What does the liver look like?

The liver is reddish-brown in color. It is about the size of a football and weighs about 3 pounds. The liver is divided into four major sections called lobes (Fig. 1–3). There are important arteries and veins that run in and out of the liver. The hepatic artery supplies the liver with oxygenated blood from the heart, while the hepatic veins carry blood back to the heart. The portal vein delivers most of the blood to the normal liver, carrying nutrients and toxins from the intestines to the liver for processing (Fig. 1–4).

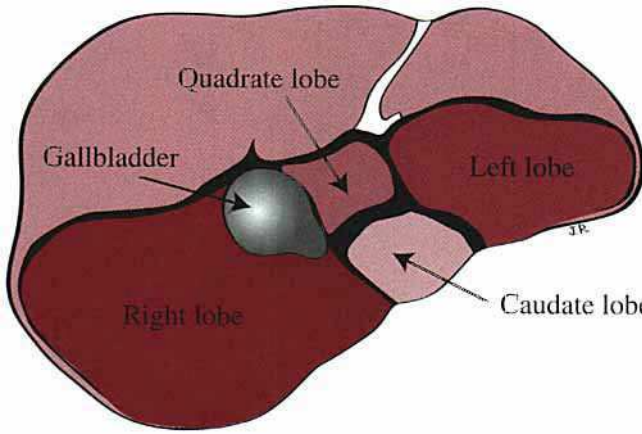

Figure 1–3 The liver is divided into four lobes.

What does the liver do?

As a food processing and chemical factory, the liver is one of the most important organs in your body. Food, drugs, and vitamins taken by mouth go through the stomach to the small intestines, where they are absorbed into the portal vein. The portal vein is the important road from the intestines to the liver. Just about everything you take by mouth is absorbed and transported to the liver by the portal vein. Once processed in the liver, the transformed food, drugs, and vitamins leave the liver by the hepatic veins, enter the heart, and are then distributed throughout the body. The liver affects the functions of the blood, lymph, bile, immune system, and chemical processes. Thousands of vital processes necessary for life are occurring in the liver at any time.

Your liver

- stores various forms of energy and vital nutrients (vitamins, minerals, and sugars) and later releases them into the bloodstream when needed by your body,
- processes drugs, absorbed from the digestive tract, into forms that your body can use and, for many drugs, controls the disposal of the agent,

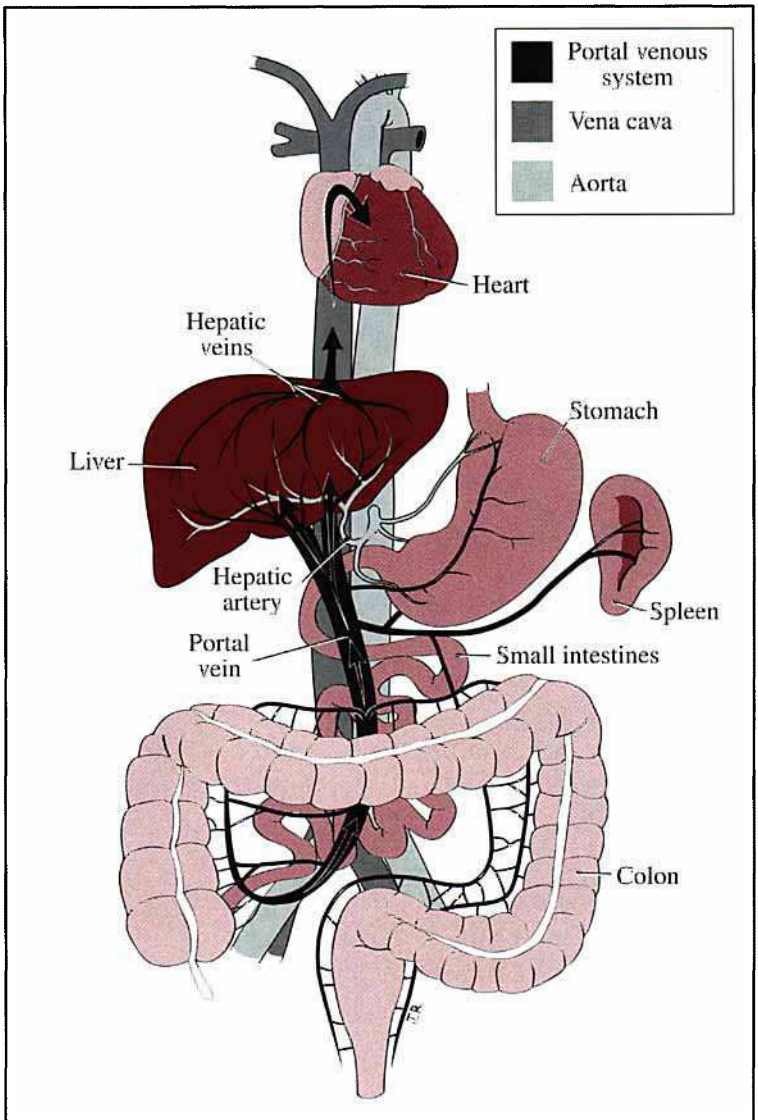

Figure 1–4 The blood supply to and from the liver.

- cleanses from the blood a variety of environmental and internally produced toxins by converting them into substances that can be eliminated from the body,
- manufactures bile, a greenish-brown fluid that is needed for digestion, and
- builds or breaks down body proteins and other compounds that are essential for life. Some of these include:
  - **Albumin**: an important protein component of blood that maintains the balance of the fluid in your body and helps prevent swelling.
  - **Bilirubin**: the yellow pigment that is released from red blood cells when they reach the end of their normal lifespan of 120 days. Bilirubin is taken up, metabolized, and excreted by the liver. When the liver is not working properly, bilirubin levels build up in blood and tissues, leading to a yellow color, called jaundice, in the skin and the whites of the eyes.
  - **Enzymes**: substances involved in chemical reactions that provide your body with fuel. The liver manufactures enzymes such as alanine aminotransferase (ALT).
  - **Clotting Factors**: proteins that are necessary for blood to clot and bleeding to stop.
  - **Cholesterol**: a vital element in the membranes of your body cells, and a building block for sex hormones and vitamins.
  - **Hormones**: substances that stimulate activity in an organ. The liver plays a major role in regulating the levels of hormones in the body, such as insulin.

LEARNING ABOUT THE HEPATITIS C VIRUS

What is hepatitis?

Hepatitis means inflammation (itis) of the liver (hepa). This inflammation can be caused by many things, including alco-

hol, viruses, drugs, toxins, and certain medications. Hepatitis C is inflammation of the liver caused by the hepatitis C virus.

What is a virus?

Unlike bacteria, which not only cause infections but also carry out a range of functions such as assisting in absorbing nutrients, viruses exist mainly to reproduce and cause infection. They do this by invading cells and using them to make more viruses. There are few, if any, redeeming features of a virus. Invasion and reproduction are the goals of a virus.

A virus is so tiny that it can only be seen under a high-powered electron microscope. It is made up of a compact string of genes surrounded by a coat of protein. When this coat attaches to a cell in the body, the genes from the virus enter the cell, where the virus takes over the cell's normal function and uses it to produce more viruses. These viruses then go on to infect other healthy cells.

Many viruses replicate quickly—some (including hepatitis C) within a few hours. While this process is occurring, the body's immune system attempts to protect the body by sending out special proteins called antibodies to neutralize the virus. Unfortunately, some viruses are able to mutate (change form) quickly so as to, at least partially, escape these antibodies.

What is the hepatitis C virus?

The hepatitis C virus (Fig. 1–5) is a spherical, enveloped, single-stranded ribonucleic acid (RNA) virus in the Flaviviridae family, a group that also includes dengue and yellow fever viruses. The hepatitis C virus replicates mainly in the liver cells (Fig. 1–6). As the virus reproduces, the liver cells are damaged, some cells die, inflammation occurs, and scar tissue (fibrosis) develops. Hepatitis C is a blood-to-blood virus and can be

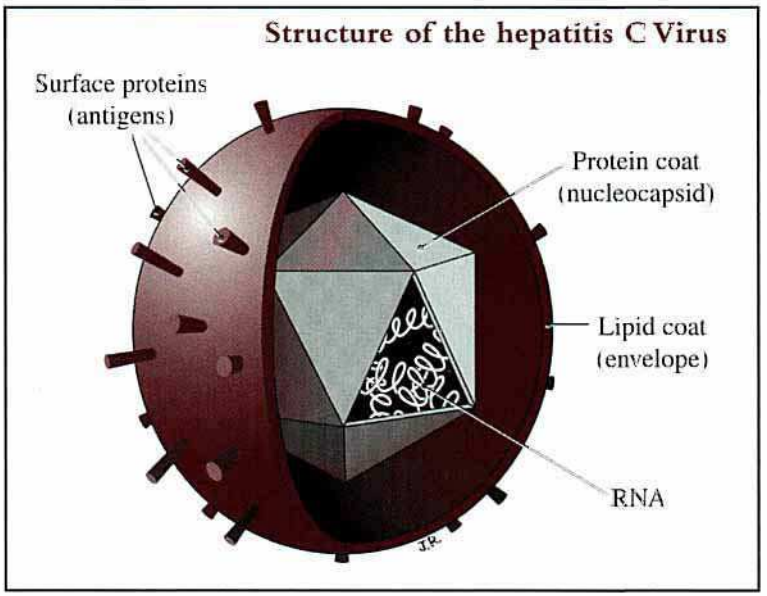

Figure 1–5 Structure of the hepatitis C virus.

transmitted through transfusions, shared drug needles, and other routes. (For more information on transmission, see Chapter 3, page 36.)

How was the hepatitis C virus discovered?

By the 1970's, scientists had identified the hepatitis A and B viruses and had developed tests to detect them. However, it became clear that these viruses didn't explain all cases of viral hepatitis, particularly those caused by blood transfusions. During the 1980's, the search continued to identify the non-A non-B virus. Many candidates came and went. Then, in 1989, a group of investigators, led by Dr. Michael Houghton of the Chiron Corporation, discovered the hepatitis C virus. In 1990, the first test for detecting the presence of the hepatitis C virus

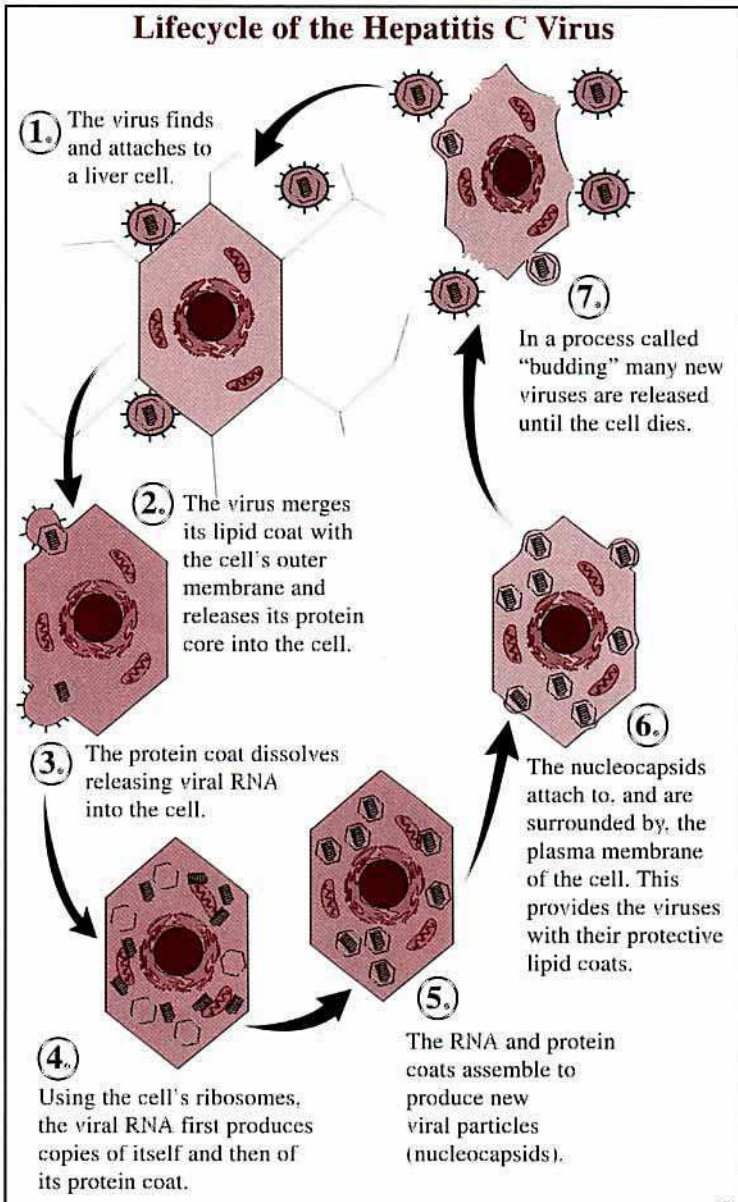

Figure 1–6 Lifecylce of the hepatitis C virus in liver cells.

became available on a commercial basis, and widespread testing began.

Do we know the genetic make-up of the hepatitis C virus?

Yes, the entire genetic information—called the genome—is known and has been reproduced (cloned) by scientists. The genome has a number of different action points. One of the most critical points is the neck of the virus, located directly behind the core region (Fig. 1–7). Called the hypervariable region, this area is where errors (mutations) are highly likely to occur as the virus is replicating, creating permanent changes to the virus's genetic code. These mutations, known as quasispecies (see below), are one of the reasons why we have difficulty treating and developing a vaccine for hepatitis C.

What is the hepatitis C "genotype"?

The hepatitis C genotype is the basic combination of genes within the hepatitis C virus. It is useful to think of a genotype as a family that is related to other families but maintains its identity.

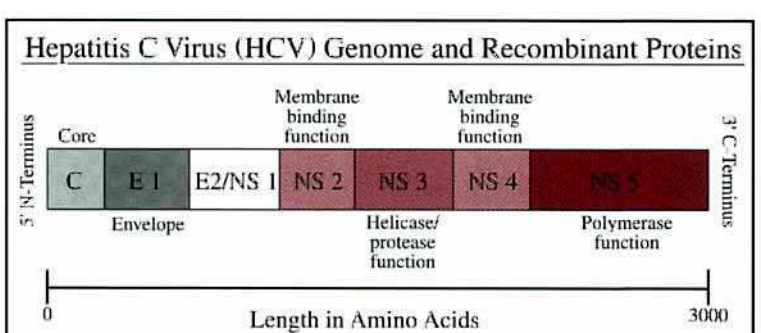

Figure 1–7 The hepatitis C genome.

There are at least six different genotypes that have been identified. Within those genotypes, a number of major subtypes have been recognized: 1a, 1b, 2a, 2b, 2c, 3a, 3b, 4a, 5a, 6a. Certain genotypes are more common in certain countries (Fig. 1–8). In the United States, 70 to 80 percent of infected patients have genotype 1; type 1a is the most common (about 58% of infected people have this subtype), with type 1b being the second most common subtype. We don't know why certain genotypes predominate in certain countries. We do know that each genotype has a different impact on the progression of liver disease and the effectiveness of treatment. For instance, people with type 1b often appear to have more rapidly progressive disease and respond less well to treatment than people with type 2 or 3.

What are quasispecies?

As discussed earlier, the hepatitis C genome can change or mutate as it is replicating, creating many errors called quasispecies. At any one time, you can have several quasispecies of the hepatitis C virus in the blood and liver, and the viruses may continue to mutate during treatment. These ongoing changes to its genetic code help the virus to escape from the body's immune system and to be resistant to some treatments. As a result, quasispecies, like genotypes, can affect whether and how quickly the liver disease will progress and how well the treatment will work.

What is the natural course of hepatitis C?

In most people, hepatitis C is a slow moving disease with no, or few, symptoms during the first few decades after they are infected. In general, hepatitis C progresses through four phases (Fig. 1–9). These phases are not always distinct from one

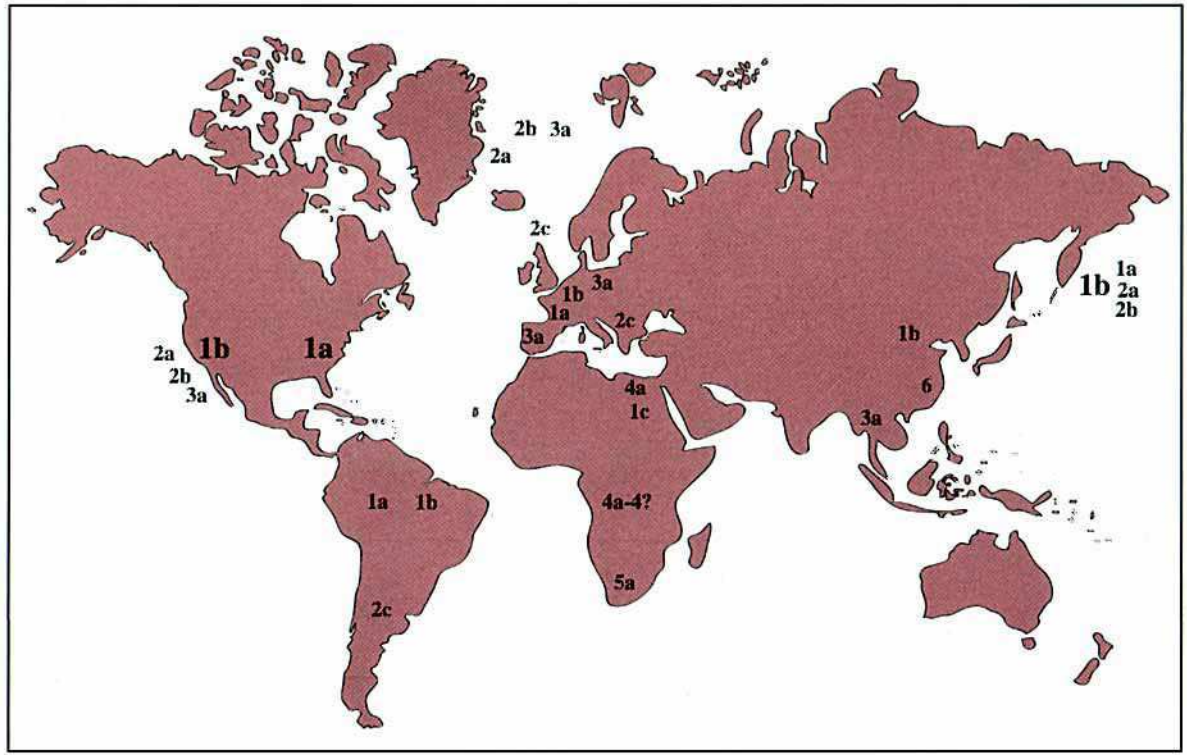

Figure 1–8 Geographic distribution of hepatitis C subtypes.

