



## LIVER CANCER

### What is cancer?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

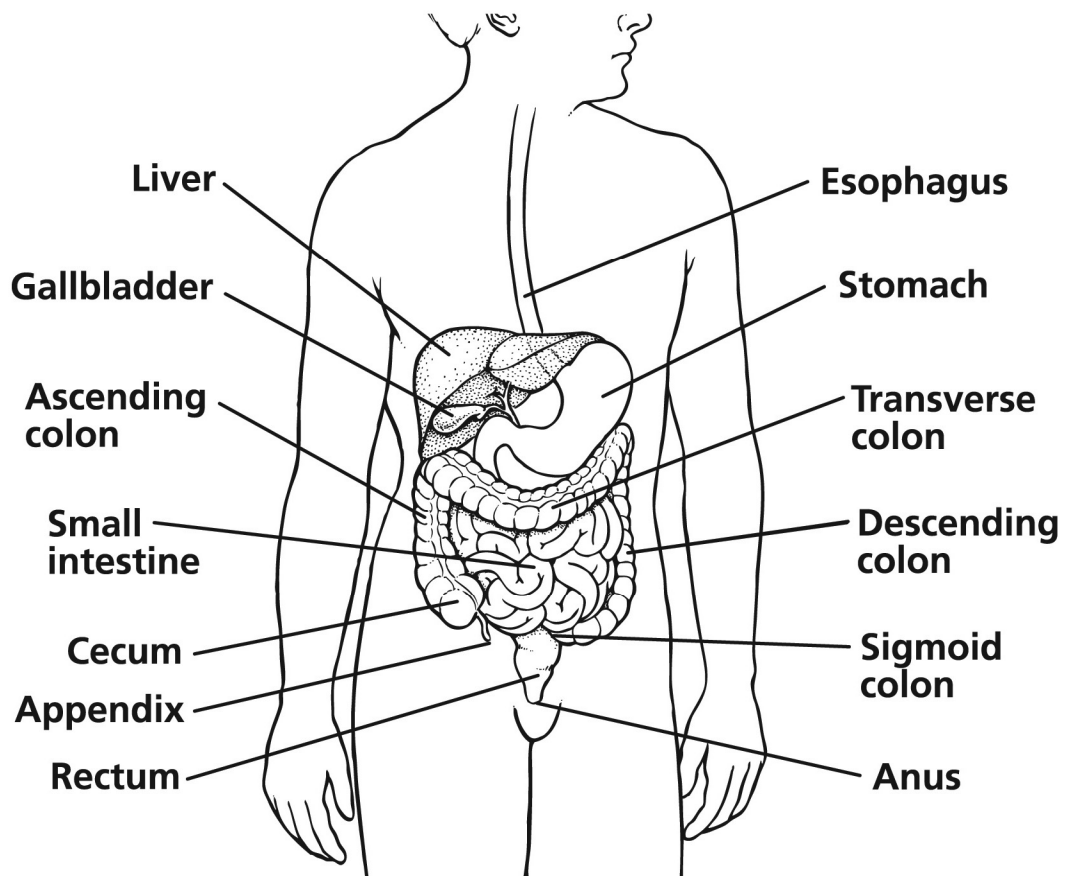
## **What is liver cancer?**

Liver cancer is a cancer that starts in the liver. To understand liver cancer, it helps to know about the normal structure and function of the liver.

### **About the liver**

The liver is the largest internal organ. It lies under your right ribs just beneath your right lung. If you were to poke your fingers up under your right ribs, you could almost touch it.

It is shaped like a pyramid and divided into right and left lobes. The lobes are further divided into segments. Unlike most other organs, the liver gets blood from 2 sources: the *hepatic artery* supplies the liver with blood rich in oxygen from the heart, and the *portal vein* carries nutrient-rich blood from the intestines.



You cannot live without your liver. It has several important functions:

- It breaks down and stores many of the nutrients absorbed from the intestine that your body needs to function. Some nutrients must be changed (metabolized) in the liver before they can be used by the rest of the body for energy or to build and repair body tissues.
- It makes most of the clotting factors that keep the body from bleeding too much when you are cut or injured.
- It secretes bile into the intestines to help absorb nutrients (especially fats).
- It plays an important role in removing toxic wastes from the body.

The liver is made up of several different types of cells. This is why several types of malignant (cancerous) and benign (non-cancerous) tumors can form in the liver. These tumors have different causes, are treated differently, and have a different prognosis (outlook).

## **Benign tumors**

Benign tumors sometimes grow large enough to cause problems, but they do not grow into nearby tissues or spread to distant parts of the body. If they need to be treated, the patient can usually be cured with surgery.

### **Hemangiomas**

The most common type of benign liver tumor, hemangiomas start in blood vessels. Most hemangiomas of the liver cause no symptoms and do not need treatment. But some may bleed and need to be removed surgically.

### **Hepatic adenomas**

These are benign tumors that start from hepatocytes (the main type of liver cell). Most cause no symptoms and do not need treatment. But some eventually cause symptoms, such as pain or a mass in the abdomen (stomach area) or blood loss. Because there is a risk that the tumor could rupture (leading to severe blood loss) and a small risk that it could eventually develop into liver cancer, most experts usually advise surgical removal if possible.

The use of certain drugs may increase the risk of getting these tumors. Women have a higher chance of having one of these tumors if they take birth control pills, although this is a rare complication. Stopping the pills can sometimes cause the tumor to shrink. Men who use anabolic steroids may also develop these. Adenomas may shrink when the drugs are stopped.

### **Focal nodular hyperplasia**

Focal nodular hyperplasia (FNH) is a tumor-like growth of several cell types (hepatocytes, bile duct cells, and connective tissue). Although FNH tumors are benign, it can be hard to tell them apart from true liver cancers, and doctors sometimes remove them when the diagnosis is unclear. If you have symptoms from an FNH tumor, it can be surgically removed and you can be cured.

Both hepatic adenomas and FNH tumors are more common in women than in men.

## **Cancerous tumors that start in the liver**

Several types of cancer can start in the liver.

## **Hepatocellular carcinoma or hepatocellular cancer**

This is the most common form of liver cancer in adults. It is also sometimes called *hepatoma* because it comes from the hepatocytes (the main type of liver cell). About 3 of 4 cancers that start in the liver are this type.

Hepatocellular cancers (HCC) can have different growth patterns:

- Some begin as a single tumor that grows larger. Only late in the disease does it spread to other parts of the liver.
- A second type seems to start as many small cancer nodules throughout the liver -- not just a single tumor. This is seen most often in people with cirrhosis (chronic liver damage) and is the most common pattern seen in the United States.

Under a microscope, doctors can distinguish several subtypes of HCC. Most often these subtypes do not affect treatment or prognosis (outlook). But one of these subtypes, *fibrolamellar*, is important to recognize. This type is rare, making up less than 1% of HCCs. The patients with this type are usually younger (below age 35), and the rest of their liver is not diseased. This subtype has a much better outlook than other forms of HCC.

## **Intrahepatic cholangiocarcinomas (bile duct cancers)**

About 10% to 20% of cancers that start in the liver are intrahepatic cholangiocarcinomas. They start in the small bile ducts (tubes that carry bile to the gallbladder) within the liver. (Most cholangiocarcinomas actually start in the bile ducts outside the liver.)