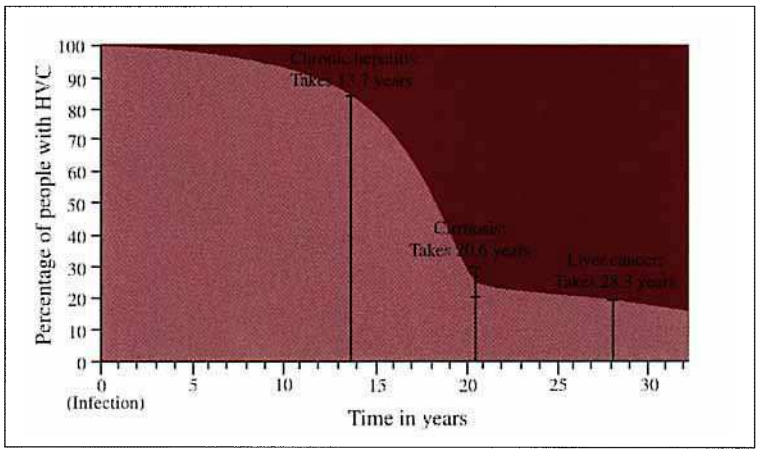

Figure 1–9 The four phases of hepatitis C. Individual responses are highly variable.

another, and it is difficult to predict accurately how a person will progress through them. This is a great variation in the course of hepatitis C from one person to the next. In some, the disease hardly progresses at all over decades, while in others cirrhosis may develop in only a few years. We know that the average time to progress from initial infection

- to chronic hepatitis takes 13.7 years,
- to cirrhosis takes 20.6 years, and
- to liver cancer takes 28.3 years.

The risk of developing liver cancer is almost completely linked to having developed cirrhosis.

Phases of Hepatitis C

Infection: As explained earlier, a virus attaches itself to a healthy cell in the body, invades it, and then begins to replicate. In the case of hepatitis C, this process occurs mainly within the liver cells, with the virus spreading through the entire liver. Your body's immune system is generally ineffective in getting rid of the hepatitis C virus.

Inflammation: During this acute initial phase, inflammation of the liver (hepatitis) begins. This phase normally lasts from 2 to 12 weeks. The human immune system is not very effective in clearing the hepatitis C virus, so most people infected can't get rid of the virus. In fact, more than 85 percent of people with acute hepatitis C progress to long-lasting (chronic) infection. Factors that appear to increase the risk of progressing to chronic hepatitis C include

- becoming infected after age 40 years,
- male gender, and
- regular use of alcohol.

Fibrosis: Eventually, inflammation and liver injury, followed by efforts to repair the damage, may lead to a build-up of scar tissue (fibrosis). With time, fibrosis begins to interfere with normal liver function.

Cirrhosis: When fibrosis is severe, the liver becomes scarred and changes in structure. This is called cirrhosis, a condition which develops in 20 to 30 percent of people with hepatitis C. When cirrhosis occurs, blood from the portal vein and even from the hepatic artery is prevented from flowing freely through the liver. Eventually, this bloodflow can be dramatically reduced; the blood that is trying to get through the liver meets great resistance and is under increasing pressure (this is called portal hypertension). The result is serious complications, such as

bleeding from the esophagus and stomach (varices),
fluid build-up and abdominal swelling (ascites),
development of new blood vessels which allow the blood to bypass the congested liver, and
build-up of toxins in the bloodstream because the blood has bypassed the liver, causing mental confusion (hepatic encephalopathy). (For more information on the signs of these complications, see Chapter 2, page 20.)

People infected with chronic hepatitis, particularly those that have developed cirrhosis, are at increased risk of liver cancer (hepatocellular carcinoma). Of those who have cirrhosis, up to 20 percent will develop liver cancer, although it may take many years for the cancer to appear. As well, it seems that men are at increased risk for this type of cancer.

How does hepatitis C differ from other types of hepatitis?

To date, five distinct hepatitis viruses have been identified: A, B, C, D, and E. A sixth virus, G, has been detected, but it has not been proved to cause hepatitis. The five viruses differ in several ways, including route of transmission, natural course, response to treatment, and suitability for an effective vaccine. Table 1–1 outlines the primary differences among these viruses.

A few hepatitis cases are attributed to unknown origins (cryptogenic) and may be due to variants of one or more unidentified hepatitis viruses. As work to identify these unknown viruses continues, it's likely that the current alphabet of hepatitis viruses will grow.

THE HEPATITIS C STORY

Why are we hearing about hepatitis C only now?

It was only relatively recently that we identified the hepatitis C virus and found a way to detect it. Two factors have played key roles in its low profile:

1. Before 1940, blood transfusions were relatively rare events. Then, during World War II, transfusions were used widely. After that, blood transfusions were commonly used for surgery, such as caesarean sections and coronary artery bypasses.
2. In the 1960's, the use of illicit intravenous drugs and sharing of needles became much more widespread.

Transfusions and illicit intravenous drugs created windows of opportunity for the blood-to-blood transmission of hepatitis C. As this disease is slow-moving with very few, if any, symptoms, many people previously exposed to the virus are being diagnosed only now. That's why the diagnosis of hepatitis C often comes as a great surprise.

In more recent years, recognition of the seriousness of hepatitis C may have been hampered and overshadowed by the intense focus on the acquired immunodeficiency syndrome (AIDS) epidemic. However, the increased understanding of the human immunodeficiency virus (HIV) that causes AIDS has also attracted public attention to the issue of viruses and blood safety. The hepatitis C field has benefited by the focus on greater blood safety and by a greater receptiveness within the medical community to identify new viruses and determine effective measures for testing and treatment.

How large is the hepatitis C problem?

If you have hepatitis C, you are not alone. Around the world, there are an estimated 150 million people who have chronic hepatitis C. From studies, we know that in the United States, there are an estimated four million people who are chronically infected, although no more than 25 percent of these people have so far been identified. During the late 1990s, nearly 30,000 new infections have been reported each year.

Hepatitis C is the most common chronic infection transmitted by blood in the United States and appears to be more prevalent among African-Americans and Hispanics than among Caucasians. The impact of hepatitis C can be seen in the following data:

Hepatitis C counts for

- 20 percent of acute hepatitis cases,
- 70 percent of chronic hepatitis cases,

Table 1–1 The family of hepatitis viruses.

	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Transmission	Food or water transmission such as fecal contamination of water supply or poor personal hygiene.	Blood-to-blood transmission such as sexual contact, needle sharing, and mother to infant exposure.	Blood-to-blood transmission such as drug transfusions and needle sharing.	Blood-to-blood transmission. An incomplete virus that needs the presence of Hepatitis B to be transmitted.	Food or water transmission such as fecal contamination of water supply or poor personal hygiene. Rarely seen in North America.
Natural Course	Does not progress to chronic hepatitis. Usually mild and symptoms resolve on their own. In rare cases, hepatitis A can cause serious liver disease. More likely to be severe and prolonged in older people.	95% of people with hepatitis B clear the infection, and maintain lifelong immunity. People with chronic infection can progress to cirrhosis and liver cancer.	85% of people with hepatitis C progress to chronic infection. Cirrhosis develops in 20-30% of people within 20 years. Serious complications and liver cancer develop in 4-8% of people who develop cirrhosis.	People with hepatitis B, who develop hepatitis D, have a greater chance of developing chronic infection, and usually have more serious disease. 80% of people with chronic infection progress to cirrhosis.	Does not progress to chronic hepatitis, and is not associated with liver cancer. Can cause severe liver disease and death in pregnant women especially during the third trimester.

Table 1–1 The family of hepatitis viruses—Continued.

Treatment	No treatment.	Most adults can fight off virus without treatment. Interferon and other antiviral therapies (such as the nucleoside analog lamivudine) are available for people with chronic infection.	Interferon, and combination interferon and ribavirin therapy are available for those with chronic infection.	Same treatment as for hepatitis B.	No treatment.
Vaccine	Vaccine available and becoming more widely used. Normally given to international travelers, military personnel, and certain people at high risk. May soon be universally recommended.	Vaccine available. Now given to all newborns. Recommended for adolescents, health care workers and travelers to endemic areas.	Not available.	Not available.	Vaccine is being developed for international travelers (particularly pregnant women) traveling to endemic areas.

- 40 percent of end-stage cirrhosis cases,
- 60 percent of liver cancer cases, and
- 30 to 50 percent of those with liver disease requiring liver transplantation.

Currently, hepatitis C results in an estimated 8,000 to 10,000 deaths per year in the United States. These numbers will likely increase during the next 10 to 20 years, as hepatitis C-infected people (who are, on average, 30 to 49 years of age) will reach the stage at which complications from chronic liver disease commonly arise.

In spite of these grim data, there is light at the end of the tunnel. The rate of new infections of hepatitis C is declining. Why?

- Transmission by blood products is almost zero, with current blood-screening programs.
- Precautions have been taken to reduce transmission in medical settings.
- Transmission through intravenous drug use, although still the primary route, is declining, to some extent, due to a greater awareness about the risk of sharing needles, and the availability in some areas of needle exchange programs.

Should everyone be screened for hepatitis C?

Many people are unaware that they have been infected with hepatitis C, so general screening of the public might seem to make sense. But the reality is that this would be a colossal and costly exercise. Instead, we recommend that screening be encouraged for high-risk groups, including

- people who have injected illegal drugs, even once or a few times many years ago;
- people with certain medical conditions such as those who received clotting factor concentrate blood products

before the early 1990s; those who receive hemodialysis; and those with abnormal results from tests, taken for any reason, which indicate an elevation of the liver enzyme, alanine aminotransferase (ALT);

- people who have received blood transfusions or organ transplants;
- healthcare workers who have been exposed to hepatitis C–infected blood through needle stick injury or have had mucous membranes exposed to infected blood, such as the lining of the nose, mouth, or throat; and
- children born of hepatitis C–positive women; screening is advised only for children age 1 year by which time any maternal antibodies received before birth through the placenta are no longer present.

How far has the field advanced since the discovery of the hepatitis C virus?

Since the discovery of the hepatitis C virus in 1989, we have amassed a great deal of information about the virus and have learned how to test and formulate treatments for it. In just a decade, we have made significant progress. The next decade holds even greater promise. The pace of research will gather speed, and our knowledge base will continue to grow. By 2010, we hope (and expect) that an effective treatment will be found for virtually everyone infected with hepatitis C. (For more information about experimental and future treatments for hepatitis C, see Chapter 8, page 89.)

CHAPTER TWO

DIAGNOSIS OF HEPATITIS C

ACUTE HEPATITIS C

What are the signs and symptoms of acute hepatitis?

As you learned in Chapter 1, the initial acute phase of hepatitis C begins after exposure to the virus, which reproduces in the liver cells. This acute phase is often not recognized because the great majority of people with acute hepatitis C do not develop specific symptoms. In those people who do, symptoms are usually mild and flu-like, such as loss of appetite, fatigue, nausea, and vomiting. In a few cases, jaundice can occur. Rarely, acute hepatitis C results in severe or fatal liver failure.

Whether or not symptoms appear, it does not help us to predict who will go on to develop chronic hepatitis C.

How long does it take for the virus to appear in my bloodstream?

The hepatitis C virus can be detected at about 7 weeks after you have been exposed to infection, although it can appear earlier or later. This is called the incubation period. If there is no sign of the virus in your bloodstream after 12 weeks following exposure, either the virus was never transmitted or it has cleared on its own, and you will not need treatment. Spontaneous clearance of the virus happens in only about 15 percent of infected people, with the remaining 85 percent going on to develop chronic hepatitis C.

Antibodies to the virus (your immune system's attempt to clear the virus) will appear at 5 to 6 weeks after exposure and remain in your bloodstream permanently. In most

people, these antibodies are not effective and provide no protection.

What are the other signs of acute hepatitis C?

The levels of ALT begin to rise. Alanine aminotransferase is manufactured by your liver (see Chapter 1, page 3), and normally its levels in the bloodstream are low. However, when the liver cells are injured, ALT leaks into the bloodstream, causing its levels to rise.

Usually, high levels of ALT indicate there is serious liver injury, while low (or no increase in) ALT levels may indicate that mild injury is occurring. However, it's important to understand that the hepatitis C virus may still be present even if ALT levels are normal and that the ALT level is not a reliable guide to the extent of injury.

If acute hepatitis is diagnosed, is it more easily treated?

We don't know for certain, but some early studies have shown that starting antiviral therapy immediately after infection with hepatitis C may be effective in clearing the virus and preventing the development of chronic hepatitis.

Treatments of immunoglobulin given within 24 hours after exposure to the hepatitis A or B virus may provide temporary protection from these viruses. Unfortunately, immunoglobulin doesn't provide the same protection against the hepatitis C virus.

CHRONIC HEPATITIS C

Do people with chronic hepatitis C experience symptoms?

It's remarkable how few symptoms there usually are during the chronic phase of hepatitis C. That's why it's called the

silent epidemic. Chronic hepatitis C can progress for years with no signs that it is present. In fact, hepatitis C is most often picked up by accident, either during screening programs of high-risk groups, during blood donation testing, or during tests done for insurance purposes.

If symptoms do arise, what are they?

Slight to moderate fatigue is the most common symptom, although, in a few cases, the fatigue associated with hepatitis C may be severe enough to interfere with work and other activities.

A dull discomfort on the right side of the abdomen is the second most common symptom. People often describe a heaviness or dragging sensation on the right side of the abdomen and under the right lower ribs (Fig. 2–1). You don't actually feel pain in your liver since it has no pain fibers. However, the covering (capsule) of the liver has them. As a result, an enlarged or inflamed liver can stretch the capsule and thus cause pain.

Other symptoms may include nausea and joint pain. Even with chronic hepatitis C, it is unusual for a person to develop jaundice.

Always remember that the presence or severity of symptoms doesn't tell us whether or not serious liver disease is present.

What can happen to my liver during chronic hepatitis C?

As explained in Chapter 1, there are several stages that your liver goes through during the natural course of hepatitis C—infection, inflammation, fibrosis, and cirrhosis. Cirrhosis will eventually develop in 20 to 30 percent of people with chronic hepatitis C, with complications of cirrhosis and liver cancer occuring in 4 to 8 percent of these people.

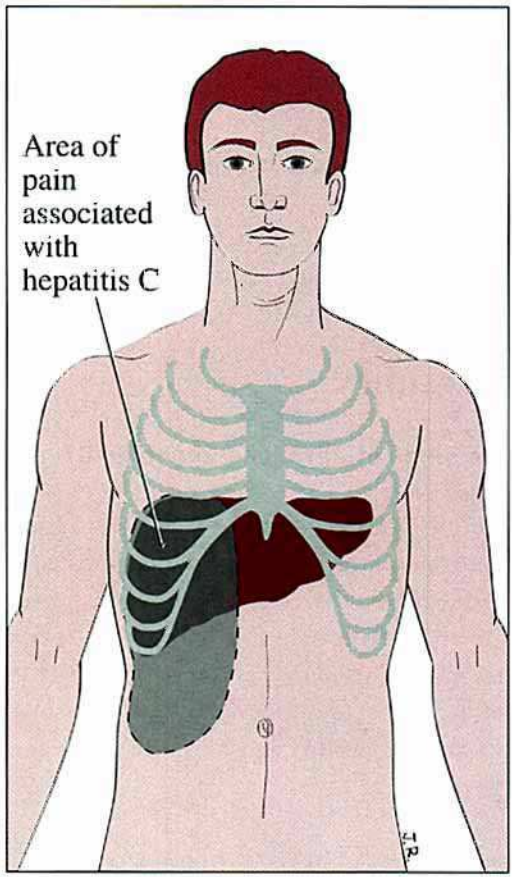

Figure 2–1 Area of pain associated with hepatitis C.

What happens to the levels of virus, antibodies, and liver enzymes in my bloodstream?

The hepatitis C virus and its antibodies can be detected throughout the course of chronic hepatitis C.

The levels of ALT can change over months or years. We believe these fluctuations are caused by ongoing waves of

injury to the liver although the ALT level often does not correlate with the extent of inflammation found on liver biopsy. About 30 to 50 percent of people with chronic hepatitis C have normal ALT levels. However, like symptoms, these normal levels do not give us a clear idea about the severity of the liver disease.

Levels of other substances in your body, including bilirubin, albumin, and clotting factors, will also be affected by hepatitis C and liver injury (see Chapter 4, page 48).

ADVANCED HEPATITIS C

What are the signs of advanced hepatitis C?

Later in the course of hepatitis C, extensive scarring (cirrhosis) becomes more widespread. The liver develops many nodules, and blood vessels are destroyed and rearranged, preventing blood from flowing freely through the liver. With severe cirrhosis, bloodflow to and from the liver is dramatically reduced, causing serious complications (described below). The appearance of these complications is a sure sign of advanced hepatitis C.