Although the rest of this document deals mainly with hepatocellular cancers, cholangiocarcinomas are often treated the same way. For more detailed information on this type of cancer, see the separate American Cancer Society document, *Bile Duct (Cholangiocarcinoma) Cancer*.

## **Angiosarcomas and hemangiosarcomas**

These are rare cancers that begin in blood vessels of the liver. People who have been exposed to vinyl chloride or to thorium dioxide (Thorotrast) are more likely to develop these cancers. See the section "What are the risk factors for liver cancer?" Other cases are thought to be due to exposure to arsenic or radium, or to an inherited condition known as hemochromatosis. In about half of all cases, no likely cause can be identified.

These tumors grow quickly and are usually too widespread to be removed surgically by the time they are found. Chemotherapy and radiation therapy may help slow the disease, but most patients do not live more than a year after the diagnosis.

## Hepatoblastoma

This is a very rare kind of cancer that develops in children, usually in those younger than 4 years old. The cells of hepatoblastoma are similar to fetal liver cells. About 70% of children with this disease are treated successfully with surgery and chemotherapy, and the survival rate is greater than 90% for early-stage hepatoblastomas.

## Secondary liver cancer

Most of the time when cancer is found in the liver it did not start there but has spread (metastasized) from somewhere else in the body, such as the pancreas, colon, stomach, breast, or lung. These tumors are named and treated based on their primary site (where they started). For example, cancer that started in the lung and spread to the liver is called lung cancer with spread to the liver, not liver cancer. In the United States and Europe, secondary (metastatic) liver tumors are more common than primary liver cancer. The opposite is true for many areas of Asia and Africa.

For more information on liver metastases from different types of cancer, refer to the American Cancer Society documents on these cancer types, and to our document, *Advanced Cancer*.

**Most of the remaining content in this document refers only to hepatocellular cancer.**

## What are the key statistics about liver cancer?

The American Cancer Society most recent estimates for primary liver cancer and intrahepatic bile duct cancer in the U.S. are for 2009:

- about 22,620 new cases (16,410 in men and 6,210 in women) will be diagnosed
- about 18,160 people (12,090 men and 6,070 women) will die of these cancers

The percentage of Americans developing liver cancer had been increasing in the second half of the 20th century, but the rate seems to have been stable in recent years. The actual number of cases has gone up, but this is in part because the population is increasing.

Liver cancer is more common in men than in women, although it is still fairly rare in the United States in both groups. An average man's lifetime risk of getting liver or intrahepatic bile duct cancer is about 1 in 100, while an average woman's risk is about 1 in 217. Most cases occur in people with certain risk factors (see the section, "What are the risk factors for liver cancer?").

The average age at diagnosis of liver cancer is 64. More than 90% of people diagnosed with liver cancer are older than 45 years of age. About 4% are between 35 and 44 years of age and less than 3% are younger than 35.

This cancer is many times more common in countries in sub-Saharan Africa and Southeast Asia than in the United States. In many of these countries it is the most common type of cancer. More than 500,000 people are diagnosed with this cancer each year throughout the world.

## **What are the risk factors for liver cancer?**

A risk factor is anything that affects your chance of getting a disease, such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for several types of cancer.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may not have had any known risk factors.

Scientists have found several risk factors that make a person more likely to develop hepatocellular carcinoma (HCC).

### **Gender**

Hepatocellular carcinoma is much more common in males than in females, although much of this is probably because of behaviors affecting the risk factors described below. The fibrolamellar subtype of HCC occurs in about equal numbers in both sexes.

### **Race/ethnicity**

In the United States, Asian Americans and Pacific Islanders have the highest rates of liver cancer, followed by American Indians/Alaska Natives and Hispanics/Latinos, African Americans, and whites.

### **Chronic viral hepatitis**

The most common risk factor for liver cancer is chronic (long-term) infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). These infections lead to cirrhosis of the liver (see

below) and are responsible for making liver cancer the most common cancer in many parts of the world.

In the United States, infection with hepatitis C is the most common cause of HCC, while in Asia and developing countries, hepatitis B is more common. People infected with both viruses have a very high risk of developing chronic hepatitis, cirrhosis, and liver cancer.

HBV and HCV are spread from person to person through sharing contaminated needles (such as in drug use), unprotected sex, or childbirth. They can also be passed on through blood transfusions, although this is rare in the United States since the start of blood product testing for these viruses. In developing countries, children sometimes contract hepatitis B infection from prolonged contact with family members who are infected.

Of the 2 viruses, infection with HBV is more likely to cause symptoms, such as a flu-like illness and a yellowing of the eyes and skin (jaundice). But most people recover completely from HBV infection within a few months. Only a very small percentage of adults become chronic carriers (and have a higher risk for liver cancer). The risk is higher in infants and small children who become infected.

HCV, on the other hand, is less likely to cause symptoms. But most people with HCV develop chronic infections, which are more likely to lead to liver damage or even cancer.

Other viruses, such as the hepatitis A virus and hepatitis E virus, can also cause hepatitis. But people infected with these viruses do not develop chronic hepatitis or cirrhosis, and are not at an increased risk of liver cancer.

## **Cirrhosis**

Cirrhosis is a disease in which liver cells become damaged and are replaced by scar tissue. People with cirrhosis have an increased risk of liver cancer. Most (but not all) people who develop liver cancer already have some evidence of cirrhosis.

There are several possible causes of cirrhosis. Most cases in the United States occur in people who abuse alcohol or have chronic HBV or HCV infections. Non-alcoholic fatty liver, a disease in which people who consume no alcohol develop a fatty liver is fairly common (it is often seen in obese people). People with a type of this disease known as non-alcoholic steatohepatitis (or NASH, for short) can go on to develop cirrhosis.

Certain types of inherited metabolic diseases (see below) can cause problems in the liver that lead to cirrhosis. Some types of autoimmune diseases that affect the liver can also cause cirrhosis.

## **Inherited metabolic diseases**

Certain inherited metabolic diseases can lead to cirrhosis. People with hemochromatosis absorb too much iron from their food. The iron settles in tissues throughout the body, including the liver. If enough iron builds up in the liver, they can get cirrhosis and liver cancer. Other rare diseases that increase the risk of liver cancer include:

- tyrosinemia
- alpha1-antitrypsin deficiency
- porphyria cutanea tarda
- glycogen storage diseases
- Wilson disease.

## **Diabetes**

Diabetes can also increase the risk of liver cancer, usually in patients who have other risk factors such as heavy alcohol consumption and/or chronic viral hepatitis.

## **Obesity**

Obesity may increase the risk of developing liver cancer, probably because it can result in fatty liver disease and cirrhosis.

## **Aflatoxins**

These cancer-causing substances are made by a fungus that contaminates peanuts, wheat, soybeans, ground nuts, corn, and rice. Storage in a moist, warm environment can lead to the growth of this fungus. Although this can occur almost anywhere in the world, it is more common in warmer and tropical countries. Developed countries such as the United States and those in Europe regulate the content of aflatoxins in foods through testing. Long-term exposure to these substances is a major risk factor for liver cancer. The risk is increased even more in people with hepatitis B or C infections.

## **Vinyl chloride and thorium dioxide (Thorotrast)**

Exposure to these chemicals raises the risk of angiosarcoma of the liver (see the section, "What is liver cancer?"). It also increases the risk of developing cholangiocarcinoma and hepatocellular cancer, but to a far lesser degree. Vinyl chloride is a chemical used in making

some kinds of plastics. Thorotrast is a chemical that in the past was injected into some patients as part of certain x-ray tests. When the cancer-causing properties of these chemicals were recognized, steps were taken to eliminate them or minimize exposure to them. Thorotrast is no longer used and exposure of workers to vinyl chloride is strictly regulated.

## **Anabolic steroids**

Anabolic steroids are male hormones used by some athletes to increase their strength and muscle mass. Long-term anabolic steroid use can slightly increase the risk of hepatocellular cancer. Cortisone-like steroids, such as hydrocortisone, prednisone, and dexamethasone, do not carry this same risk.

## **Arsenic**

Chronic exposure to drinking water contaminated with naturally occurring arsenic, such as that from some wells, increases the risk of some types of liver cancer. This is more common in parts of East Asia but might also be a concern in some areas of the United States.

## **Factors with uncertain, controversial, or unproven effects on liver cancer risk**

### **Birth control pills**

Birth control pills, also known as oral contraceptives, are a cause of benign tumors called hepatic adenomas. But it is not known if they increase the risk of hepatocellular cancer. Some of the studies that have looked at this issue have suggested there may be a link, but most of the studies were not of high quality and looked at types of pills that are no longer used. Current birth control pills use different types of estrogens, different estrogen doses, and different combinations of estrogens with other hormones. It is not known if the newer pills increase liver cancer risk.

### **Tobacco use**

Some studies have found a link between smoking and liver cancer, but the extent of this is not known. This link seems to be strongest among people with viral hepatitis or who drink a lot of alcohol.

## **Do we know what causes liver cancer?**

Although several risk factors for hepatocellular cancer are known, the exact way in which these factors cause normal liver cells to become cancerous is only partially understood.

Cancers develop when damage occurs to the DNA of cells. DNA is the chemical in each of our cells that makes up our *genes* -- the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. However, DNA affects more than how we look. It also can influence our risk for developing certain diseases, such as some kinds of cancer.

Some genes contain instructions for controlling when cells grow and divide. Genes that promote cell division are called *oncogenes*. Genes that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*. Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes.

Certain chemicals that cause liver cancer, such as aflatoxins, are known to damage the DNA in liver cells. For example, studies have shown that aflatoxins can damage the p53 tumor suppressor gene, which normally works to prevent cells from growing too much. Damage to p53 DNA can lead to increased growth of abnormal cells and formation of cancers.

Infection of liver cells with hepatitis viruses can also damage DNA. These viruses have their own DNA, which carries instructions on how to infect cells and produce more viruses. In some patients, this viral DNA can insert itself into a liver cell's DNA, where it may affect the cell's genes. But scientists still don't know exactly how this leads to cancer.

Although scientists are starting to understand how liver cancer develops, much more must be learned. Liver cancer clearly has many different causes, and there are undoubtedly many different genes involved in its development. In recent years, scientists have created new tools that allow them to look at the activity of thousands of genes in a liver tumor sample at the same time. This is likely to have a major effect on the study of liver cancer in the near future. It is hoped that a more complete understanding will help doctors develop ways to better prevent and treat liver cancers.

## **Can liver cancer be prevented?**

Many liver cancers can be prevented by public health measures that reduce exposure to known risk factors for this disease.

### **Avoiding and treating hepatitis infections**

Worldwide, the most significant risk factor for liver cancer is chronic infection with hepatitis B virus (HBV) and hepatitis C virus (HCV).

A vaccine to help prevent hepatitis B infection has been available since the early 1980s. The Centers for Disease Control and Prevention (CDC) recommends that all children, as well as adults at risk (health care workers, those whose behaviors may put them at risk, etc.) get this vaccine to reduce the risk of hepatitis and liver cancer.

There is no vaccine for hepatitis C. Preventing HCV infection, as well as HBV infection in people who have not been immunized, is based on understanding how these infections occur. These viruses can be spread through sharing contaminated needles (such as in drug use), unprotected sex, and through childbirth.

Blood transfusions were once a major source of infection as well, but this has become extremely rare. Blood banks in the United States test donated blood to look for these viruses. All infected blood is discarded. Because of screening, the risk of getting a hepatitis infection from a blood transfusion in the United States is extremely low.

People at high risk for hepatitis B or C should be tested for these infections so they can be watched for liver disease and treated if needed. Several drugs can be used to treat hepatitis B and C.

Two drugs, interferon alfa and ribavirin, are often used to treat chronic hepatitis C. Interferon can be given alone or along with ribavirin. Combined treatment using a newer form of interferon (called *peg-interferon*) and ribavirin seems to be the most effective treatment at this time. Treatment usually lasts for 6 months to a year and can eliminate the hepatitis C virus in many people. One of the problems with this treatment is that it can cause severe side effects, including flu-like symptoms, fatigue, depression, and low blood counts, which can make it hard to take.

A number of drugs can be used to treat chronic hepatitis B, including interferon (and peg-interferon), lamivudine (Epivir-HBV), adefovir (Hepsera), entecavir (Baraclude), telbivudine (Tyzeka), and tenofovir (Viread). These drugs have been shown to reduce the number of viruses in the blood and lessen liver damage. Although they do not cure the disease, they lower the risk of cirrhosis and may lower the risk of liver cancer, as well.

## **Limiting alcohol and tobacco use**

In the United States, alcohol abuse remains a major cause of the cirrhosis that can lead to liver cancer. Prevention of liver cancers linked with alcohol abuse remains a challenge. Quitting smoking may also slightly lower the risk of liver cancer, as well as lowering the risk for many other life-threatening diseases.

## **Limiting exposure to cancer-causing chemicals**

Changing the way certain grains are stored in tropical and subtropical countries could reduce exposure to cancer-causing substances such as aflatoxins. Many developed countries already have regulations to prevent and monitor grain contamination.

Most developed countries also have regulations to protect consumers and workers from known cancer-causing chemicals. These regulations have essentially eliminated certain chemicals as a cause of liver cancer. The U. S. Environmental Protection Agency (EPA) recently lowered the allowable level of arsenic in drinking water in the United States. But this may continue to be a problem in areas of the world where naturally occurring arsenic commonly gets into drinking water.

## **Treating diseases that increase liver cancer risk**

Certain inherited diseases can cause cirrhosis of the liver, increasing the risk for liver cancer. Finding and treating these diseases early in life could lower this risk. For example, all children in families with hemochromatosis should be screened for the disease and treated if they have it. Treatment lowers their iron intake and removes small amounts of blood to use up the body's excess stores of iron.

## **Can liver cancer be found early?**

Because signs and symptoms of liver cancer do not usually appear until it is in its later stages, it is seldom diagnosed early. Small liver tumors are hard to detect on a physical exam because most of the liver is covered by the right rib cage. By the time a tumor can be felt, it may already be quite large.

Many patients who develop liver cancer have long-standing cirrhosis (scar tissue formation due to liver cell damage). If a patient with cirrhosis gets worse for no apparent reason, doctors should suspect that liver cancer may be the cause and do appropriate tests.

If a person is known to have cirrhosis, whatever the cause, most doctors recommend liver cancer screening every 6 months with tests of alpha-fetoprotein (AFP) and ultrasound. But it's not yet clear if screening will result in more effective treatment of liver cancer.