Varices

When blood can't flow freely through the liver, the pressure mounts, and the blood is forced to find alternative routes to travel—much like cars exiting off a jammed freeway onto side streets. In this process, new vessels (varices) develop in the lower esophagus and upper stomach so that the blood can continue to flow (Fig. 2–2). These varices have thin walls, and when the pressure within the vessels increases, they can burst easily, causing internal bleeding.

Ascites

When the blood "backs up" in the portal vein and other veins in the abdomen behind the congested liver, fluid is forced out

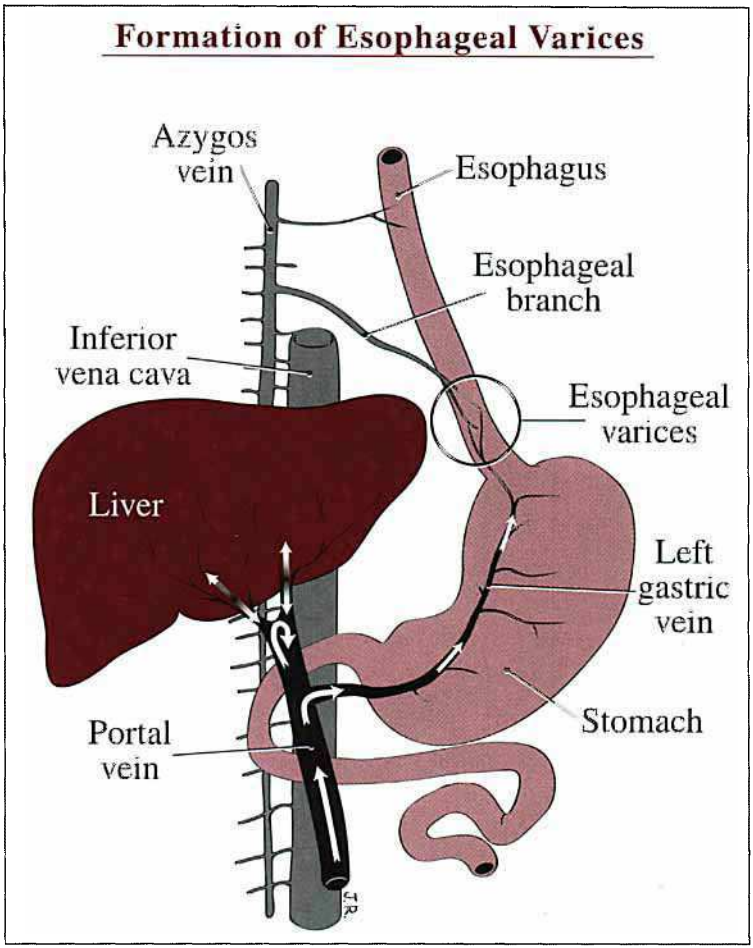

Figure 2–2 The process of esophageal varices formation.

of the vessels and collects in the hollow part of the abdomen (peritoneal cavity), causing swelling. This condition is called ascites (Fig. 2–3). The abdomen can become so swollen that the blood vessels in the gut also swell and become porous, possibly allowing bacteria to travel from the gut to the bloodstream. This can cause serious infection.

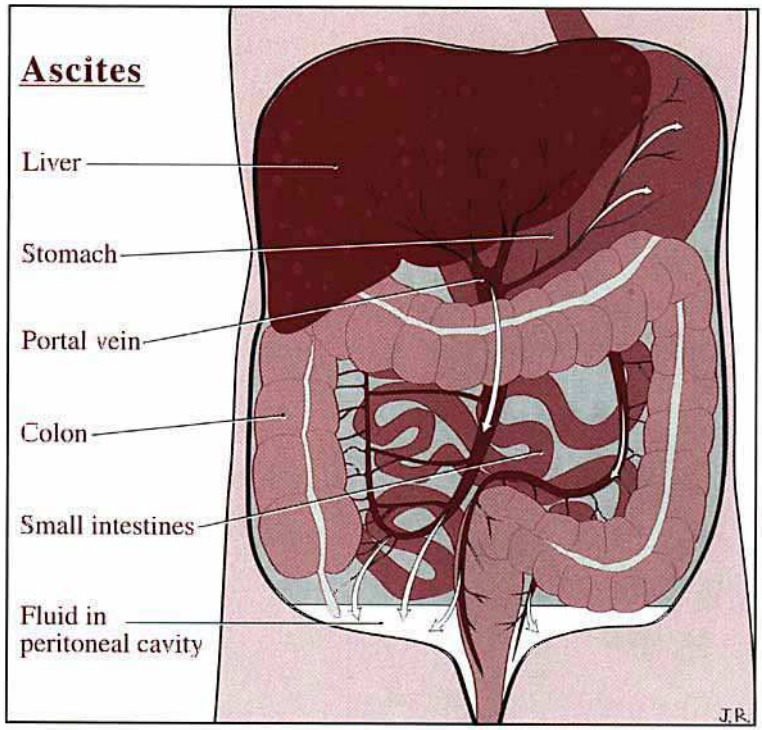

Figure 2–3 Fluid in the peritoneal cavity causes ascites.

Hepatic Encephalopathy

When the liver is severely injured, it loses its ability to clear toxins from the blood. Some of the blood that is meant to go through the liver for processing bypasses it and goes through the varices. This blood, along with the toxins, directly enters the body's circulation. Constant, severe itching is often an early sign that toxins are building up in the blood. The itching can affect all body surfaces or, more specifically, the palms of the hands and soles of the feet. If the level of certain toxins gets too high, mental confusion (hepatic encephalopathy) and even coma can occur.

Jaundice

When the liver isn't working properly, it fails to break down the yellow pigment bilirubin. Bilirubin is produced when red blood cells are broken down. Red blood cells live for 120 days and are then replaced. As the aging cells break down, bilirubin is released and is cleared by the liver (Fig. 2–4A). As the liver damage progresses, there often is a shortening of the lifespan of red blood cells, thereby adding to the bilirubin load. When the liver is damaged, however, bilirubin levels build up, causing the skin, whites of the eyes, and other tissues to turn yellow (Fig. 2–4B).

Blood Clotting Problems

A severely damaged liver fails to produce some of the proteins (blood clotting factors) that help the blood to clot and stop bleeding. Even with minor cuts or scrapes, people with advanced hepatitis C may bruise and bleed excessively.

Osteoporosis

Osteoporosis (a disease in which bones become thinner and more prone to breaks or fractures) commonly affects people with advanced hepatitis C.

OTHER DISEASES ASSOCIATED WITH HEPATITIS C

What other diseases can be a sign of hepatitis C?

Chronic hepatitis C not only injures the liver but also many other parts of the body, such as the joints, skin, and kidneys. Diseases that result from this injury are often the first sign of hepatitis C and may be recognized by physicians such as dermatologists (skin specialists) and rheumatologists (arthritis specialists). These diseases associated with hepatitis C (extrahepatic diseases) are discussed below.

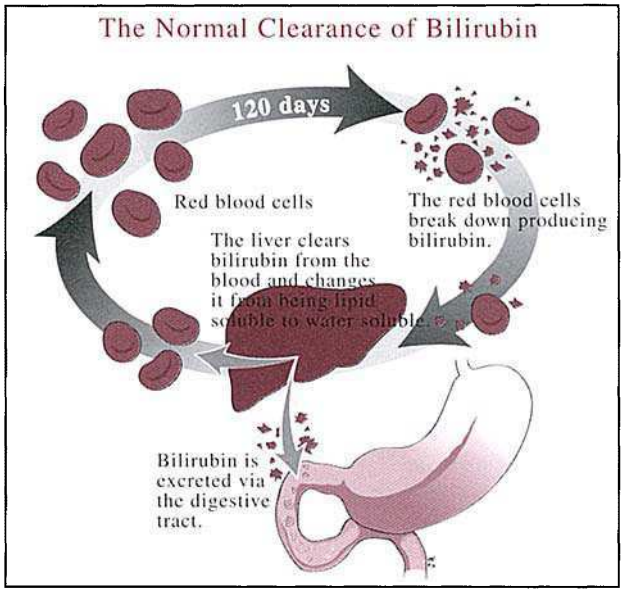

Figure 2–4A Clearance of bilirubin by the healthy liver.

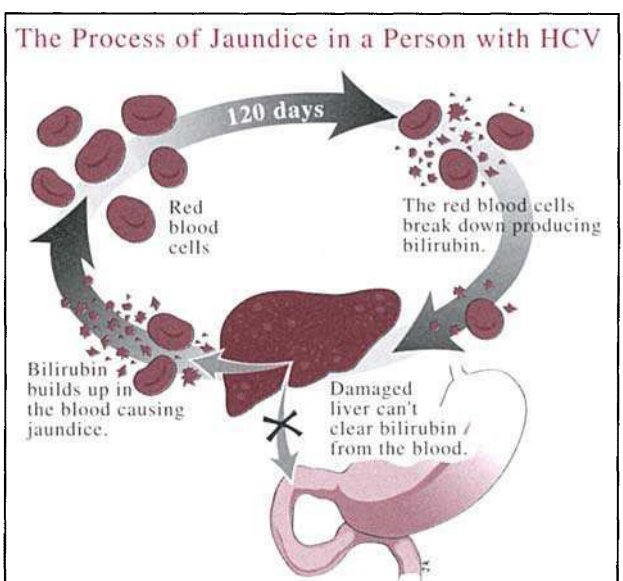

Figure 2–4B Buildup of bilirubin in a damaged liver.

Cryoglobulinemia

When a person is infected with the hepatitis C virus, the body's immune system sends a group of sticky proteins (cryoglobulins) to attach to the virus and kill it. Unfortunately, these cryoglobulins aren't usually successful. Instead, they combine with the virus and other proteins, forming immune complexes, which affect certain parts of the body and leads to excessive fatigue, joint pain, and a red raised rash often more prominent on the lower legs. This is called cryoglobulinemia.

Membranoproliferative Glomerulonephritis

When the immune complexes (described above) deposit in the kidney, they can cause inflammation and damage, which interferes with the kidney's ability to absorb proteins. The unabsorbed proteins leak into the urine, leading to fewer proteins in the blood, and swelling in the ankles or abdomen. This condition is called membranoproliferative glomerulonephritis.

Skin Conditions

The hepatitis C virus is associated with several serious skin conditions, including porphyria cutanea tarda, which causes blistering over the hands or any other extremity exposed to the sun. Anywhere from 20 to 70 percent of people worldwide who have this skin disease also have hepatitis C. Porphyria cutanea tarda is also associated with the regular use of alcohol. Other skin disorders which have been associated with hepatitis C are lichen planus, which involves reddish-brown raised spots, about 1 to 2 cm in diameter, that are sometimes itchy and scaly and lichenoid dermatitis, which involves scaly, reddish flat areas, usually larger than 2 cm in diameter, which can be itchy.

Thyroid Disease

In comparison with the general population, thyroid disease is more common in people with hepatitis C, especially occur-

ring after they have begun antiviral treatment. Interferon seems to interfere with the functioning of the thyroid, although we don't know how. Hypothyroidism (underactive thyroid) is the most common problem, although hyperthyroidism (overactive thyroid) can also occur. Signs of hypothyroidism include sluggishness, dry skin, coarse hair, and mental confusion. Palpitations, sweating, and poor concentration often signal hyperthyroidism. All people with hepatitis C who receive interferon therapy should have a thyroid test before beginning treatment and at regular intervals throughout treatment (Fig. 2–5).

Hepatitis C and its treatment are also associated with diabetes mellitus and certain autoimmune conditions, such as polyarteritis nodosa (inflammation of blood vessels in the abdomen, liver, and kidney), hemolytic anemia (red blood cells breaking down too rapidly), and rheumatoid arthritis (inflammation, stiffness, and pain in the joints).

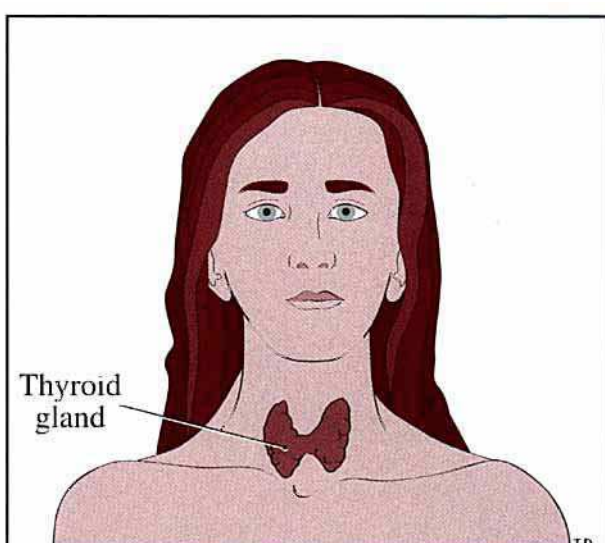

Figure 2–5 Location of the thyroid gland.

TESTING FOR HEPATITIS C

How is hepatitis C first picked up?

Testing the levels of ALT in the blood is the single most important test that leads to a diagnosis. As discussed, elevated ALT levels may be a sign of liver inflammation. If your physician finds your levels are high, other testing will be done to find out why.

In the past, many physicians did not recognize that slight elevations in ALT levels needed to be investigated, as other factors, such as obesity or reactions to therapeutic drugs, can also cause these levels to rise. However, we now know that hepatitis C is a large enough problem to warrant further testing of all people with elevated ALT levels.

Keep in mind that not all people with hepatitis C will have elevated ALT levels. About 30 to 50 percent of people will have normal ALT levels, even though the virus is active in their body.

What other tests are done to confirm the diagnosis of hepatitis C?

There are several tests now available that detect the antibodies to hepatitis C, as well as the virus itself. The tests you undergo will be determined by many factors, including your prior test results and risk factors for having hepatitis C. (For more information on risk factors, see Chapter 3, page 36.)

Enzyme-Linked Immunosorbent Assay

Enzyme-linked immunosorbent assay (ELISA), the most important test for diagnosing hepatitis C, detects the presence of antibodies to the virus. This test was developed shortly after the discovery of hepatitis C in 1989. The first version, ELISA 1,

detected antibodies directed against a single hepatitis C antigen (Fig. 2–6). (Antigens are protein components to which the antibodies are attracted). In the case of the hepatitis C virus, its antigens are seen as foreign and stimulate the body's immune system to send antibodies to attack them.) Because ELISA 1 only used a single antigen to detect hepatitis C antibodies, it produced many false-positive and false-negative results.

Since then, the test has been improved, although it is still not accurate in every case (Fig. 2–7). ELISA 2, developed in 1993, uses four antigens to detect the hepatitis C antibodies. In people at high risk for hepatitis C, the test is greater than 95 percent accurate, but for low-risk people (such as those who have no risk factors and voluntarily donate blood), the accuracy rate drops to 40 percent or lower. In these people, ELISA is said to be "false-positive," if more sensitive tests are negative. These individuals need to be reassured that they do *not* have hepatitis C.

An improved ELISA 3 is now used in Europe. In the United States, its use is currently limited to blood banks, although it will likely replace ELISA 2 throughout the community eventually.

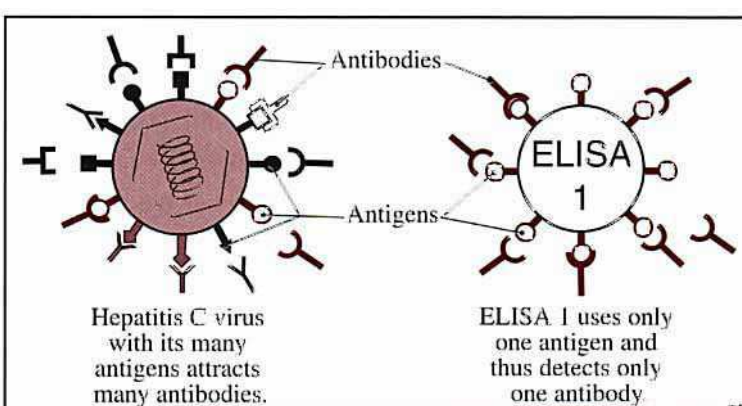

Figure 2–6 The ELISA 1 test uses only one antigen.

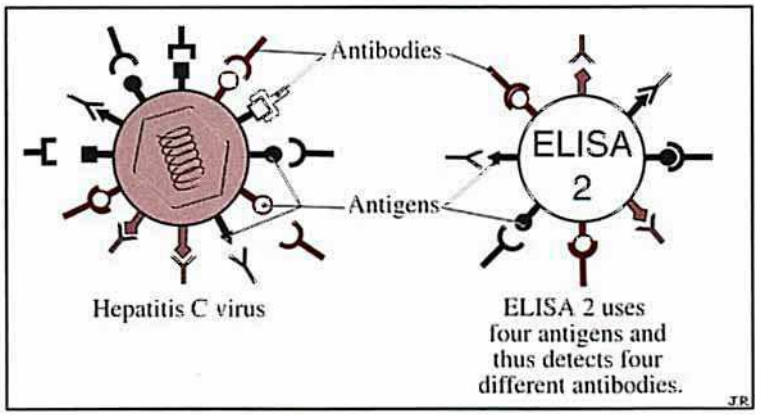

Figure 2–7 The ELISA 2 test uses four antigens.

Recombinant Immunoblot Assay

If you test positive on ELISA 2, your physician may choose to confirm the diagnosis of hepatitis C with recombinant immunoblot assay (RIBA). This test also measures the presence of hepatitis C antibodies using four antigens that are placed as separate bands on a strip (Fig. 2–8). The reaction between the antibodies in the blood and the antigens can be seen on the strip. If you produce antibodies to only one antigen, it's likely you don't have hepatitis C, and, therefore, you have a "false-positive" ELISA 2 test. If you produce antibodies to several antigens, you probably have been infected with the virus.