## **Alpha-fetoprotein blood test**

Alpha-fetoprotein (AFP) is a protein that is normally present at high levels in the blood of fetuses but disappears shortly after birth. If it is found in the blood of adults, it suggests they may have liver cancer or some types of germ cell tumors of the testicle (in men) or ovary (in women). It can also be found in the blood of pregnant women and can be used to help diagnose some birth defects and other problems with the fetus before birth.

Tests for AFP are used to look for early tumors in people at high risk for liver cancer. But it is usually not advised as a routine test to screen for liver cancer in people at average risk because there are potential problems with using it:

- Some liver tumors do not make a lot of this protein.
- Often by the time the AFP level is elevated, the tumor is too large to be removed or it has spread outside the liver.
- Some non-cancerous liver diseases can also raise AFP levels.

In areas where liver cancer is very common, using the AFP blood test for screening has detected many tumors at an earlier stage. Still, many experts feel that AFP testing isn't sensitive enough for people living in the U. S. and Europe, and recommend ultrasound (see the next section) as the main test, although the AFP level may still be measured along with it.

## Ultrasound

Ultrasound is a test that uses sound waves and their echoes to produce a picture of internal organs or masses. A small instrument called a transducer emits sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into a black-and-white image that is displayed on a video screen. This test can show masses (tumors) growing in the liver, which can then be tested for cancer, if needed.

This is a very easy procedure to have. It uses no radiation, which is why it is often used to look at developing fetuses. For most ultrasound exams, you simply lie on a table while the transducer (which is shaped like a wand) is placed on the skin over the part of your body being looked at. Usually, the skin is first lubricated with gel.

This test is used in people with certain liver cancer risk factors to help find cancers earlier. Many experts recommend that the test be done every 6 or 12 months. But no one knows for certain how often is really best.

### **Who should be screened?**

Screening for liver cancer is not recommended for people who are not at increased risk. At this time there are no screening tests that doctors consider to be accurate enough for screening in the general population.

People at higher risk for liver cancer may be helped by screening. Many doctors recommend testing for certain groups. This includes people with cirrhosis (from any cause), especially if the cirrhosis is so severe that the patient is on the waiting list to receive a liver transplant. Without screening, while the person is waiting for a transplant, a cancer may develop and

become so advanced that it is incurable. Finding cancer early usually makes it more likely that the patient will survive longer. Early cancer will also move the person up on the transplant waiting list.

Most doctors also recommend that certain people with chronic HBV or HCV infections be screened, especially those with a family history of liver cancer. In other groups at increased risk, the benefits of screening may not be as clear. If you think you are at increased risk for liver cancer, talk to your doctor about whether screening is a good option for you.

## **How is liver cancer diagnosed?**

Many liver cancers are not found until they start to cause symptoms, at which point they may already be at an advanced stage.

## **Signs and symptoms of liver cancer**

Although signs and symptoms are usually not present until the late stages of liver cancer, sometimes they may show up early and lead to an early diagnosis. If you go to your doctor when you first notice symptoms, your cancer might be diagnosed and treated while it is curable. Or, at the least, you could live longer with a better quality of life. Some of the most common symptoms of liver cancer are:

- weight loss (without trying)
- loss of appetite
- feeling very full after a small meal
- nausea or vomiting
- fever
- an enlarged liver, felt as a mass under the ribs on the right side
- an enlarged spleen, felt as a mass under the ribs on the left side
- constant pain in the abdomen
- swelling or fluid build-up in the abdomen
- itching
- yellowing of the skin and eyes (jaundice)
- enlarged veins on the belly that become visible through the skin
- worsening of your condition if you have chronic hepatitis or cirrhosis

Many of the signs and symptoms of liver cancer can also be caused by other conditions. Still, if you have any of these problems, it's important to see your doctor right away so the cause can be found and treated, if needed.

Some liver tumors make hormones that act on organs other than the liver. These hormones may cause:

- high blood calcium levels (hypercalcemia), which can cause nausea, confusion, constipation, weakness, or muscle problems
- low blood sugar levels (hypoglycemia), which can cause fatigue or fainting
- breast enlargement (gynecomastia) and/or shrinking of the testicles in men
- high counts of red blood cells (erythrocytosis) which can cause someone to look red and flushed

These unusual findings may cause doctors to suspect a disease of the nervous system or an endocrine (hormone-producing) gland, rather than a liver cancer.

If you have one or more of these symptoms, your doctor will try to find if they are caused by liver cancer or something else.

## **Medical history and physical exam**

Your doctor will take your complete medical history to check for risk factors and symptoms. Your doctor will also examine you to look for signs of liver cancer and other health problems. He or she will probably pay special attention to your abdomen.

If symptoms and/or the results of the physical exam suggest liver cancer might be present, more involved tests will likely be done. These might include imaging tests, lab tests, and other procedures.

## **Imaging tests**

Imaging tests use x-rays, magnetic fields, or sound waves to create pictures of the inside of your body. Imaging tests may be done for a number of reasons, including to help find a suspicious area that might be cancerous, to learn how far cancer may have spread, and to help determine if treatment has been effective.

### **Ultrasound**

This test is used to look for masses in the liver. It is described in the section "Can liver cancer be found early?"

### **Computed tomography (CT)**

The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. This test is very useful in identifying many types of liver tumors. It can provide precise information about the size, shape, and position of any tumors in the liver or elsewhere in the abdomen.

Instead of taking one picture like a standard x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these into images of slices of the part of your body that is being studied.

Before any pictures are taken, you may be asked to drink 1 to 2 pints of a liquid called *oral contrast*. This helps outline the intestine so that certain areas are not mistaken for tumors. You may also receive an IV (intravenous) line through which a different kind of contrast (IV contrast) is injected. This helps better outline structures in your body.

The injection can cause some flushing (redness and warm feeling). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have any allergies or ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you have to lie in while the pictures are being taken.

For a CT scan with portography (pictures of the portal vein which is the large vein leading into the liver from the intestine), contrast material is injected into veins that lead to the liver, to help find tumors in the area.

### **Magnetic resonance imaging (MRI)**

Like CT scans, MRI scans provide detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. A contrast material called *gadolinium* is often injected into a vein before the scan to see details more clearly.

MRI scans can be very helpful in looking at liver cancers. Sometimes they can tell a benign tumor from a malignant one.

MRI scans may be a little more uncomfortable than CT scans. They often take up to an hour. You may be placed inside a large cylindrical tube, which is confining and can upset people with a fear of enclosed spaces. Newer, more open MRI machines can help with this if needed. The MRI machine makes buzzing and clicking noises that you may find disturbing. Some places will provide earplugs to help block these noises out.

## **Angiography**

Angiography is an x-ray procedure for looking at blood vessels. Contrast medium, or dye, is injected into an artery before x-ray images are taken. The dye outlines the blood vessels on x-ray pictures. Angiography can be useful in showing the arteries that supply blood to a liver cancer. This can help surgeons decide whether a cancer can be removed and if so, it can help in planning the operation.

Angiography can be uncomfortable because you must stay very still while the doctor puts a small catheter (a flexible hollow tube) into the artery leading to the liver to inject the dye. Usually the catheter is put into an artery in your inner thigh and threaded up into the liver artery. A local anesthetic is often used to numb the area before inserting the catheter. Then the dye is injected quickly to outline all the vessels while the x-rays are being taken.

Angiography may also be done with a CT scanner (CT angiography) or an MRI scanner (MR angiography). These techniques give information about the blood vessels in the liver without the need for a catheter, although you may still need an IV line so that a contrast dye can be injected into the bloodstream during the imaging.

For more information on these imaging procedures, see the separate American Cancer Society document, *Imaging (Radiology) Tests*.

## **Other procedures**

### **Laparoscopy**

In this procedure, a doctor uses a thin, lighted tube with a small video camera on the end to look at the liver and other internal organs. The tube is inserted through a small incision in the front of the abdomen. Laparoscopy provides a view of organs, which can help in planning surgery or other treatments. Doctors can also use small instruments through this tube to remove tissue samples (biopsies) to look at under the microscope.

Laparoscopy is usually done at an outpatient center but it is still an operation. You will be sedated (made sleepy), and the area where the incision will be made will be numbed. Because the surgeon only makes a small incision to insert the tubes, you should not have much pain after surgery. You should be able to go home after you recover from the anesthesia.

### **Biopsy**

In most cases, the only way to be certain that liver cancer is present is to take a biopsy (sample of the tumor tissue) and look at it under a microscope. But in some cases, if imaging

studies (CT or MRI) show a tumor mass in the liver that is probably cancerous and a blood test reveals the AFP level is very high, a biopsy may not be needed.

Several biopsy methods can be used to take samples of liver tissue.

**Surgical biopsy:** In some cases, a biopsy sample may not be obtained until surgery that is meant to treat the tumor. An incisional biopsy (removing a piece of the tumor) or an excisional biopsy (removing the entire tumor and some surrounding normal liver tissue) can be done during an operation. But since doctors usually prefer to know the exact type of tumor before surgery, other types of biopsy methods are often used.

**Needle biopsy:** If the tumor is large or has spread throughout the liver, a hollow needle can be placed through the skin in the abdomen and into the liver. The skin is first numbed with local anesthesia before the needle is placed.

Different sized needles may be used. For a *fine needle aspiration (FNA) biopsy*, tumor cells are sucked into a very thin needle with a syringe. This can usually confirm a cancer, but it doesn't provide much information about how the cancer cells are arranged. For this reason, doctors often use a slightly larger needle to get a bigger sample. This is known as a *core needle biopsy*.

If the tumor is smaller, the doctor may use ultrasound or CT scanning to guide the needle. With this approach, the doctor slowly advances the needle while its position is checked by one of these imaging tests. When the images show that the needle is in the tumor, a sample is removed and sent to the lab to be looked at under a microscope.

**Laparoscopic biopsy:** Biopsy specimens can also be taken during laparoscopy. This allows the doctor to see the surface of the liver and take samples of abnormal-appearing areas.

## Lab tests

Your doctor may order lab tests for a number of reasons:

- to help diagnose liver cancer
- to determine how well the liver is working, which may affect what types of treatments you can have
- to get an idea of your general health and how well your other organs are working, which also may affect what types of treatments you can have
- to see how well treatment is working
- to look for signs that the cancer has come back after treatment

## **Alpha-fetoprotein blood test**

This test is described in the section "Can liver cancer be found early?" It can be helpful in determining if a liver mass might be cancer, although it is not accurate in every case. A low or normal value on this test does not mean that cancer isn't present, but a very high level can mean that liver cancer is there. It can also be useful in people diagnosed with liver cancer. The alpha-fetoprotein (AFP) level can help determine what treatment options might be appropriate. The test can also be used to help give an idea of how well a treatment is working, as the AFP level should fall after treatment. It can be used after treatment as well, to look for possible signs that the cancer may have come back (recurred).

## **Other blood tests**

**Liver function tests (LFTs):** Because liver cancer often develops in damaged livers, doctors need to know the condition of your liver before starting your treatment. A series of blood tests can help with this. These tests can assess the condition of the part of your liver not affected by the cancer. They measure levels of certain substances in your blood, such as bilirubin, albumin, alkaline phosphatase, AST, ALT, and GGT. If your liver is not healthy, you may not be able to have curative surgery, as the surgery might require removal of a large part of your liver. This is a common problem in people with liver cancer.

**Blood clotting tests:** The liver also makes proteins that help blood clot when you are bleeding. A damaged liver may not make enough of these clotting factors, which could increase your risk of bleeding. Your doctor may order blood tests, such as a prothrombin time (PT), to assess this risk.

**Tests for viral hepatitis:** If liver cancer has not yet been diagnosed, your doctor may also order other blood tests, such as tests for hepatitis B and C. Results showing you have been infected with either of these viruses may make it more likely that liver cancer is present.

**Kidney function tests:** Tests of blood urea nitrogen (BUN) and creatinine levels are often done to assess how well your kidneys are working.

**Complete blood count (CBC):** This test measures levels of red blood cells, white blood cells (which fight infections), and platelets (which help the blood clot). It gives an idea of how the bone marrow, a substance found inside certain bones where new blood cells are made, is functioning.

**Electrolytes and blood chemistry tests:** The blood calcium level may be checked, since liver cancer can cause this level to rise. Liver cancer can sometimes cause the cholesterol level to go up, so this may be checked as well.

## How is liver cancer staged?

Staging is the process of finding out how widespread a cancer is. The stage of a liver cancer is one of the most important factors in considering treatment options.

A staging system is a standardized way for the cancer care team to summarize information about how far a cancer has spread. Doctors use staging systems to get an idea about a patient's prognosis (outlook) and to try to determine the most appropriate treatment.

There are several staging systems for liver cancer, and not all doctors use the same system.

### The American Joint Committee on Cancer (AJCC) TNM system

The American Joint Committee on Cancer (AJCC) TNM system is a major system used to describe the stages of liver cancer. It is based on the results of the physical exam, imaging tests (ultrasound, CT or MRI scan, etc.) and other tests, which are described in the section "How is liver cancer diagnosed?"

The TNM system for staging contains 3 key pieces of information:

- **T** describes the number and size of the primary **tumor(s)**, measured in centimeters (cm), and whether the cancer has grown into organs next to the tumor.
- **N** describes the extent of spread to nearby (regional) lymph **nodes**.
- **M** indicates whether the cancer has **metastasized** (spread) to other organs of the body. (The most common sites of liver cancer spread are the lungs and bones.)

Numbers or letters that appear after T, N, and M provide more details about each of these factors:

- The numbers 0 through 4 indicate increasing severity.
- The letter X means "cannot be assessed" because the information is not available.

#### T groups

- **TX:** Primary tumor cannot be assessed
- **T0:** No evidence of primary tumor
- **T1:** A single tumor (any size) that hasn't grown into blood vessels
- **T2:** Either a single tumor (any size) that has grown into blood vessels, OR more than one tumor where no tumor is larger than 5 cm (about 2 inches) across
- **T3:** Multiple tumors that are greater than 5 cm (about 2 inches) across, OR a tumor that has grown into a major branch of the large veins of the liver (the portal and hepatic veins)

- **T4:** The tumor has grown into a nearby organ (other than the gallbladder), OR the tumor is growing into the thin layer of tissue covering and surrounding the liver (called the *visceral peritoneum*)

### **N groups**

- **NX:** Regional lymph nodes cannot be assessed.
- **N0:** The cancer has not spread to the regional (nearby) lymph nodes.
- **N1:** The cancer has spread to the regional lymph nodes.