While false-positive and false-negative results are possible, the new RIBA 3 will likely offer improved accuracy.

Why do false results occur with these two tests?

Since these tests measure the presence of hepatitis C antibodies and not the virus itself, results can sometimes be misleading.

False-positive results can occur for several reasons:

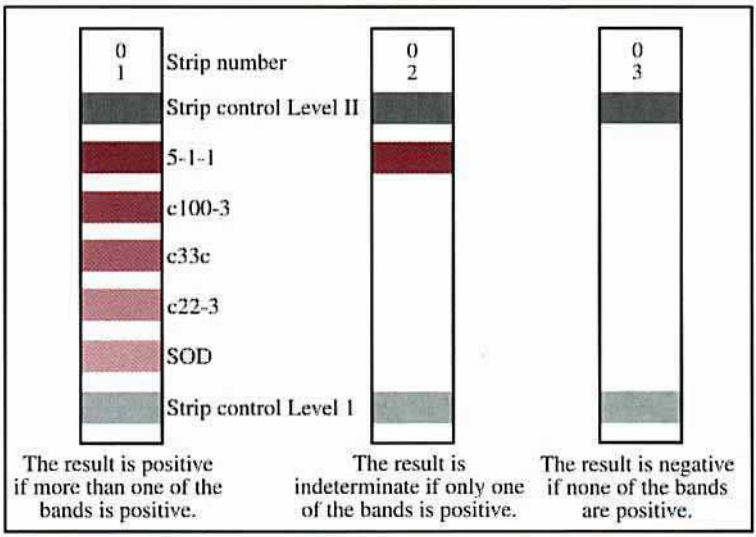

Figure 2–8 The RIBA test strip showing different results.

- Antibodies may be present even though you may be immune to the virus (remember that 15 percent of people clear the hepatitis C virus on their own).
- Antibodies may stay in your bloodstream even after the infection has been cleared by treatment.
- Infants may receive hepatitis C antibodies from their mothers through the placenta (these antibodies will clear within several months following birth).
- Other types of antibodies may react to the hepatitis C antigens or to an enzyme called superoxide dismutase; a reaction against this enzyme can cause a false-positive result.

False-negative results usually occur because the test has been done too early; antibodies only develop 5 to 6 weeks after exposure to the hepatitis C virus.

What tests detect the hepatitis C virus itself?

The hepatitis C virus can be detected in the blood and liver within 2 to 4 weeks after infection, using the reverse transcriptase polymerase chain reaction (PCR) test or the branch DNA (bDNA) test. Either test is used to confirm the presence of hepatitis C virus.

PCR Test

There are two types of the PCR test for detecting the hepatitis C virus:

1. Qualitative—checks if virus is present or absent; and
2. Quantitative—determines how much virus is present (this is called the viral load).

The qualitative PCR test is often done to confirm the diagnosis of hepatitis C.

The quantitative test can then help your physician to estimate how well you will respond or are responding to treatment. It is also used for monitoring your response to treatment (see Chapter 5, page 55 for more information). Some PCR quantitative tests can detect as few as 10 to 100 particles per milliliter of blood.

bDNA Test

This test also measures the presence and quantity of the hepatitis C virus. However, it is not as accurate as the PCR tests at measuring low levels of the virus; it only detects levels higher than 200,000 viral particles per milliliter of blood. Further refinements in the bDNA test are being developed.

CHAPTER THREE

HOW YOU GOT HEPATITIS C AND HOW TO AVOID INFECTING OTHERS

THE SPREAD OF HEPATITIS C

What are the most common ways that the hepatitis C virus is spread?

Hepatitis C is passed on (transmitted) primarily by the exchange of blood. About 60 percent of hepatitis C infections today result from direct exposure to infected blood through current or past illegal drug use. It is estimated that more than 75 percent of people who now use or previously used intravenous drugs may have hepatitis C.

Sharing needles contaminated with infected blood has been the most common way for the virus to be spread. More recently, we have learned that "straws" used for snorting cocaine may be another route for transmitting the virus (Fig. 3–1). People who regularly use cocaine may have open sores (erosions) in the lining of their nose. As a result, drops of blood may be deposited on the straw and then passed on to other people.

Is the hepatitis C virus still transmitted through blood products?

Before widespread blood screening programs were introduced in 1990, hepatitis C was commonly spread through blood products. In fact, hepatitis C accounted for at least 90 percent of liver disease that developed after blood transfusions. The good news is that blood screening programs have dramatically improved the safety of blood products, almost eliminating transfusion as a route for the spread of hepatitis C. The risk of contracting the infection through transfusions is almost nil and

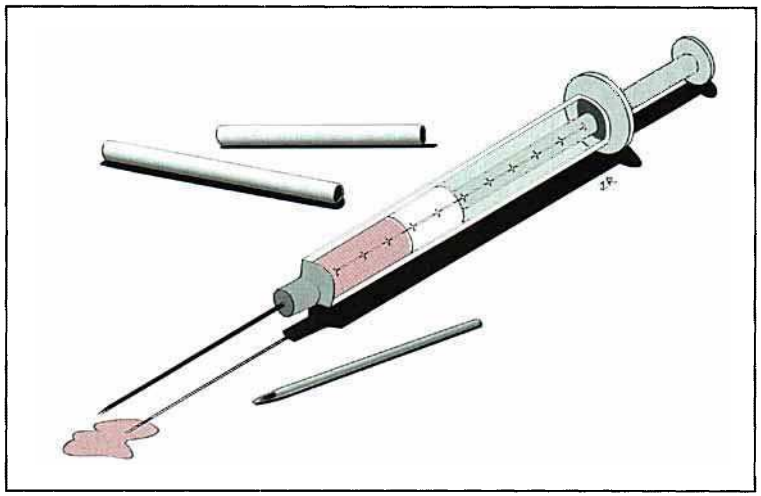

Figure 3–1 Intravenous needles and cocaine straws can spread the virus.

is now considered an exceedingly rare event. The risk will never be completely eliminated because blood donors may give blood before antibodies have appeared in their blood (about 5 to 6 weeks after exposure). At this time, blood screening programs only test for antibodies using ELISA (see Chapter 2, page 31).

Are there other ways for the hepatitis C virus to spread?

We believe that instruments used for body piercing, tattoos, and acupuncture may transmit the hepatitis C virus if they aren't sterilized properly. There are similar concerns regarding the sharing of razors, nail clippers, tooth brushes, and even hair brushes with infected people (Fig. 3–2). However, it is important to note that the hepatitis C virus is hardly ever spread to nonsexual partners in the home.

Figure 3–2 Many household articles should be used with caution.

What about sexual activity?

Hepatitis C may be passed on by sexual contact, although not very often. In part, that's because the hepatitis C virus circulates in your blood at low levels. As well, the hepatitis C virus has been detected at only low levels—or not at all—in body fluids such as semen, vaginal fluid, and saliva.

If you're in a monogamous (single partner) relationship, the chances of passing on the virus to your partner is very low—much less than 5 percent. However, if you have many sexual partners, it's a different story, and it appears that you are at greater risk of being exposed to hepatitis C. We also know that some sexual practices that may injure body tissues (such as anal intercourse, which injures the lining of the rectum) may cause infected blood to enter the bloodstream of a sexual partner.

Can the hepatitis C virus be passed from a pregnant woman to her child?

In a very few instances (about 1 to 3 percent), a mother infected with hepatitis C can pass the virus to her newborn child. This most likely occurs during birth when a mother's blood is mixed with her baby's blood. The type of delivery (caesarean section or vaginal delivery) doesn't appear to have any impact on the risk of the hepatitis C virus being spread from mother to child.

Can the hepatitis C virus be spread through breast milk?

Breast milk has not been proved to spread the virus from mother to child, so women with chronic hepatitis C are not discouraged to breastfeed (Fig. 3–3). Keep in mind that cracked, bleeding nipples (which some women experience initially when breastfeeding) may present a way for the virus to be transmitted.

Is the virus transmitted in health-care settings?

People who work in health-care settings may be at a slightly higher risk for hepatitis C through accidental needle stick injury or injury during surgical operations. Fortunately, the risk is low. If medical instruments are not properly sterilized, hepatitis C virus may be spread from one patient to another. Similarly, laboratory workers, paramedics, policemen, and firemen may occasionally be exposed.

Does everyone know how they got hepatitis C?

Not everyone with hepatitis C remembers any high-risk behavior or event when they may have been exposed to the virus. In some cases, the source of the hepatitis C infection is never identified. In fact, 30 to 50 percent of people with hepatitis C don't know how they got infected.

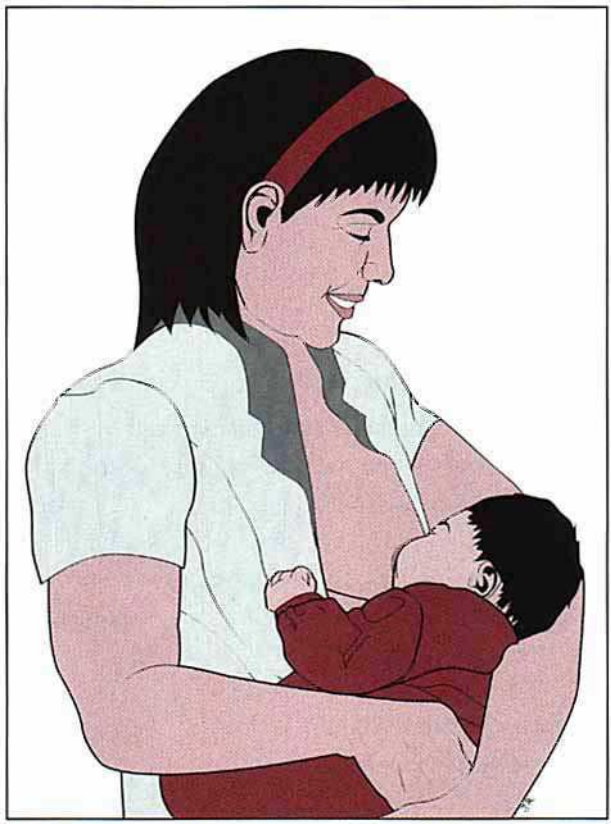

Figure 3–3 Infected women are not discouraged from breastfeeding.

HOW TO AVOID INFECTING OTHERS

Should condoms be always used during sexual contact?

As discussed, there is a very low risk of transmission of the hepatitis C virus between monogamous sexual partners, so barrier precautions (such as latex condoms) are generally not needed.

If you have many sexual partners, safe sexual practices (including the use of latex condoms) are strongly recommended.

Since menstrual blood can carry the virus, it's wise to avoid sexual relations during menstruation. The virus is generally not spread by saliva, so kissing your partner is not a risky activity, unless either one of you has gum disease with bleeding gums. To prevent gum problems, practice good dental care including regular visits to your dentist.

Can an infected woman have a baby?

The risk of passing the virus to a newborn baby is extremely low, so women with hepatitis C are not discouraged when considering pregnancy. A child born to a mother who has hepatitis C should be tested at 1 year of age for the virus, but not before (see Chapter 1, page 19).

It appears that the virus is not spread through breast milk. Unless you have cracked, bleeding nipples, breastfeeding appears to be safe.

How can I avoid infecting other family members or colleagues?

As we've said, the hepatitis C virus is hardly ever spread to nonsexual partners in the home, at work, or in social environments, so you don't need to avoid close contact with them. Hugging, kissing on the cheek, and shaking hands will *not* spread the virus. Sharing food or drink is perfectly safe, too.

Still, there are some commonsense precautions that you can take to help ensure the virus is not transmitted to others.

- Don't share shaving razors, nail clippers, or other manicure tools, depilitating (hair removal) equipment, tooth

brushes, and eating utensils. Some experts also believe that hairbrushes or combs should not be shared, especially in case of scabs on the scalp.
- Always cover open wounds with a bandage.
- Clean any blood stains with a disinfectant.
- Carefully dispose of any injection needles used for treating hepatitis C.

Taking these precautions will protect your family members and give you peace of mind. It's important to understand that having hepatitis C need not interfere with your daily life at home. It also shouldn't stop you from taking part in social, educational, and employment activities.

Can I infect my doctor or dentist?

Health-care workers are at some risk of getting hepatitis C during procedures that involve needles or any other sharp tools. That's why it's important to explain to doctors, nurses, dentists, laboratory technicians, and all other health-care workers that you have hepatitis C before any procedures are done. Make sure that they follow the proper infection control steps, such as wearing gloves and masks and heat-sterilizing all instruments.

What precautions should other people take to avoid being exposed to the hepatitis C virus?

There are precautions everyone should take to avoid exposure to hepatitis C:
- If going to a tattoo artist, ear piercing establishment, acupuncturist, or esthetician, be sure they always use clean, sterilized equipment. If in doubt, ask.

- Ensure that all doctors, dentists, and other health care workers use sterilized or disposable equipment. Be observant, and don't be shy in asking.
- Never share needles or cocaine straws.

CHAPTER FOUR

AFTER YOUR DIAGNOSIS

WHAT TO DO

I find it hard to believe I have hepatitis C. Is this a common reaction?

People experience a wide range of emotions when they learn they have hepatitis C—from disbelief to shock to fear, and everything in between. Whatever you're feeling is perfectly normal and understandable.

The first thing to do is try and calm yourself. Remember, in most people, hepatitis C is a slow-moving disease and only 20 to 30 percent of patients will advance to cirrhosis. Many people will never progress to cirrhosis or will not do so for at least 20 to 30 years. In most cases, we have the time to carefully consider the best course of action for you and with you.

We have many good treatments for hepatitis C, and more are on the way. The results of treatment are improving every year. Even if you don't respond to the treatments available now, research is moving so fast that you may well respond to newer treatments and regimens that are on the way (see Chapter 8, page 89).

Who will be treating me?

Although some family physicians are comfortable treating hepatitis C, most people are sent to a specialist, at least initially. You might be referred to a

- hepatologist (a specialist in liver disease),
- gastroenterologist (a specialist in diseases of the digestive system),
- infectious diseases expert, or
- general internist (a specialist in diseases of the internal organs).

Once your specialist has done the necessary tests and worked out your treatment regimen, your family physician may take over and supervise your treatment. Only occasional visits to the specialist are usually needed.

It's important to find a physician you feel comfortable with and have confidence in. Take the time to get to know your physician. Building a good working relationship means you can work together to treat your condition more effectively. View the treatment as a partnership between you and your physician.

What should I talk to my doctor about?

Your doctor will make sure all the important bases are covered, but it is helpful for you to be prepared with the questions you want answered. You will probably discuss how you may have been exposed to the virus, the tests and treatments you will undergo, and precautions you should take to avoid infecting others. If there is anything you don't understand, be sure to ask. You might prepare a list of questions before each visit, so that you don't forget anything.

Above all, try to be honest with your doctor about your past behaviors (such as intravenous drug use). This may help your doctor pinpoint when you were infected with the virus. Knowing how long you have had hepatitis C will help your doctor evaluate how your disease is progressing and decide on a treatment plan (Fig. 4–1).

MORE TESTS

What tests will be done before my treatment starts?

Thyroid Test

Before your treatment begins, you will be given a test to check how well your thyroid is working. This is done because

Figure 4–1 Talk to your doctor about hepatitis C.

1 to 3 percent of people will develop thyroid disease during treatment that includes interferon. We need to know if you have an existing thyroid problem before we start treatment.

Complete Physical Examination

Your doctor will do a complete physical examination to check

- if your liver or spleen is enlarged (this occurs when scarring blocks the flow of blood through the liver, and the pressure in the spleen is increased);
- if you have rash or joint pain, which may be a sign that you have an extrahepatic disease, such as cryoglobulinemia (see Chapter 2, page 29) that may be related to hepatitis C; and

- if your urine contains any protein that may mean cryoglobulin containing complexes (related to hepatitis C) are affecting the kidneys.

Will a test be done to see how much virus is present in my bloodstream?

Yes, as discussed in Chapter 2 (page 31), there are qualitative tests that detect the hepatitis C virus in the blood. There are also quantitative tests that tell how much virus is present. This is called the viral load. Most physicians are now measuring the viral load. Determining your viral load before treatment provides a benchmark, which can be compared with levels measured during treatment to see how you are responding.

We know that people with a lower viral load generally respond better to treatment than those with a higher viral load. A level of two million virus particles per milliliter of blood has been chosen by researchers as an arbitrary cut-off point; a level below this point is considered a low viral load, while a level above it is considered a high viral load. However, it's important to understand that this figure is only a guideline, and some people with a high viral load may respond well to treatment.

Will I be tested to see which hepatitis C genotype I have?

A test to determine genotype (see Chapter 1, page 9) is not absolutely necessary, and results do not affect the decision to treat. However, identifying your genotype is of interest. The use of the test is becoming more widespread, in part because it is becoming established that the different genotypes may require different treatment schedules. We know that certain genotypes respond better to treatment. For instance, genotype subtypes 2 and 3 generally respond better than subtype 1. Furthermore, genotypes 2 and 3 may respond to 6 months of

therapy, while 1 year of treatment appears to be more effective for genotype 1.

What tests will be done before and during treatment to check on my liver function?

Enzymes

After diagnosis and throughout treatment, your doctor can obtain a good picture of your liver function by measuring the enzymes produced by your liver, including

- alanine aminotransferase (ALT) (see Chapter 2, page 21),
- aspartate aminotransferase (AST),
- gamma-glutamyltransferase (GGT), and
- alkaline phosphatase.

These enzymes are leaked into your bloodstream when the liver is damaged, usually within several hours or days of the damage occurring. Most people with hepatitis C have elevated ALT and AST levels, although the GGT and alkaline phosphatase may remain normal. It is important to remember that levels of ALT do not always correspond to the degree of liver damage. For instance, ALT levels may be normal even though cirrhosis is present (see Chapter 2, page 21).