### **M groups**

- **MX:** Distant spread cannot be assessed.
- **M0:** The cancer has not spread to distant lymph nodes or other organs.
- **M1:** The cancer has spread to distant lymph nodes or other organs.

### **Stage grouping**

The T, N, and M groups are then combined to give an overall stage:

**Stage I:** T1, N0, M0: There is a single tumor (any size) that has not grown into any blood vessels.

**Stage II:** T2, N0, M0: Either there is a single tumor (any size) that has grown into blood vessels; OR there are several tumors, and all are less than 5 cm (2 inches) in diameter.

**Stage IIIA:** T3, N0, M0: Either there are several tumors, and at least one is larger than 5 cm (2 inches) in diameter; OR a tumor is growing into a branch of the major liver blood vessels (portal vein or hepatic vein).

**Stage IIIB:** T4, N0, M0: A tumor is growing into a nearby organ (other than the gallbladder); OR a tumor has grown into the outer covering of the liver.

**Stage IIIC:** Any T, N1, M0: The cancer has invaded nearby lymph nodes. (Tumors can be any size or number.)

**Stage IV:** Any T, Any N, M1: The cancer has spread to other parts of the body. (Tumors can be any size or number, and nearby lymph nodes may or may not be involved.)

### **Other liver cancer staging systems**

The staging systems for most types of cancer depend only on the extent of the cancer, but liver cancer is complicated by the fact that most patients have liver damage along with their cancer. This also has an effect on treatment options and prognosis.

Although the TNM system defines the extent of liver cancer in some detail, it does not take liver function into account. Several other staging systems have been developed that include both of these factors:

- the Barcelona-Clinic Liver Cancer (BCLC) system
- the Cancer of the Liver Italian Program (CLIP) system
- the Okuda system

These staging systems have not been compared against each other, and at this time there is no single staging system that all doctors use. If you have questions about the stage of your cancer or which system your doctor uses, be sure to ask.

## Child-Pugh score (cirrhosis staging system)

The Child-Pugh score is a measure of liver function, especially in people with cirrhosis. Because people with liver cancer often have 2 diseases, their cancer and cirrhosis, doctors treating liver cancer need to know the extent of liver function. This system looks at 5 factors, the first 3 of which are blood tests:

- blood levels of bilirubin (the substance that can cause yellowing of the skin and eyes)
- blood levels of albumin (a major protein normally made by the liver)
- the prothrombin time (measures how well the liver is making blood clotting factors)
- whether there is fluid (ascites) in the abdomen
- whether the liver disease is affecting brain function

Based on the score, liver function is divided into 3 classes. If all these factors are normal, then liver function is called *class A*. Mild abnormalities are *class B*, and severe abnormalities are *class C*. People with liver cancer and class C cirrhosis are generally too sick for any treatment.

The Child-Pugh score is actually part of the BCLC and CLIP staging systems mentioned previously.

## Localized resectable, localized unresectable, and advanced liver cancer

For treatment purposes, doctors often classify liver cancers by whether or not they can be entirely cut out (resected). Resectable is the medical term meaning "able to be removed by surgery."

**Localized resectable cancers:** Only a small number of patients with liver cancer have tumors that can be completely removed by surgery. This would include most stage I and some stage II cancers in the TNM system, in patients who do not have cirrhosis.

**Localized unresectable cancers:** Cancers that have not spread to the lymph nodes or distant organs but cannot be completely removed by surgery are classified as localized unresectable. This would include some early stage cancers, as well as stage IIIA and IIIB cancers in the TNM system. There are several reasons that it might not be possible to safely remove a localized liver cancer. If the non-cancerous part of your liver is not healthy (due to cirrhosis, for example), surgery might not leave enough liver tissue behind for it to function properly. Also, curative surgery may not be possible if your cancer is spread throughout the liver or is close to the area where the liver meets the main arteries, veins, and bile ducts.

**Advanced cancers:** Cancers that have spread to lymph nodes or other organs are classified as advanced. These would include stage IIIC and stage IV cancers in the TNM system. Most advanced liver cancers cannot be treated with surgery.

## Survival rates for liver cancer

The numbers below come from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database, and are based on patients who were diagnosed with liver cancer (hepatocellular type) between 1996 and 2001. There are some important points to note about these numbers:

- The *5-year survival rate* refers to the percentage of patients who live *at least 5 years* after being diagnosed with cancer. Many of these patients live much longer than 5 years after diagnosis. Five-year relative survival rates assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This is a more accurate way to describe the prognosis for patients with a particular type and stage of cancer.
- The SEER database does not divide liver cancer survival rates by AJCC stages. Instead, it groups cancer cases into summary stages. Localized means only one or 2 tumors in one lobe of the liver, and includes stage I and some stage II cancers. Regional means many tumors, spread to other lobes or parts of the liver, and/or spread to lymph nodes (includes some stage II cancers and all stage III). Distant means that the cancer has spread to distant organs or tissues and is the same as stage IV.
- These numbers were taken from patients treated several years ago. Although they are among the most current numbers we have available, improvements in treatment since then mean that the survival rates for people now being diagnosed with these cancers may be higher.
- Although survival statistics can sometimes be useful as a general guide, they may not accurately represent any one person's prognosis. A number of other factors, including other tumor characteristics and a person's age and general health, can also affect

outlook. Your doctor can tell you how these numbers may apply to you, as he or she is familiar with the aspects of your particular situation.

<b>Stage</b>	<b>5-year Relative Survival Rate</b>
Localized	21%
Regional	6%
Distant	2%

For all stages combined, the relative 5-year survival rate from liver cancer is about 10%. Part of the reason for this low survival rate is that most patients with liver cancer also have other liver problems such as cirrhosis, which itself can be fatal.

Studies have shown that patients with small, resectable tumors who do not have cirrhosis or other serious health problems, are likely to do well if their cancers are removed. Their overall 5-year survival is over 50%.

## How is liver cancer treated?

*This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.*

*The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.*

*Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.*

The first part of this section describes the various types of treatments used for liver cancer. This is followed by a description of the most common approaches used for these cancers based on their stage.

## Making treatment decisions

After liver cancer is diagnosed and staged, the cancer care team can recommend your treatment options. Choosing a treatment plan is a major decision, so it is important to take time and think about your choices.

In creating your treatment plan, an important factor to consider is the stage (extent) of the cancer. But you and your cancer care team will also want to take into account your age, general state of health, and personal preferences.

If time permits, it may be a good idea to seek a second opinion, especially from doctors experienced in treating liver cancer. A second opinion might provide more information and help you feel more confident about the treatment plan being considered.

## Surgery

At this time, surgery, either with resection (removal of the tumor) or a liver transplant, offers the only reasonable chance to cure liver cancer. If all known cancer in the liver is successfully removed, you will have the best outlook for survival.

### Partial hepatectomy

Surgery to remove part of the liver is called *partial hepatectomy*. This operation is only attempted if all of the tumor can be removed while leaving enough healthy liver behind to function. Unfortunately, complete removal of most liver cancers is not possible. Often the cancer has spread beyond the liver, it has become quite large or is present in too many different parts of the liver, or the person is not healthy enough for surgery.

More than 4 out of 5 people with liver cancer in the United States also have cirrhosis. If you have severe cirrhosis, removing even a small amount of liver tissue at the edges of your cancer might not leave enough liver behind to perform essential functions. People with cirrhosis are eligible for surgery only if the cancer is small and they still have a reasonable amount of liver function left. Doctors often assess this function by assigning a Child-Pugh score (see the section "How is liver cancer staged?"), which is a measure of cirrhosis based on certain lab tests and symptoms. Patients who fall into class A are most likely to have enough liver function to have surgery. Patients in class B are less likely to be eligible for surgery. Surgery is not typically an option for patients in class C.

**Possible risks and side effects:** Liver resection is a major, serious operation that should only be done by skilled and experienced surgeons. Because people with liver cancer usually have damage to the other parts of their liver, surgeons have to remove enough of the liver to try to get all of the cancer, yet leave enough behind for the liver to function adequately.

A lot of blood passes through the liver at any given time, and bleeding after surgery is a major concern. On top of this, the liver normally makes substances that help the blood clot. Damage to the liver (both before the surgery and during the surgery itself) can add to potential bleeding problems.

Other possible problems are similar to those seen with other major surgeries and can include infections, complications from anesthesia, and pneumonia.

Another concern is that because the remaining liver still contains the underlying disease that led to the cancer, sometimes a new liver cancer can develop afterward.

## **Liver transplant**

When it is available, a liver transplant has become the best option for some people with small liver cancers. At the present time, liver transplants are reserved for those with small tumors (either 1 tumor smaller than 5 cm or 1 to 3 tumors no larger than 3 cm) that cannot be totally removed, either because of the location of the tumors or because the liver is too diseased for the patient to withstand removing part of it.

According to the Organ Procurement and Transplantation Network, more than 6,000 liver transplants are done each year in the United States. About 10% of these are done in people with liver cancer. The 5-year survival for these patients is around 60%. Not only is the risk of a second new liver cancer significantly reduced, but the new liver will function normally.

Unfortunately, the opportunities for liver transplants are limited. Not many livers are available for patients with cancer because they are generally used for patients with more curable diseases. Increased awareness about the importance of organ donation is an essential public health goal that could make this treatment available to more patients with liver cancer and other serious liver diseases.

An option that has become more popular in recent years is having a living donor give a part of their liver for transplant to a close relative. This can be successful, but it carries risk for the donor. About 300 living donor transplants are done in the United States each year. Only a small percentage of them are for patients with liver cancer.

People needing a transplant must wait until a liver is available, which can take too long for some people with liver cancer. Some doctors suggest a limited resection or other treatments first and then a transplant if the cancer comes back.

**Possible risks and side effects:** Like partial hepatectomy, a liver transplant is a major operation with potential risks (bleeding, infection, complications from anesthesia, etc.). But there are some additional risks after this surgery.

People who get a liver transplant have to be given drugs to help suppress the immune system and prevent the body from rejecting the new organ. These drugs have their own risks and side effects, especially the risk of getting serious infections. By suppressing the immune system, these drugs can also allow any remaining cancer to grow even faster than before. Some of the drugs used to prevent rejection can also cause high blood pressure, high cholesterol, diabetes, and can weaken the bones and kidneys. After a liver transplant, regular blood tests are important to check for signs of rejection. Sometimes liver biopsies are also taken to see if rejection is occurring and if changes are needed in the anti-rejection medicines. Future advances are expected to reduce the risk of liver rejection and the severity of side effects caused by these drugs.

## **Tumor ablation**

Ablation refers to local methods that destroy the tumor without removing it. These techniques are often used in patients with only a few small tumors that cannot be resected. They are not usually considered curative but may produce survival rates equal to surgery in people with small tumors. These treatments are often good options for patients whose disease cannot be cured with surgery. They are also sometimes used to treat cancers in patients waiting for a liver transplant. Ablation is not used for large tumors, it is best for tumors no larger than 2 cm (a little less than an inch) across.

### **Radiofrequency ablation**

This procedure uses high-energy radio waves for treatment. A thin, needle-like probe is placed through the skin and into the tumor. Placement of the probe is guided by ultrasound or CT scans. The tip of the probe releases a high-frequency current that heats the tumor and destroys the cancer cells. This has become a major treatment method for small tumors.

### **Ethanol (alcohol) ablation**

This is also known as percutaneous ethanol injection. In this procedure, concentrated alcohol is injected directly into the tumor to kill cancer cells. This is usually done through the skin using a needle guided by ultrasound or CT scans.

### **Microwave thermotherapy**

In this procedure, microwaves are used to heat and destroy the abnormal tissue.

### **Cryosurgery (cryotherapy)**

This procedure destroys a tumor by freezing it with a metal probe. The probe is guided through the skin and into the tumor using ultrasound. Then very cold gasses are passed through the probe to freeze the tumor, killing the cancer cells. This method may be used to treat larger tumors than the other ablation techniques, but it sometimes requires general anesthesia (where you are asleep).

## **Embolization therapy**

### **Arterial embolization**

Arterial embolization, also known as *transarterial embolization* (or TAE), is another option for tumors that cannot be removed. Embolization can be used for larger tumors -- up to 5 cm (2 inches) -- than the ablative methods. This technique is used to reduce the blood flow to the cancer cells by blocking the artery feeding the area of the liver containing the tumor. This artery is a branch of the hepatic artery, the artery that feeds the liver. Blood flow is blocked

(or reduced) by injecting materials that plug up the artery. Most of the healthy liver cells will not be affected because they get their blood supply from the portal vein.

In this procedure a catheter is put into an artery in the inner thigh and threaded up into the liver. A dye is usually injected into the bloodstream at this time to allow the doctor to monitor the path of the catheter via angiography, a special type of x-ray. Once the catheter is in place, small particles called *microspheres* are injected into the artery to plug it up.

Embolization also reduces some of the blood supply to the normal liver tissue. This may be dangerous for patients with diseases such as hepatitis and cirrhosis in parts of the liver not affected by cancer.

### **Chemoembolization**

This approach, also known as *transarterial chemoembolization (or TACE)* combines embolization with chemotherapy. This is done either by coating the microspheres with chemotherapy drugs before injection, or by giving chemotherapy through the catheter directly into the artery, then plugging up the artery. Studies are looking to see if chemoembolization is more effective than embolization alone.

### **Radioembolization**

This technique combines embolization with radiation therapy. In the United States, this is done by injecting small radioactive beads into the hepatic artery. The beads travel to the tumor and give off small amounts of radiation only at the tumor sites. These techniques are still fairly new and the best ways of doing them is still being studied.

One approach uses microspheres attached to a radioactive element (yttrium-90). Once infused, these beads lodge in the blood vessels near the tumor, where they give off radioactivity for a short while. This treatment has been approved by the FDA and is available through several cancer treatment centers. Long-term data on its use isn't yet available, but in one study more than 40% of patients treated had their tumors shrink.

Another way of delivering radiation to the tumor is in the form of an oil that contains radioactive iodine-131. This substance, known as I-131 lipiodol, is also infused directly into the hepatic artery. One clinical trial found this type of radioembolization may be effective, but more studies are needed to confirm this. It is not available in the United States at this time.