Bilirubin

As discussed in Chapter 1 (page 5), bilirubin is the yellow pigment that is a by-product of red blood cells when they reach the end of their lives and break down. In some patients who have liver disease, the lifespan of the red blood cells is shortened, thereby adding to the bilirubin load that the liver must process. When damaged, your liver is unable to clear the bilirubin from your bloodstream. The bilirubin builds up, causing your skin and whites of the eyes to turn yellow. This condition is called jaundice.

In most people with hepatitis C, the levels of bilirubin will be normal or only slightly increased, although levels may be quite high if advanced liver disease or cirrhosis is present. Your doctor will measure your bilirubin levels regularly as another way to monitor how your liver is functioning.

Albumin

Albumin, a protein made by your liver, helps to maintain the balance of fluid in your body and helps prevent swelling in the legs or other areas. When your liver isn't working properly, the levels of albumin in your bloodstream will drop. If these levels go low enough, fluid may leak out of your blood vessels and into nearby tissues, causing swelling.

Levels of albumin don't usually fall until chronic liver injury has been present for at least several weeks. Ongoing low levels may indicate poor liver function and cirrhosis. Your albumin levels will be checked regularly.

Complete Blood Count

Low blood counts, particularly white blood cells and platelets, may mean your liver is severely scarred. This scarring disrupts the flow of blood through the liver. As a result, blood backs up into the spleen, which enlarges. White blood cells and platelets are trapped in the enlarged spleen, removing them from circulation and causing blood levels to fall.

Your blood counts will be checked regularly during treatment.

Clotting Factors

The liver produces vital proteins called clotting factors, which maintain the function of blood clotting in your body. When your liver is damaged, the levels of clotting factors can decrease rapidly. This lengthens the time it takes for your blood to clot. One of the more common tests measures the prothrombin

time and, like the other tests discussed above, indicates how well your liver is functioning.

Heart Check

Older people and those with a history of heart problems will have their heart function checked before treatment is started and periodically during treatment. In some people, this evaluation will include a stress test. The heart tests are especially important if your doctor is considering using combination therapy of interferon and ribavirin (see Chapter 5, page 60). The regular use of ribavirin leads to a fall in hemoglobin by causing a type of anemia called nonimmune hemolytic anemia (where the red blood cells break down too rapidly). Anemia may put extra strain on the heart.

LIVER BIOPSY

What is a liver biopsy?

A liver biopsy is a procedure which removes a tiny piece of the liver (less than 1/50,000) for analysis under a microscope.

Why is a liver biopsy important?

A liver biopsy is the only certain way to confirm the presence and extent of liver damage caused by hepatitis C. A physician is greatly helped by knowing the extent of damage, especially the amount of scarring. It also allows the physician to rule out other disorders such as granulomatous liver disease, infections, biliary tract disorders, or liver cancer.

Many doctors will do a liver biopsy in a person with hepatitis C, especially if the person has high ALT levels, which suggest that the liver is inflamed. The biopsy will help confirm the cause and severity of the problem.

A liver biopsy is also a useful tool for measuring your response to treatment.

How is a liver biopsy done?

Nowadays, a liver biopsy is an outpatient procedure that only takes a few minutes to perform.

- If you're feeling anxious before the biopsy, you will be given a mild sedative to help you relax, although you will be awake during the entire procedure.
- We anesthetize the skin over the right side of the lower rib cage. In some cases, the location of the liver is determined using ultrasonography (a procedure that creates images of your liver using sound waves).
- A small biopsy needle is inserted through the anesthetized skin and into the liver (Fig. 4–2). You will feel strong pressure but little or no pain when the needle is inserted.
- With the needle, the physician removes a tiny piece of liver.
- You'll remain in the clinic for a few hours to make sure there are no complications. If you develop pain after the biopsy, your doctor may give you medication to relieve it. If you develop any complications (see below), you will have to stay in hospital overnight.

What are the risks of a liver biopsy?

A liver biopsy is a safe procedure that gives us important information about your liver. Rarely, after a liver biopsy, bleeding can occur from the surface of the liver (fewer than 1 in 1,000 people [0.1 percent] will develop this complication). The only other risk is a biopsy needle puncturing a bile duct, lung, or other organ (again, this risk is less than 0.1 percent). If you choose a physician who regularly performs liver biopsies, it is highly unlikely this will occur.

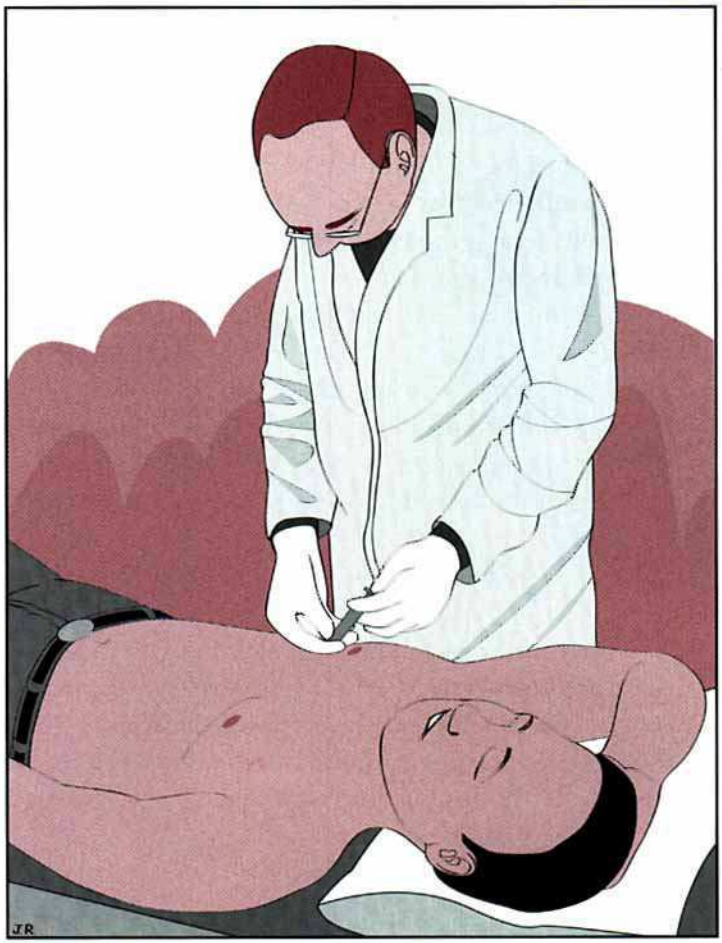

Figure 4–2 Insertion of liver biopsy needle.

What do my biopsy results mean?

After your biopsy has been examined under a microscope, you will be given results in terms of histologic stages ("histologic" refers to the microscopic structure of your liver tissue).

There are four histologic stages of liver injury caused by hepatitis C.

1. Inflammation is present, but fibrosis (scar tissue) has not yet occurred.
2. Inflammation and early fibrosis are present in one part of the liver.
3. Fibrosis is spreading throughout the liver.
4. Cirrhosis (generalized scarring with nodule formation) is present.

It's important to understand that these stages don't necessarily correspond to how long you have had hepatitis C. Nor do they correlate with symptoms, a person with no symptoms could show extensive liver damage on biopsy. That's why it's so vital to have a liver biopsy if your physician recommends it.

MEDICATIONS AND VACCINATIONS

Now that I know I have hepatitis C, should I avoid any prescription or over-the-counter drugs?

As a general rule, no one should take any drugs unless absolutely necessary or advised to do so by their doctor. The more drugs you take, the more likely that you will take a combination that might have a negative interaction. (An interaction means a change in the effect of one drug when taking a second drug with it.)

Most drugs are processed by the liver. Given that your liver is already under pressure from hepatitis C, it makes sense to be careful about the type and number of drugs you take. In particular, the combination of alcohol and acetaminophen (a common ingredient in over-the-counter pain relievers and cold medications) can be very harmful to your liver, and the combination should *always* be avoided.

Should I be vaccinated for hepatitis A and B?

Although it is not fully proved, we believe that if you have one type of hepatitis, you are more likely to become severely ill and develop a greater degree of liver damage if you acquire another type of viral hepatitis. That's why we advise that people with hepatitis C get the hepatitis A vaccine (two injections) and the series of hepatitis B vaccine (three injections). You may be tested first to see if you have hepatitis A or B antibodies. If you do, you won't need a vaccine, as you are already immune to these viruses from previous exposure.

Hepatitis A and B vaccines do not harm your liver and are generally well tolerated and have no side effects. In a few cases, these vaccines may cause mild side effects, such as minor skin irritation at the place of injection.

CHAPTER FIVE

TREATMENT OF HEPATITIS C

THE DECISION TO TREAT

Who receives treatment for hepatitis C?

Deciding whether or not to treat a person with hepatitis C is a complex process and must take into account many factors, such as age, general state of health, stage of the liver disease, risk of cirrhosis, likelihood of response to treatment, and other medical conditions (such as heart disease), which indicate that some treatments should not be used.

It's important that any treatment decisions are made by you and your doctor after a clear and complete discussion about the risks and benefits involved.

As a general guideline, the following criteria determine whether a particular person is a good candidate for treatment:

- Detectable hepatitis C virus, as shown by the PCR qualitative test (see Chapter 2, page 35);
- Persistently elevated ALT levels (at least 1.5 times above normal levels);
- Blood components and other substances made by the liver fall within the following counts: platelets > 70,000/microliter, white blood cells > 3,000/microliter, polymorphonuclear leucocytes > 1,500/microliter, hemoglobin > 11 grams/deciliter, bilirubin < 3 milligrams/deciliter, albumin > 3 grams/deciliter, prothrombin time < 2 to 3 seconds beyond the control value;
- No sign of complications of cirrhosis, such as varices, ascites, or encephalopathy (see Chapter 2, page 24); and
- No medical conditions, such as previous or present major depression (interferon therapy commonly causes depression).

Who should not be treated?

On the basis of the current state of knowledge and proven responses to presently available therapies, hepatitis C should not be treated in every person. Generally, treatment is not given to people who

- continue to drink alcohol in large amounts—we know that alcohol increases the amount of hepatitis C virus in the body and interferes with response to treatment (see Chapter 6, page 70),
- continue to use intravenous drugs, as they have a greater risk of being infected again and have continuing suppression of their immune systems,
- have complications of cirrhosis—there is no evidence that treatment will be helpful to them,
- have mild liver disease of known long duration, especially those over 60 years of age with other health problems,
- have chronic kidney failure,
- have, or used to have, severe depression, and
- have a known autoimmune disease.

As discussed earlier (Chapter 4, page 47), people with a higher viral load are less likely to respond to treatment; however, this is never a reason to deny treatment. The same goes for genotype. Although people with genotype 1 often do not respond as well, they are never denied treatment for this reason.

People with chronic hepatitis C in whom the ALT levels are persistently normal represent a special category in which the benefits of treatment are less certain. It has been established that individuals who have normal ALT levels generally have less evidence of ongoing liver injury on liver biopsy and have less severe disease. However, some of these individuals will have significant liver injury (even cirrhosis) on liver

biopsy. The results of treatment in this group have often been less favorable. The only endpoints to measure are decreases in HCV–RNA levels and changes on liver biopsy. Many studies are ongoing in this important group and the treatment recommendations are being updated constantly. Presently, it is recommended that people with chronic hepatitis C who have normal ALT levels enter clinical trials so that we can more confidently assess the benefits of treatment.

What are the goals of treatment?

When treating hepatitis C, the primary goal is to clear the virus from your body for long-term remission. In this way, further damage to your liver is prevented.

If ridding the virus is not possible, the secondary goal is to slow down the disease and reduce the liver damage that leads to cirrhosis, liver cancer, and the need for liver transplantation. Treatment may favorably affect the manifestations of extrahepatic diseases (see Chapter 2, pages 27–30) even if some virus remains.

INTERFERON

What is interferon?

Interferon is a small protein (cytokine) that was discovered in 1957. It is a natural substance that helps the body protect itself from "foreign invaders." When interferon is given in a dose far greater than the body normally produces, it has two main effects:

- Antiviral—it works to destroy certain viruses; and
- Antiproliferative—it stops the viruses from reproducing. Unfortunately, it also affects other cells like white

blood cells (which puts you at greater risk of infections) and platelets (which puts you at greater risk of bleeding).

There are three types of interferon: alpha (the most effective for treating hepatitis C), beta (less effective), and gamma (not effective).

The Food and Drug Administration (FDA) has approved three alpha interferons to treat hepatitis C in the United States:

1. Interferon alfa-2b (Intron A, made by Schering Plough)
2. Interferon alfa-2a (Roferon, made by Roche)
3. Interferon alfacon-1 (Infergen, made by Amgen)

These alpha interferons appear to be approximately equally effective in treating hepatitis C.

How is interferon given?

Interferon is given by a needle under the skin (subcutaneously). Your doctor will show you how to give yourself injections. Most people quickly learn the proper injection technique and have few, if any, problems. If you don't want to inject yourself, we can teach your partner, other family members, or a friend to do it for you.

How often is interferon taken and for how long?

The approved schedule is three times a week at a dose of three million units or equivalent: three million units of interferon alfa-2b, three million units of interferon alfa-2a, or 9 micrograms of interferon alfacon-1.

Interferon is taken for 6 months to 1 year. People with genotypes 2 or 3 (who usually respond better to treatment) are often on interferon for 6 months (although in some a longer

course is needed), while those with genotype 1 are usually treated for 12 months.

What are the side effects of interferon?

Not everyone experiences the same side effects, and some have few, if any. But, on the whole, interferon will make you feel "bad," at least initially. You may experience

- 'flu-like illness—fever, joint and muscle aches, headache, fatigue,
- reduced appetite, nausea, vomiting, diarrhea,
- depression,
- rash,
- temporary hair loss,
- thyroid problems, and
- reduced platelet and white blood cell counts.

Fortunately, many of these side effects will diminish and even disappear in a few weeks. Until then and for those in whom the side effects are a continuing problem, there are always ways to lessen the unpleasant side effects caused by interferon so that you can continue with your treatment and carry on with all or most of your usual activities. (See Chapter 7, page 74 for more about managing side effects.)

How effective is interferon?

We have found that 40 percent of people treated with interferon alone had their ALT levels return to normal. Unfortunately, relapses (the return of the disease) are frequent. Only 7 to 20 percent of people have a long-term sustained response. (For an explanation of responses, see page 64.) Responses to interferon therapy are sometimes improved when therapy is given for 12 to 18 months, rather than for only 6 months.

COMBINATION THERAPY

What is combination therapy?

Combination therapy consists of alfa-2b interferon and another antiviral drug called ribavirin (Rebetron combination therapy: Intron A and Rebetrol capsules made by Schering Plough).

Ribavirin is a nucleoside analogue, which acts against some RNA and DNA viruses. Initially, researchers used ribavirin on its own for treating people with hepatitis C. The drug used alone was found to lower ALT levels but didn't clear the virus itself. Interest in ribavirin waned until researchers combined it with interferon and achieved impressive results.

After that, two large parallel studies—one in the United States (led by Dr. John G. McHutchison) and one internationally (led by Dr. Thierry Poynard)—tested this combination therapy and reported improved responses to treatment across the board.

In June 1998, combination therapy was approved by the FDA for treating people with hepatitis C who had responded to interferon treatment but had relapsed after it was completed. Later that same year, combination therapy was approved for people with hepatitis C who had never received antiviral treatment.

Ribavirin appears to work synergistically with interferon, that is, together they produce an effect that neither produces alone. Combination therapy is a major breakthrough and is now the favored therapy for most people with hepatitis C.

How is combination therapy given?

Interferon is given by a needle under the skin (subcutaneously), and ribavirin is a capsule that you swallow.

How often is combination therapy taken and for how long?

The approved schedule for interferon is three times a week at a dose of three million units. Ribavirin is taken by mouth twice a day, morning and night, at a dose of 600 to 1200 mg depending on your weight—for those under 75 kg (165 pounds), the dose is usually 1,000 mg per day; for those above 75 kg, the dose is usually 1,200 mg per day. However, many people can't tolerate the higher doses, as their hemoglobin drops too low and they become anemic (see below). If this happens, the dose of ribavirin is reduced, while the dose of interferon remains the same. It is likely that lower doses of ribavirin (800 mg) will prove to be equally effective and better tolerated.

The length of time you take combination therapy may depend on your hepatitis C genotype and viral load, as shown in Table 5–1.

What are the side effects of combination therapy?

When you take combination therapy, you will experience the same side effects of interferon (discussed above), such as headache, fatigue, and depression, as those when interferon is used alone.

One of the most important side effects of ribavirin is a significant drop in hemoglobin (the oxygen-carrying red cells in the blood), which can cause anemia. Signs of anemia include weakness, fatigue, and difficulty breathing. Because of this drop in hemoglobin, many people cannot take ribavirin, including those with anemia, cardiovascular disease, or chronic renal failure.

Ribavirin can cause serious birth defects or loss of pregnancy. That's why we do not prescribe ribavirin to both men and women who are unwilling to follow proper contracep-

Table 5–1 The Duration of Combination Therapy for Hepatitis C

Genotype	Viral Load*	Duration of Treatment
2 or 3	High and low	6 months
1	High	12 months
1	Low	6 to 12 months

*A high viral load is more than 2 million copies per milliliter of blood. A low viral load is less than 2 million copies per milliliter of blood.

tion. Women must have pregnancy tests before and during treatment. And couples must use contraception during treatment and for 6 months after completion of treatment.

Other side effects caused by ribavirin include itching, rash, and shortness of breath. These side effects will likely disappear within a couple of weeks. If not, they can be managed by reducing the dose or, if necessary, stopping the use of ribavirin altogether.

How effective is combination therapy?

Combination therapy is far more effective than interferon alone, as it improves your chances of clearing the virus on a sustained basis, returning ALT levels to normal, and preventing further liver damage. In patients who have not been previously treated, combination therapy leads to a sustained virologic response (an explanation of these response measurements is provided below) in almost 40% of patients who are treated for a year. Even in people who have genotype I (the type most resistant to treatment), 28% of patients responded.

RESPONSE TO TREATMENT

How will my response to treatment be measured?

As shown in Table 5–2, the effectiveness of treatment will be measured by two different responses in your body and two distinct timeframes.

The highest standard of response is a sustained virologic response (that is, you are still clear of the virus 6 months after treatment is finished). A sustained biologic response is good news, too, as it means there is probably no active inflammation occurring in the liver.

If you have achieved a sustained virologic response, you have a 90 percent chance of maintaining this response 5 years after stopping treatment. Keep in mind that there is always a chance that the virus will return; that's why we use the phrase "long-term remission" rather than "cure."

What tests will be done to monitor my response to treatment?

The tests outlined in Chapter 2 (page 31) will be done regularly to assess your response to treatment and identify any troublesome side effects, such as a fall in blood counts.

The most important tests to see how you're responding to treatment are

- ALT levels, which indicates (not always reliably) the degree of liver inflammation;
- quantitative PCR, which detects the amount of virus in your body; and
- follow-up liver biopsy, which shows the extent of inflammation in your liver and is the "gold standard" regarding the status. It is the best indication of how treatment has affected your liver.

Table 5–2 Measuring Effectiveness of Combination Therapy

Response	Timeframe
Biochemical response: ALT levels return to normal	End of treatment response: A response on the last day of treatment
Virologic response: The hepatitis C virus is undetectable	Sustained response: A response 6 months after treatment has finished

When will these tests be done?

The timing of these tests depends on the type of treatment you are taking and the type of response we are measuring.

Initial Response to Interferon Therapy

After 3 months of treatment, you likely will be tested for hepatitis C virus, using a quantitative or qualitative PCR test.

Initial Response to Combination Therapy

After 6 months of treatment, you will be tested for hepatitis C virus, using a quantitative or qualitative PCR test.

End-of-Treatment Response (Both Therapies)

Just before stopping treatment, your ALT levels will be measured, and you will be tested for hepatitis C virus, using a quantitative or qualitative PCR test.

Sustained Response (Both Therapies)

At 6 months after treatment has finished, your ALT levels will be measured, and you will be tested for hepatitis C virus, using a quantitative or qualitative PCR test.

Your doctor may choose to recommend a follow-up liver biopsy, although many wait to perform it until a year or more after completion of therapy. Some choose to monitor the patient without a follow-up biopsy.

Other tests and evaluation will also be done during treatment to detect side effects from treatment:

- A complete blood count (CBC) will be done every several months, although for the first 4 weeks, it will be done weekly in people on combination therapy in order to keep a close watch on blood counts (Fig. 5–1).
- Thyroid tests will be done every 3 to 6 months during treatment, and then 6 months after treatment.
- Your emotional state, especially any depressive feelings, will be checked regularly.

What is breakthrough?

In some cases, people initially respond to interferon-only treatment and then relapse before the end of treatment. This is called "breakthrough". We don't know why this happens, although we think that the virus mutates and produces an interferon-resistant quasispecies (see Chapter 1, page 10). In this situation, combination therapy will likely be started.

What happens if I respond to treatment and then relapse?

Sometimes after treatment is finished, the hepatitis C virus can be detected again and/or ALT levels will rise. This is called a relapse. With interferon-only treatment, this happened in about 50 percent of people. Now with combination therapy, the risk of relapse is much lower.

If you were taking interferon alone and have relapsed, there are two options:

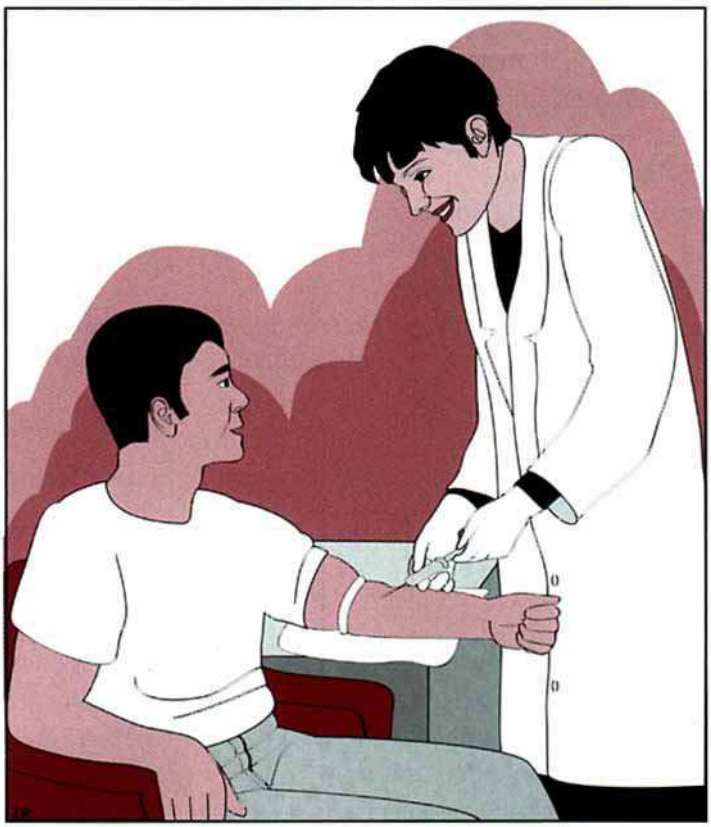

Figure 5–1 Samples of your blood will be taken for testing purposes.

- you will most likely be treated with combination therapy for 6 months or longer (as long as you are able to take ribavirin), *or*
- you will be treated with high doses of another type of interferon for 6 to 12 months.

When is the decision made to stop treatment?

Interferon-Only Treatment

If you respond, you almost certainly will do so in 3 months. Treatment will be stopped after 3 months if your ALT levels haven't returned to normal and if the PCR test shows that the hepatitis C virus hasn't been cleared.

Combination Therapy

Again, if you respond, you will likely do so in 3 months. However, we know that about 15 percent of people will respond between 3 and 6 months, so the decision to stop combination therapy should not be made until 6 months, at which time ALT levels must have returned to normal and the hepatitis C virus cleared, as measured by the PCR test.

Cirrhosis with Complications

If you have cirrhosis and develop complications, such as bleeding from varices, ascites, or encephalopathy (see Chapter 2, page 24), treatment will be stopped, as it will no longer be helpful to you. At this point, liver transplantation may be considered (see page 69).

Why do some people not respond to therapy?

We don't know why some people don't respond to therapy; they may be in the later stages of the disease, or they may have a genotype (or quasispecies) that is relatively unresponsive. (Remember that genotype 1 is the hardest to treat—see Chapter 1, page 10.)

Another reason people don't respond to treatment is lack of compliance (not taking medication as prescribed). Usually, this happens because the side effects have been too troublesome. It's important to tell your physician whether you took your full course of medication. If you didn't, the first option

is to take a full, standard course. If you aren't able to do that, your physician might consider reducing the dose to minimize side effects.

What can be done for people who don't respond to treatment?

If you haven't responded to interferon-only treatment, you will be treated with combination therapy (as long as you can tolerate ribavirin). We don't know yet how effective this therapy is for people who don't respond to interferon-only treatment, but early research shows that up to 20 percent or more of people may respond.

If you can't take ribavirin, you might consider entering a therapeutic trial to try an experimental approach, such as long term maintenance interferon therapy (see Chapter 8, page 90). This approach may be helpful for people who are at most risk for progressive liver disease.

People with mild disease who don't respond to treatment

- may be monitored without further treatment, recognizing that new approaches are being developed;
- given combination therapy (if they can take ribavirin); or
- enrolled in a clinical trial to try one or several experimental approaches being studied.

LIVER TRANSPLANTATION

What is the role of liver transplantation?

While liver transplantations provide hope to people who have cirrhosis with complications or liver cancer, the reality is that these procedures are available to only a few. There is a shortage of donor organs in the United States—roughly 5,000 people will have liver transplantation annually, while over 20,000 are on the waiting list.

That is why the thrust of hepatitis C treatment is to avoid the need for liver transplantation by identifying the virus early, if possible, and treating it aggressively to stop or slow down the progression of liver disease.

If a liver transplantation is done, does the hepatitis C virus infect the new liver?

Yes, hepatitis C returns in almost everyone who receives a transplanted liver, although only 5 percent of people will develop serious, fast-moving disease. We have been studying whether to treat people with interferon or combination therapy after transplantation. At this point, we cannot definitely say that treatment will have an impact, although early results suggest some benefit, particularly with combination therapy.

How well do people do after liver transplantation?

The overall survival rate following liver transplantation in people who have had chronic hepatitis C is as good as the survival rate for liver transplantations taken as a whole. In fact, people have a better than 90 percent chance of being alive up to 3 years after a successful liver transplantation.

Importantly, the quality of life is excellent after transplantation. People go from suffering terrible symptoms, such as jaundice, itching, fluid build up, and mental confusion, to being able to lead a full, productive life again in most cases. After the transplantation, medications are needed to prevent rejection of the transplanted liver. These medications do have side effects, but they can usually be minimized by reducing the dose or changing to another medication.

CHAPTER SIX

ALCOHOL AND HEPATITIS C

WHAT YOU NEED TO KNOW

This chapter is brief but has important information you need to know—facts about alcohol and hepatitis C. You must understand that alcohol not only injures your liver but also interferes with the treatment of hepatitis C. The bottom line is hepatitis C and alcohol don't mix!

How does alcohol affect the liver?

One of the longest known facts in medicine is that drinking too much alcohol over a long period of time causes liver disease. Here are some important things we have learned about alcohol and liver disease.

- In many people, regular drinking causes fat to build up in the liver. In a few people, it causes liver injury and cirrhosis.
- Alcohol interferes with the liver's ability to regenerate itself.
- How much alcohol you drink is important in determining whether you will develop liver disease.
- The type of alcohol you drink appears to make no difference. Whether it's wine, beer, or spirits, drinking any type of alcohol on a regular, long-term basis is harmful to your liver (Fig. 6–1).

How does drinking alcohol affect hepatitis C?

In many ways, hepatitis C and alcohol are a lethal combination. We know that the effects of alcohol and hepatitis C on the liver are additive, that is, they do more damage together than each does alone.

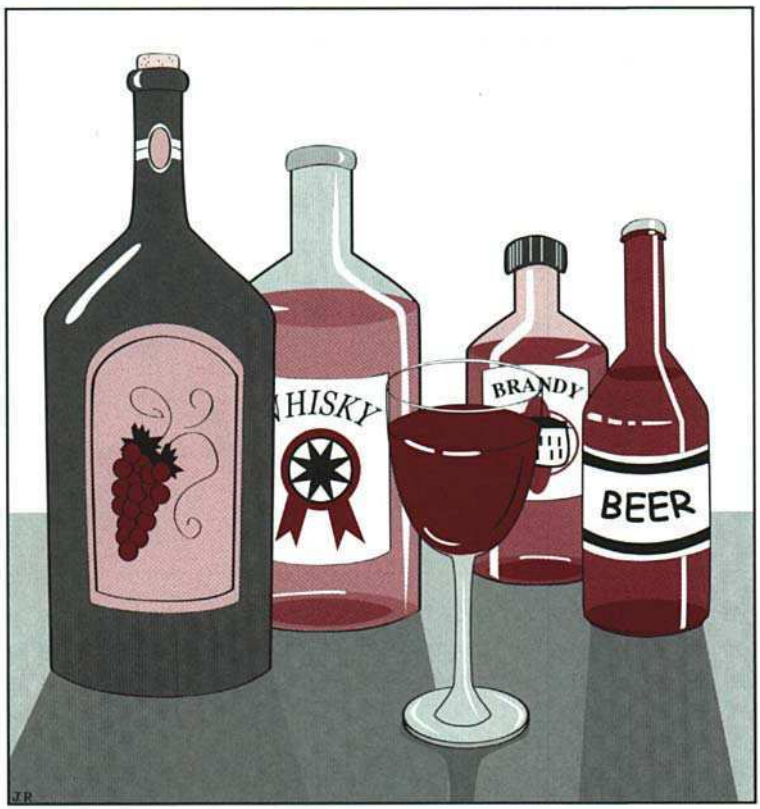

Figure 6–1 All types of alcohol are harmful to your liver.

The excessive use of alcohol can dramatically worsen the long-term outlook of hepatitis C. The development of cirrhosis and liver cancer are much more likely in people with hepatitis C who are alcoholics.

However, alcoholism is not the only cause of trouble. Even the regular use of alcohol—more than two or three drinks each week—appears to reduce the effectiveness of treatment and decreases the chances of having a sustained response.

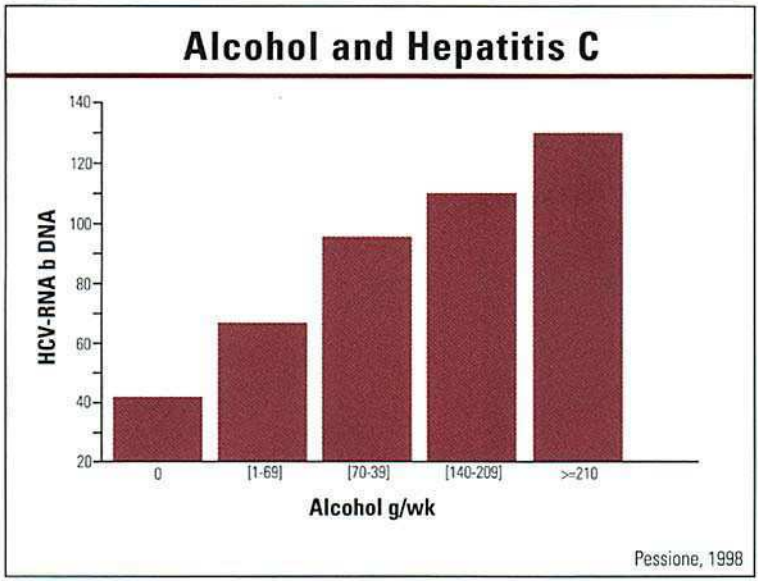

Figure 6–2 The level of hepatitis C virus increases with alcohol consumption. There are approximately 10 grams of alcohol in a bottle of regular beer, 4 ounces of wine, or 1 ounce of 86 proof liquor.

Regular drinking also raises the level of the hepatitis C virus in the body (Fig. 6–2).

Another concern is vitamins. People with hepatitis C who drink regularly may become deficient in important vitamins, especially thiamine and folate.

Is the effect of alcohol different for men and women?

Yes. Studies have shown that women develop liver disease more easily, and at a lower quantity of alcohol as compared with men. We don't know why this is so, although lower body weight and a slower metabolism of alcohol in women may be part of the reason.

Should I stop drinking completely?

You should try to limit alcohol as much as you can. Better yet, try to cut it out completely, particularly if you have severe liver inflammation. We don't know what a safe drinking level is for people with hepatitis C.

If you find you can't stop drinking alcohol completely, limit yourself to no more than an occasional drink—1 to 2 glasses of wine, beer, or spirits per week.

There is no doubt that alcohol is a common and accepted part of many people's lives—from celebrations to stress relief. Trying to cut down or stop drinking is not always easy, but it's certainly worth the effort.

This is the one lifestyle change you can make that may have a big impact on the treatment of hepatitis C.

Can alcohol interact with any drugs I'm taking?

The combination of alcohol and acetaminophen is very harmful to your liver. Acetaminophen is an ingredient in some over-the-counter pain relievers and in many cold medications. Combining alcohol and acetaminophen can cause liver failure, so people with hepatitis C should *always* avoid taking them together. If you're ever unsure whether the medications you take may contain acetaminophen, ask your doctor or pharmacist.

Will I receive treatment if I continue to drink regularly?

As we've said, alcohol interferes with the treatment of hepatitis C and decreases your chances of achieving a sustained response. As a result, a physician generally will not treat persons with hepatitis C if they refuse to stop drinking. No one can successfully treat hepatitis C in the face of ongoing alcohol consumption.

CHAPTER SEVEN

MANAGING HEPATITIS C

COPING WITH SIDE EFFECTS OF TREATMENT

Will I have side effects from hepatitis C treatment?

Less than 5 percent of people develop severe side effects from hepatitis C treatment, although most will experience mild to moderate side effects that can be bothersome especially in the beginning. Fortunately, within a few weeks, many of these effects will subside, once you have developed a tolerance for the medication.

Still, at first, you'll be bothered by side effects and may become discouraged with your treatment, particularly if you had not experienced any symptoms from hepatitis C beforehand. Some people get so discouraged that they skip doses of their medication or stop taking it entirely.

It's vital that you don't allow this to happen. If you skip or stop treatments, your tolerance to the medication will be lost, and side effects will reappear when you start therapy again.

Is there anything I can do to lessen the side effects?

Yes, there are many steps you and your doctor can take to lessen the impact of side effects until you develop tolerance to the medication.

'Flu-Like Symptoms (fever, chills, headache, and muscle aches)

- Take the interferon component of your medication at 7 or 8 o'clock just after your evening meal. This way the side effects will peak at night while you are asleep.
- Take a low dose of acetaminophen (without any alcohol) or a nonsteroidal anti-inflammatory drug before you take your interferon.

- Drink plenty of fluids (at least 6 to 8 glasses of water a day), and get regular, moderate exercise (see page 79).

Gastrointestinal Effects (decreased appetite, nausea, vomiting, and diarrhea)

- Try eating several small meals throughout the day.
- Eat dry crackers, drink weak tea or flat ginger ale, or suck on candies.
- Avoid foods that are spicy, greasy, or deep fried.
- Stay away from citrus juices, such as orange juice, as the acid can upset your stomach.

If these measures don't work, your doctor can prescribe drugs called antiemetics, which prevent nausea and vomiting. Diarrhea can be treated with antidiarrheal medications.

You might experience taste changes caused by your medication or by the liver disease. Red meat, for instance, may taste unpleasant. Since it is important to get enough protein in your diet, try chicken, fish, beans, eggs, or peanut butter if you find it difficult to eat red meat.

Longer-Term Side Effects (fatigue, poor memory, and irritability)

- Conserve your energy by planning ahead for activities, getting help with chores, and setting regular time aside for rest.
- Eat a healthy, well-balanced diet (see page 76).
- Get regular, moderate exercise (see page 79).
- Devise ways to reduce your stress levels—relaxation tapes, deep breathing exercises, meditation, massage therapy, yoga, or journal writing are good choices.

Depression is a common side effect of interferon. It's important to recognize the early signs of depression and

understand how it can be treated. (See page 88 for more information.)

NUTRITION

Should I be eating in a particular way during treatment?

The treatment period is no time to go on a fad diet. There is no particular food we know of which makes any difference to the treatment of hepatitis C. In general, a well-balanced diet is all that is needed for people with hepatitis C. The Food Guide Pyramid (Fig. 7–1) from the U.S. Department of Agriculture (USDA) provides a guide to healthy eating.

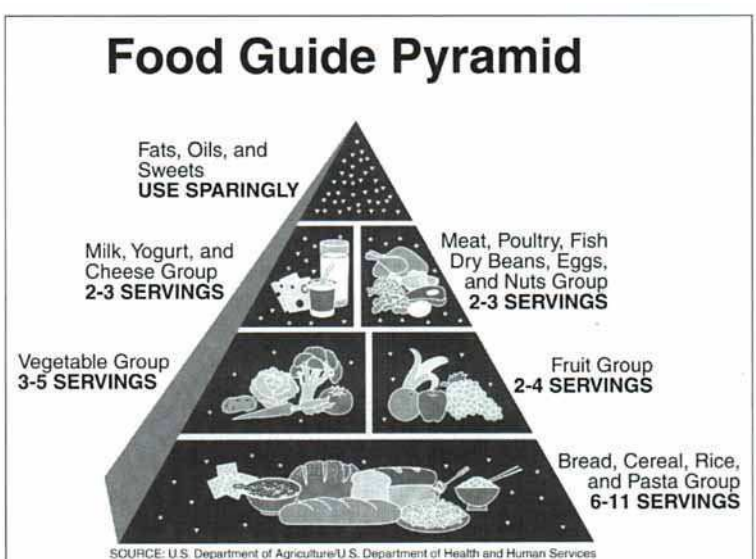

Figure 7–1 Follow the USDA Food Guide Pyramid for a healthy diet.

The Pyramid recommends eating a variety of foods to get the nutrients you need and enough calories to keep to a healthy weight. In general, you should try to eat

- plenty of breads, cereals, and pasta (6 to 11 servings);
- 3 to 5 servings of vegetables and 2 to 4 servings of fruits;
- 2 to 3 servings from the milk group; and
- 2 to 3 servings from the meat group.

Remember to go easy on fats, oils, and sweets.

Calcium-rich foods (such as dairy products) are particularly important for people with advanced hepatitis C. As liver disease progresses, osteoporosis can develop. Osteoporosis is a disease in which bones become thinner and more prone to breaks or fractures. Getting enough calcium through your diet and, if necessary, a supplement is important in preventing osteoporosis from worsening. Regular, moderate exercise is helpful, too.

If you want more in-depth, personalized information to help you plan your diet, your doctor can refer you to a registered dietitian who is specially trained to advise you on proper nutrition.

Is there anything I shouldn't eat?

As stated above, you should avoid high-fat, high-sugar foods. If you have cirrhosis, you may need to limit the amount of salt you eat and, if necessary, the amount of fluid you drink. Cirrhosis interferes with the kidneys' control of salt and water in your body. As a result, fluid can build up in certain tissues and body parts. Some people may need extra help in getting rid of this fluid. Diuretics, which are medications to stimulate the kidneys to lose salt, and water may be used.

If your physician has advised you to cut down on salt, you'll need to pay special attention to food labels when you

shop. Many foods contain hidden salt, such as canned foods, cold cuts, frozen dinners, and condiments including ketchup.

If you have decompensated cirrhosis (cirrhosis with complications), you may have to cut down on protein. Why? Normally, when protein is broken down some potentially toxic products are formed. Your liver removes the toxins from the bloodstream. However, with decompensated cirrhosis, the liver is so damaged that it cannot do its job properly, and the toxins build up in the bloodstream, causing mental changes (encephalopathy, see Chapter 2, page 26).

Should I lose excess weight?

Obviously, the closer you are to your ideal weight, the better your overall health will be. There is no evidence that being overweight makes any difference to the treatment of hepatitis C, although obesity itself can raise ALT levels. This can pose problems when your doctor is assessing your response to treatment.

EXERCISE

Is fitness important during treatment?

Regular, moderate exercise is good for everyone, including people with hepatitis C. Although exercise hasn't been shown to improve the effectiveness of treatment, it can certainly help reduce side effects. Try to become more aware of your body, and learn how to keep it working well. Keep in mind, however, that this is not the time to start a vigorous exercise program to get into shape.

What kind of exercise should I do?

We used to think that only vigorous exercise could improve fitness; we now know that moderate, regular exercise is just as beneficial. Walking (Fig. 7–2), swimming, cycling, and low-impact aerobics are good choices.

How often and for how long should I exercise?

How often and how long you exercise are more important than how hard you do it. You may not know that exercise does not have to be continuous—three 10-minute sessions per day are just as good for you as one 30-minute session. Normal activity counts, too. Gardening, walking the dog, or choosing the stairs over the escalator will get your heart pumping and keep you active.

To avoid injuries, always remember to warm up and cool down whenever you exercise. A warm-up can include 5 minutes of brisk walking followed by light, gentle stretches. Do the same after you have finished exercising until your heart rate has returned to normal and you feel "cool."

Never exercise to the point of pain or exhaustion. Stop exercising right away if you feel:

- a tight feeling in your chest;
- pain in your chest, arms, or jaw;
- severe shortness of breath;
- a rapid throbbing or fluttering of your heart; and
- dizzy, faint, or sick to your stomach.

Remember to talk to your doctor before you begin any type of exercise program.

Figure 7–2 Exercise may help reduce the side effects of hepatitis C.

HERBAL REMEDIES AND VITAMINS

Should I consider taking herbal remedies for hepatitis C?

If you do, you're not alone. In the United States, there are probably more people with hepatitis C using herbal remedies

than the standard, proved treatments. However, being "part of the crowd" is not a wise decision in this case. The worst thing you can do is replace the standard medical treatment with an unproved herbal remedy. If you do, you will miss the chance to clear the hepatitis C virus from your body.

What type of herbal remedies do people with hepatitis C take?

Milk thistle, blessed thistle, dandelion root, fringetree bark, gentian, yellow dock, and various Chinese remedies are only a few of the products used (Fig. 7–3).

Milk thistle (silymarin) is probably the most widely used herbal remedy for hepatitis C. It is an antioxidant, a substance that takes away oxygen "radicals" that can damage tissues. Several reputable scientists have shown that milk thistle can protect the liver in artificial systems, although there have been no controlled trials in humans to prove that it is beneficial.

The advantage of milk thistle is that it is relatively safe. The disadvantage is we don't know if it is effective. Moreover, it can be costly.

What should I keep in mind when considering herbal remedies?

- Don't assume that just because a herbal remedy is natural and available at health food stores, it is safe. Roots and herbs, particularly those from outside the United States, may contain active ingredients that can be harmful to you. Also, these products are not standardized in many cases, and ingredients can vary from bottle to bottle.
- Always tell your doctor about any herbal remedies you plan to take.

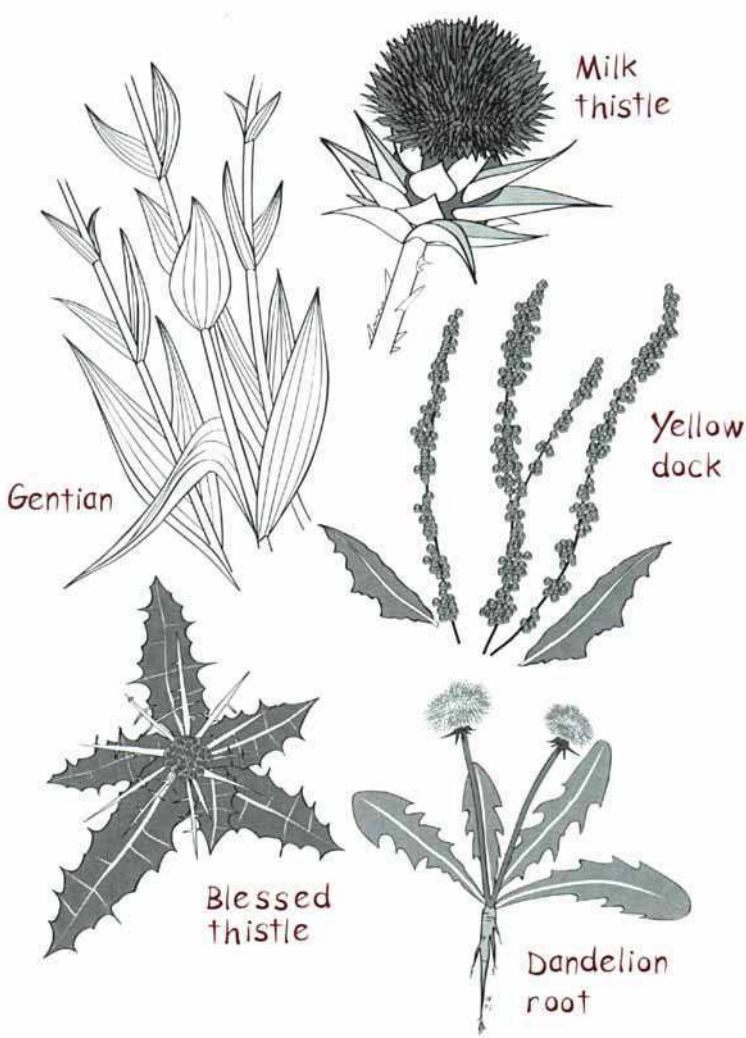

Figure 7–3 Herbal remedies are used by many hepatitis C patients.

- *Never* stop your standard hepatitis C treatment and depend solely on herbal remedies.
- Remember that herbal remedies can be a burden on your pocketbook.

Should I take extra vitamins?

We don't know of any definite evidence that you will benefit from vitamins if you have a balanced diet.

Still, there seems to be no question that antioxidant vitamins are helpful in small doses in preventing damage to the cardiovascular system. Since there are similarities with the mechanisms of heart damage and liver damage, it stands to reason that antioxidants might benefit the liver. It is perfectly reasonable to take an antioxidant multivitamin once a day. As well, you can consider taking 400 IU of vitamin E and 1,000 mg of vitamin C daily.

Are there vitamins I should avoid?

You should avoid high doses of vitamin A (which can harm your liver) and high doses of vitamin D (which can interfere with your calcium-phosphorus metabolism). It is important not to create other problems while using vitamins to treat hepatitis C.

Unless you are anemic (your hemoglobin level is too low) and your doctor specifically recommends iron, do not take any vitamin supplement that contains iron. Too much iron in your liver may make it more difficult for hepatitis C treatments to work.

Like herbal remedies, it's important to talk to your doctor before taking vitamin supplements.

YOUR EMOTIONS

How can I deal with all the emotions I feel?

First of all, allow yourself to feel whatever emotions arise. Coming to terms with the diagnosis of a chronic illness and

learning to manage its treatment are not easy. Your response may be shock, denial, anger, or embarrassment. Whatever you feel is perfectly normal and understandable.

Your feelings may ebb and flow and, sometimes, you might feel you're alone on an emotional rollercoaster. So, the second most important thing is to seek help from family, friends, and support groups (Fig. 7–4).

I'm worried about telling other people that I have hepatitis C. How do I do it?

It's normal to worry about how others will react to the news that you have hepatitis C. After all, most people know very little about this disease and may have many misconceptions about it.

Deciding whom you will tell can be difficult. Think about it carefully. You need to be able to trust the people you tell, and have confidence in their support.

There's almost no way to spread hepatitis C through normal contact, so there's no need to tell everyone you know. For those you do choose to tell, explain hepatitis C in simple terms and how the virus can—and can't—be transmitted. Tell them about the side effects you can expect from treatment, so that they can be prepared. If you want to, share this book with them.

Whether to tell a boyfriend or girlfriend is sometimes a difficult decision. It may depend on how serious the relationship is, but honesty is the best policy. Trust in any relationship—whether old or new—is vital.

The prospect of telling people that you have hepatitis C is difficult, no matter whom you tell. But it is worth it. Others can support you through the emotional hurdles of having hepatitis C (Fig. 7–5). Equally importantly, they can help out

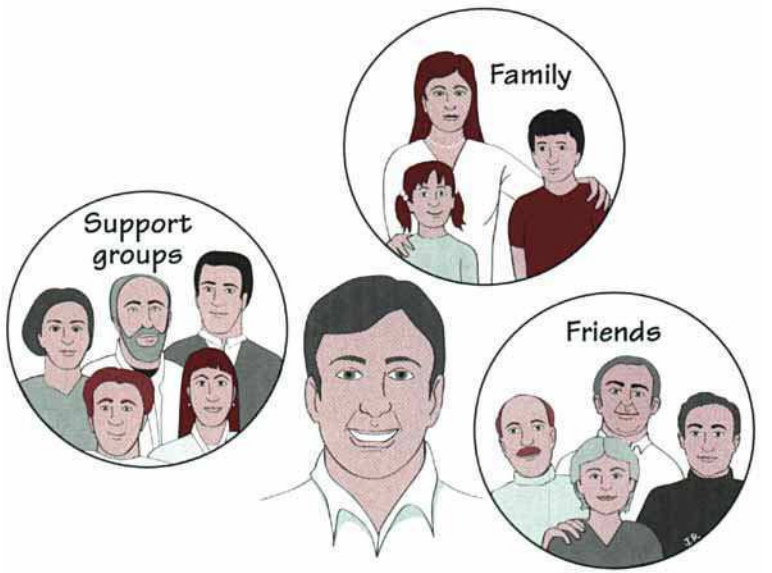

Figure 7–4 Support groups, family, and friends can help you through these emotional times.

with the demands of daily living, such as cooking, cleaning, and visiting the doctor.

How will my family react?

The response will depend on your family members, but, no matter how supportive they may be, a chronic illness can take its toll on those around you. It can upset your family's balance and routine. In some cases, the relationship with your spouse/partner may become strained when he/she learns of your illness and tries to adjust to it.

Try to keep the lines of communication open so that you can work together as a family to cope with hepatitis C. If you need outside help to do this, don't be afraid to ask for it. There are hepatitis C support groups in many areas. A range of

Figure 7–5 Emotional support can help you deal with hepatitis C.

health-care professionals, including psychiatrists, psychologists, social workers, and professional counselors, can help. Ask your doctor for a referral or recommendation.

Is depression common among people being treated for hepatitis C?

Yes, in fact, depression is a side effect of interferon therapy. This treatment appears to temporarily upset the balance of chemicals in your brain, causing depression. Try to prepare yourself by acknowledging there is a good chance you will get depressed. Then, be alert for the early signs, including

- feelings of profound sadness or irritability,

- loss of interest or pleasure in activities you enjoyed before,
- problems with sexual function,
- disrupted sleep patterns,
- inability to concentrate,
- fatigue or loss of energy,
- persistent feelings of guilt, hopelessness, or worthlessness, and
- thoughts of suicide or death.

You can do many things to help fight depression

- Keep active.
- Try to work through the day, so that you're more likely to sleep at night.
- Don't hesitate to use an antidepressant medication as recommended by your doctor. A newer class of drugs called selective serotonin reuptake inhibitors (eg, Prozac, Zoloft, or Paxil) are very effective in treating depression and have been proved to be safe for your liver.
- If necessary, see a mental health professional, who can help you deal with depression and build a positive attitude.

Are support groups a good idea? How do I find out about a group near me?

Most people find support groups are an invaluable way to learn more about hepatitis C and how to cope with diagnosis, treatment, side effects, emotions, and much more. These groups are also an opportunity to meet other people who are going through the same difficulties. And since so much is happening in the hepatitis C field, support groups can help you get up-to-date information on new advances in treatment.

Some support groups are informal, with people meeting to share their personal experiences of hepatitis C. Others are more formal and include health-care professionals trained to

cope with all the aspects of hepatitis C. Choose the type best suited to your needs.

Your doctor or nurse can tell you how to locate a support group in your area. Or you can contact the American Liver Foundation (see Appendix II, page 100).

CHAPTER EIGHT

THE PRESENT AND THE FUTURE

CURRENT TRENDS IN TREATMENT

You should take heart that there is a vast amount of work going on in the hepatitis C field. It's been only a decade since the discovery of the hepatitis C virus, and already we have some effective treatments. The trend towards combination therapies—a valuable lesson learned from the treatment of HIV infection—will continue to expand, and several promising therapies and regimens are on the horizon.

What experimental treatments and regimens are being tested?

Improved Interferon

The next generation of interferon, called PEGylated interferon, is undergoing clinical trials and should be available in the year 2000. When PEGylated interferon is manufactured, special pieces are attached to the interferon molecule that prevents it from being excreted in the urine. As a result, the interferon stays in the bloodstream longer, providing a more stable level of drug over a longer period of time. PEGylated interferon may only need to be given in weekly or biweekly doses, and hopefully side effects will be reduced. Researchers believe that the prolonged effect of PEGylated interferon may be more effective in clearing the hepatitis C virus.

New Treatment Schedules for Interferon

Higher doses of interferon (about the 3 million units or equivalent) and daily induction doses of interferon (higher daily dose of up to 10 million IU for the first few weeks of treatment) are being tested right now. These approaches are based on the philosophy of "hit it hard and hit it early," but they have

not been proved to produce an increase in sustained response (see Chapter 5, page 59). And, as side effects of interferon are related to the dose, side effects likely will worsen if the dose is raised or given more frequently. Studies of these new interferon treatment schedules are currently considered as "work in progress."

Maintenance Therapy

Maintenance interferon therapy means treatment that is continued for a longer period than is the standard practice. Many studies have shown that people who did not fully respond to interferon (by achieving normal ALT levels and a clearance of the virus) still had a reduction in their viral load, ALT levels, and evidence of liver inflammation from a liver biopsy. This may help to slow their disease and prevent liver cancer. Maintenance therapy is being evaluated in clinical trials. Some physicians are recommending maintenance therapy now, although at this point, its benefits are speculative.

Treating People with Normal ALT levels

There are many people with hepatitis C who have normal ALT levels (see Chapter 2, page 24) and we're not sure to what extent these individuals will benefit from currently available therapy. Clinical trials are underway now to assess their response to treatment. In time, there will undoubtedly be effective treatment for people who have hepatitis C and normal ALT levels. For now, there is a wide range of opinions among specialists as to whether (more likely when and with what) to treat.

Amantadine

Combination therapy using amantadine (an experimental antiviral drug that is used to treat influenza) is being studied. At this time, the answers are not in. Until definitive studies are available, it is unlikely that amantadine will enjoy widespread support as an effective treatment for hepatitis C.

What new antiviral therapies are on the "drawing board?"

Some of the most promising candidates are antiviral therapies that are directed at sites on the hepatitis C virus that are responsible for replication. The following therapies are now being investigated by researchers:

- Ribozyme: a new designer molecule that attaches itself to the hepatitis C virus and breaks it open, preventing the virus from replicating.
- Helicase inhibitors: helicase is an enzyme that causes the hepatitis C virus to wind up into a helix and reproduce. If this enzyme is blocked by an agent called a helicase inhibitor, the virus would be unable to replicate.
- Protease inhibitors: we know there is an important enzyme on the hepatitis C virus called the protease. The virus needs the protease to reproduce itself, so researchers are looking for a drug that will block the protease and reduce the viral replication. Similar agents, called polymerase inhibitors, are also being investigated.

What other approaches are being studied?

Reducing iron in the blood through repeated venesection (withdrawing blood from a vein) may improve ALT levels and, with the addition of interferon therapy, may lead to larger decreases in the hepatitis C virus. However, it is not proven that this approach is more effective in achieving the ultimate goal of a sustained response. Further studies are underway to investigate the role of iron removal in the treatment of hepatitis C. For the time being, iron removal should be considered an experimental treatment.

Nonsteroidal anti-inflammatory drugs (NSAIDs) may improve the response to interferon-based treatments, while the use of the hydrophilic bile acid, and ursoodeoxycholic

acid may have a beneficial effect on the chronic inflammatory conditions of the liver. Many people receiving ursoodeoxycholic acid have a decrease in ALT levels, but there is no evidence that the drug has any effect on the hepatitis C virus. Some physicians use ursoodeoxycholic acid in people who have not responded to other treatments in the hope of producing an anti-inflammatory effect. Fortunately, urosodeoxycholic acid is safe and well tolerated. Like iron removal, these approaches require further study.

HEPATITIS C VACCINE

What are the prospects for a hepatitis C vaccine?

Unfortunately, an effective vaccine to prevent hepatitis C is unlikely to become available in the foreseeable future. The reason for this is the nature of the hepatitis C virus. The human body is unable to produce a sufficient immune response to the virus. It appears that there are no naturally occurring antibodies that work effectively against hepatitis C. Furthermore, the virus is constantly mutating, producing many quasispecies (see Chapter 1, page 10). As a result, a single vaccine is not likely to be effective against all forms of the virus.

There are other obstacles to developing a vaccine:

- Animal studies needed to test a vaccine are limited because chimpanzees are the only species (other than humans) that can be infected by the hepatitis C virus.
- The virus does not replicate well in laboratory conditions; therefore, there is much we don't know about how it functions.

Still, there is hope for a vaccine in the future; new approaches that stimulate the immune system to produce highly effective antibodies are under study.

LOOKING AHEAD

Can I be hopeful about the future?

You can—and should—be very hopeful. Hepatitis C will be better understood and more effective therapies will become available. Recognize that you are part of a big segment of society that is moving, as a group, through life with a virus. This virus may hinder your normal life, or it may never bother you.

The hepatitis C virus has been identified, research is going on in many centers, and there is great hope that the successes already obtained are just early signs of what will be available in the future (Fig. 8–1).

Figure 8–1 Research into treatments for hepatitis C is ongoing.

Significant advances in hepatitis C treatment are occurring at a rapid rate and it's likely that by the year 2010, we'll have an effective treatment for everyone. We don't know which one it will be yet, but with so many good candidates, one of them is almost sure to work. As we've mentioned, there is also hope for a vaccine.

In the meantime, learn all you can about hepatitis C, take an active role in your treatment, and build a positive attitude. By doing so, you can take concrete steps toward "conquering" hepatitis C (Fig. 8–2).

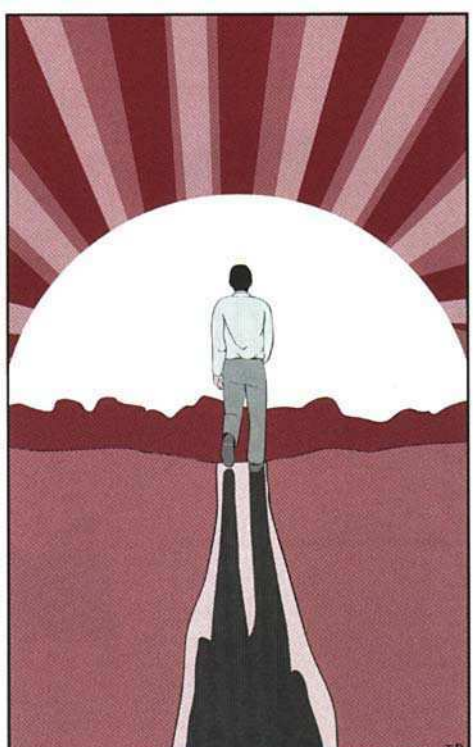

Figure 8–2 Maintain a positive outlook.

APPENDIX I

QUICK REFERENCE TO COMMON QUESTIONS

At the time of diagnosis and throughout treatment, you will have many questions. Some of the more common questions and answers to them are listed below. If you have others, be sure to ask your doctor. The more you know, the more in control you will feel.

1. Can tests used to diagnose hepatitis C be wrong?

Nowadays, the tests that diagnose hepatitis C are much more accurate then they were in the past; however, there is always a chance that they may be wrong. False-positive and false-negative results are possible with every laboratory test. If your doctor is in any doubt, further tests will be done to make sure your diagnosis is accurate. For more information on testing for hepatitis C, turn to Chapter 2, page 31.

2. Can I feel pain in my liver?

You don't actually feel pain in your liver because it has no pain fibers. However, its covering (capsule) does contain pain fibers. If your liver is enlarged or inflamed, it can stretch or expand the capsule, causing pain in your upper right abdomen and under the right lower ribs.

3. What are the chances that I can infect my children or my colleagues?

Virtually nil. The hepatitis C virus is hardly ever spread to nonsexual partners in the home or at work, and you don't need to avoid close contact with them. Hugging, kissing on the cheek, and shaking hands will *not* spread the virus. Shar-

ing food or drink is perfectly all right, and there is no need for separate washing of dishes or clothes used by a person with hepatitis C. There are some commonsense precautions you should take in the home (such as not sharing razors or tooth brushes). You can learn more about these precautions in Chapter 3, page 40.

4. How safe is it for me to continue having sex?

Hepatitis C is transmitted (passed on) primarily by the exchange of blood. (Read more about the routes of transmission in Chapter 3, page 36.) The virus has been detected in very low levels, or not at all, in body fluids such as semen, vaginal fluid, and saliva. As a result, the virus is not easily spread through sexual contact.

If you're in a monogamous (single-partner) relationship, the chances of passing on the virus to your partner is very low—much less than 5 percent. As a result, we believe that barrier precautions (such as latex condoms) are generally not needed in monogamous relationships.

People with many sexual partners may be at increased risk of being exposed to hepatitis C. We also know that some sexual practices that may injure body tissues (such as anal intercourse injuring the lining of the rectum) may allow infected blood to enter the bloodstream of a sexual partner. If you have many sexual partners, you should practice safe sex by using barrier precautions, such as latex condoms. By doing so, you are also protecting yourself from many other sexually transmitted diseases.

5. Can I have a baby? What about breastfeeding?

Only rarely does a mother infected with hepatitis C pass the virus to her newborn child (about 1 to 3 percent). So women

with hepatitis C are not discouraged to get pregnant. Remember that a baby born to a mother with hepatitis C should be tested at 1 year of age. By this time all the antibodies passed from the mother to the child before birth will be gone, and it will be possible to determine if the baby is one of the few who acquired hepatitis C.

Breast milk has not been proved to spread the virus from mother to child, so women with chronic hepatitis C are not discouraged to breastfeed. Keep in mind that cracked, bleeding nipples (which some women experience when first breastfeeding) may be a way for the virus to be passed on. So, if you have cracked, bleeding nipples, stop breastfeeding until they heal.

6. Why should I take a treatment that makes me feel sick when I feel fine right now?

You might feel fine right now (in fact, most patients do); however, hepatitis C can be damaging your liver without your knowing it. Hepatitis C is a "silent" disease which progresses slowly. The damage from hepatitis C often becomes noticeable only after many years. There is a constant battle between the virus, which destroys cells, and the body's immune system, which fights the infection and repairs the damage.

Keep in mind that the success rates of treatment are now up to 40 percent with combination therapy (see Chapter 5, page 60). By undergoing treatment, you are taking out an "insurance policy" on the future. And even if treatment doesn't clear the virus from your body, it can slow down your liver disease and help prevent cirrhosis and the later risk of developing liver cancer. While it's true that the side effects of treatment can be troublesome, it makes much more sense to try and prevent a disease in its early stages, rather than in its later, more dangerous stages.

7. What happens if I skip one or two doses of my medication?

Usually, people skip doses of the medicine because they aren't able to deal with the side effects. You should try to avoid doing this. If you keep taking your medication, your body will develop at least some tolerance, and within a few weeks, the side effects should begin to subside. However, if you skip a dose or two, you may lose this tolerance, and the side effects will return once you restart your medicine. Talk to your doctor if you can't bear the side effects. The doctor may be able to adjust the dosage to lessen the side effects. There are also techniques you can try to better cope with the side effects (see Chapter 7, page 74).

8. I've heard that milk thistle can help treat hepatitis C. Is that true?

Milk thistle (silymarin) is widely used to treat hepatitis C and has been shown to protect the liver in artificial systems. However, you should understand that there have been no controlled studies in humans to prove its effectiveness.

The advantage of milk thistle is that it is relatively safe, and if you want to try it, you can. But before you do so, *be sure* to tell your doctor. Keep in mind that milk thistle can be costly. (For more on herbal remedies, see Chapter 7, page 80.)

9. Can any type of food have a positive effect on hepatitis C?

No one food has been proved to help in the treatment of hepatitis C. The best advice is to eat a healthy, balanced diet (see Chapter 7, page 76). There are some vitamins that might be beneficial, including an antioxidant multivitamin, 400 IU

of vitamin E, and 1,000 mg of vitamin C daily. However, you *must* avoid high doses of vitamin A and vitamin D. Again, be sure to tell your doctor if you plan to take vitamins.

We don't recommend going on extreme diets to lose weight while you are receiving treatment for hepatitis C. It's best to focus first on hepatitis C and make every effort to get rid of the virus.

10. If a treatment for hepatitis C doesn't work for me, will there be another treatment that will?

You can be hopeful that there will be an effective treatment for you within the next several years, even if you don't have a good response on your first try. There is an extraordinary amount of research underway to find new and improved treatments, and it appears that exciting advances are on the way. If something doesn't work for you now, there is bound to be something soon that will.

APPENDIX II

RESOURCES

WHERE TO FIND MORE INFORMATION

The following organizations are reliable sources of accurate information about liver disease and hepatitis C.

American Liver Foundation
75 Maiden Lane, Suite 603
New York, NY 10038
Tel: 1-800-GO-LIVER (1-800-465-4837)
Website: http://www.liverfoundation.org

Centers for Disease Control (CDC) Hepatitis Branch
1600 Clifton Road NE
Atlanta, Georgia 30333
Tel: 1-888-4HEPCDC (1-888-443-7232)
Website: http://www.cdc.gov/ncidod/diseases/hepatitis

Hepatitis Foundation International
30 Sunrise Terrace
Cedar Grove, NJ 07009-1423
Tel: 1-800-891-0707 or 1-973-239-1035
Website: http://www.hepfi.org

National Institute of Allergy and Infectious Diseases
Office of Communications and Publications
Building 31, Room 7A50
31 Center Drive MSC 2520
Bethesda, MD 20892-2520
Tel: 1-301-496-5717
Website: http://www.niaid.nih.gov

HEPATITIS C: SOME COMMON TERMS

The following words are commonly associated with liver disease and hepatitis C. You may, however, hear other terms that you don't understand. If so, be sure to ask your doctor for a clear and simple definition.

ALT	Alanine aminotransferase (ALT) is an enzyme made by the liver. When the liver is damaged, ALT leaks into the bloodstream, causing levels to rise. Testing these levels can help identify the presence of liver damage.
Antibody	A protein in the blood that is part of the immune system. Antibodies work to fight infections that enter the body.
Asymptomatic	No obvious signs or symptoms of a disease.
Cirrhosis	A condition where the liver becomes scarred and changes in structure. If scarring becomes severe, bloodflow through the liver is dramatically altered and reduced, causing serious complications.
Cryoglobulins	A group of sticky proteins produced and sent by the immune system to try to kill the hepatitis C virus. In most cases, the cryoglobulins are unsuccessful. Instead, they combine with parts of the hepatitis C virus and other proteins to make an immune complex that spreads to parts of the body, causing

	excessive fatigue, joint pain, and a raised rash. This condition is called cryoglobulinemia.
Diagnosis	Identifying a disease by examining symptoms and the results of laboratory tests.
DNA	Deoxyribonucleic acid is the part of the cell that carries the genetic information.
End-of-treatment response	A response that is found on the last day of treatment.
Gastroenterologist	A specialist in diseases of the digestive system.
HCV	The hepatitis C virus.
HCV antibodies	Antibodies in the blood stream that are a sign of previous exposure to the hepatitis C virus.
Hepatitis	Inflammation of the liver.
Hepatocellular cancer	Cancer of the liver.
Hepatologist	A specialist in liver diseases.
Immune system	The system your body uses to fight against foreign substances invading it.
Interferon	A family of small, naturally occurring proteins that both destroy viruses and stop them from reproducing. A man-made version of interferon is used to treat hepatitis C.

Jaundice	When the liver doesn't function properly, it slows the clearing of the yellow pigment, bilirubin, from the blood. A build-up of bilirubin causes your skin and the white part of your eyes to turn yellow. This is called jaundice.
Perinatal transmission	When a disease is transferred from mother to child before, during, or after birth.
Prognosis	An estimation of the course of a disease.
Ribavirin	A man-made nucleoside analogue that is used with interferon to treat hepatitis C.
RNA	Ribonucleic acid in cells serves as the platform on which new proteins are produced.
Serum	The liquid part of blood.
Sustained response	A long-term, positive result of medical treatment.
Transmission	The method by which a disease is spread from one person to another.
Virus	A tiny microorganism that can only be seen under a high-powered electron microscope. A virus exists mainly to reproduce and cause infection. It does this by invading cells and using them to make more viruses.

BIBLIOGRAPHY

Everson GT, Weinberg H. Living with hepatitis—a survivor's guide. New York: Hatherleigh Press; 1998.

Davis, GL. Hepatitis C. In: Schiff ER, Sorrell MR, Maddrey WC, editors. Schiff's diseases of the liver, 8th ed. Philadelphia: Lippincott-Raven Publishers; 1998.

Herrera, JL. Chronic hepatitis C: an overview. Am J Managed Care 1998; 4(Suppl): S691–700.

Bernstein D, Schiff ER. Hepatitis C. In: Feldman M, editor. Gastroenterology and hepatology: the comprehensive visual reference. Maddrey WC, editor. Vol 2: The Liver. Philadelphia: Current Medicine; 2000.

Keefe EB, Iwarson S, McMahon BJ, et al. Safety and immunogenicity of hepatitis A vaccine and patients with chronic liver disease. Hepatology 1998;27:881–6.

Davis GL, Estaban-Mur R, Rustgi V, et al. Interferon alfa-2b alone or in combination with ribavirin for the treatment of relapse of chronic hepatitis C. N Engl J Med 1998;339: 1493–9.

McHutchison JG, Gordon SC, Schiff ER, et al. Interferon alfa-2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C. N Engl J Med 1998;339: 1485–92.

Marcellin P, Boyer N, Gervais A, et al. Long-term histologic improvement and loss of detectable intrahepatic HCV RNA in patients with chronic hepatitis C and sustained response to interferon-α therapy. Ann Intern Med 1997; 127:875–81.

Poynard T, Bedossa P, Opolon P, for the OBSVIRC, METAVIR, CLINVIR, and DOSVIRC groups. Natural history of liver fibrosis progression in patients with chronic hepatitis C. Lancet 1997; 349:825–32.

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