### **Radiation therapy**

Radiation therapy uses high-energy rays to kill cancer cells. There are different kinds of radiation therapy.

## **External beam radiation therapy**

This type of radiation therapy focuses radiation delivered from outside the body on the cancer. With liver cancer, this type of radiation therapy can be used to shrink the cancer to relieve symptoms such as pain. But it has not been shown to improve survival. Although liver cancer cells are sensitive to the radiation, this treatment can't be used at very high doses because normal liver tissue is also easily damaged by radiation.

Radiation therapy is much like getting an x-ray, but the radiation is more intense. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time -- getting you into place for treatment -- usually takes longer. Most often, radiation treatments are given 5 days a week for several weeks.

Three-dimensional conformal radiation therapy (3D-CRT) is a newer form of external-beam radiation therapy that uses sophisticated computers to map the location of a tumor precisely. The patient is fitted with a plastic mold resembling a body cast to keep the body still so that the radiation can be aimed more accurately. Radiation beams are then shaped and aimed at the tumor from several directions. This allows doctors to reduce radiation damage to normal liver tissue and therefore direct higher doses of radiation at tumors. When available, conformal radiation therapy is usually preferred over standard radiation therapy.

## **Radioembolization**

As mentioned in the "Embolization therapy" section, a newer treatment technique is to inject small radioactive beads into the hepatic artery. They lodge in the liver near tumors and give off small amounts of radiation that travel only a short distance.

## **Possible side effects of radiation therapy**

Side effects of external radiation therapy might include sunburn-like skin problems where the radiation enters the body, nausea, vomiting, and fatigue. Often these go away after treatment. Radiation might also make the side effects of chemotherapy worse.

## **Targeted therapy**

As researchers have learned more about the changes in cells that cause cancer, they have been able to develop newer drugs that specifically target these changes. Targeted drugs work differently from standard chemotherapy drugs (which are described in the next section). They often have different (and less severe) side effects.

Like chemotherapy, these drugs work systemically, that is, they enter the bloodstream and reach all areas of the body, which makes them potentially useful against cancers that have spread to distant organs. Because standard chemotherapy has not been effective in most patients with liver cancer, doctors have been looking at targeted therapies more.

## **Sorafenib (Nexavar)**

Sorafenib is a targeted drug that works by blocking both angiogenesis (new blood vessel growth in tumors) and growth-stimulating molecules in cancer cells. This drug has been shown to slow the progression of advanced liver cancer and to help some patients with advanced liver cancer live longer (by an average of about 3 months). But it has not been studied in people who already have poor liver function.

Sorafenib is taken daily as a pill. The most common side effects seen with this drug include rash, diarrhea, high blood pressure, and redness, pain, swelling, or blisters on the palms of the hands or soles of the feet.

## **Chemotherapy**

Chemotherapy is treatment with drugs to destroy cancer cells. Systemic (whole body) chemotherapy uses anti-cancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment potentially useful for cancers that have spread to distant organs.

Unfortunately, liver cancer resists most chemotherapy drugs. The drugs that have been most effective in shrinking the tumors are doxorubicin (Adriamycin), 5-fluorouracil, and cisplatin. But even these drugs shrink less than 1 in 5 tumors, and the responses often do not last long. Researchers continue to study using combinations of drugs, but in most studies, systemic chemotherapy has not helped patients live longer.

## **Hepatic artery infusion**

Because of the poor response to systemic chemotherapy, doctors have studied putting chemotherapy drugs directly into the hepatic artery to see if it might be more effective. This technique is known as hepatic artery infusion (HAI). The chemo goes to the entire liver through the hepatic artery, but the healthy liver breaks down most of the drug before it can reach the rest of the body. This gets more chemo to the tumor than systemic chemo without increasing side effects. The drugs most commonly used include floxuridine (FUDR), cisplatin, mitomycin C, and doxorubicin.

Although early studies have found that HAI is effective in shrinking tumors, more research is still needed. This technique may not be useful in all patients because it often requires surgery to insert a catheter into the hepatic artery, an operation that many liver cancer patients may not tolerate well.

## **Possible side effects of chemotherapy**

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are taken. Common side effects include:

- hair loss
- mouth sores
- loss of appetite
- nausea and vomiting
- increased chance of infections (due to low white blood cell counts)
- easy bruising or bleeding (due to low blood platelet counts)
- fatigue (due to low red blood cell counts)

These side effects are usually short-term and go away after treatment is finished. There are often ways to lessen these side effects. For example, there are drugs that can be given to help prevent or reduce nausea and vomiting. Be sure to ask your doctor or nurse about drugs to help reduce side effects, and let him or her know when you do have side effects so they can be managed effectively.

## **Clinical trials**

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at <http://clinicaltrials.cancer.org>. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at [www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials).

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

## Complementary and alternative therapies

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

### What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

**Complementary methods:** Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven to not be helpful, and a few have even been found harmful.

**Alternative treatments:** Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

### Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

### **The choice is yours**

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

## **Treatment of liver cancer by stage**

Although the AJCC (TNM) staging system is often used to precisely describe the spread of a liver cancer, doctors use a more practical system to determine treatment options. Liver cancers are divided into 3 categories: localized resectable, localized unresectable, and advanced.

### **Localized resectable liver cancer (some T1 or T2, N0, M0 tumors)**

If your cancer is at an early stage and the rest of your liver is healthy, surgery (partial hepatectomy) may cure you. Unfortunately, only a small number of people with liver cancer fall into this category. An important factor affecting outcome is the size of the tumor and whether it has grown into blood vessels. A large tumor (more than 2 inches across) or one that invades blood vessels is more likely to come back in the liver or spread elsewhere after surgery. The function of the rest of the liver and the person's general health are also important.

Clinical trials are now looking at whether patients getting surgery will be helped by getting other treatments in addition to surgery. One study showed that chemoembolization before surgery helped some patients live longer after surgery. Another study found that patients given interferon after surgery were more likely to be alive one year after surgery. Still, not all studies agree and more studies are needed to know the value (if any) of adding other treatments to surgery.

### **Localized unresectable liver cancer (some T1 to T4, N0, M0 tumors)**

Localized, unresectable cancers include tumors that haven't spread but are too large to be removed safely. This also includes cancers that are in certain areas that make it hard to remove them, cancers with 2 or more tumors, or cancers in patients with unhealthy livers. Treating these patients with a partial hepatectomy is often not a good option. These patients may instead be treated with a liver transplant if it is possible. This is a major operation where the liver is removed and replaced with one from a donor. Although this is a very difficult operation, it has helped many people. Transplant can cure the cancer and any underlying liver disease. The 5-year survival rate for patients who had a liver transplant for liver cancer is about 60%.

If you are not a candidate for a transplant, your doctor may recommend ablation of the tumor(s) using one of the methods discussed earlier. Other options may include embolization (with or without chemotherapy or radiation), targeted therapy with sorafenib, chemotherapy (either systemic or via hepatic artery infusion), and/or conformal radiation therapy.

Although it is very unlikely that treatment other than transplantation will cure the cancer, it can reduce symptoms and may prolong life. Because these treatments are not known to be curative, a clinical trial is still a good choice.

### **Advanced liver cancer (includes all N1 or M1 tumors)**

Advanced cancer has spread throughout the liver or outside of the liver (either to the lymph nodes or to other organs). Because these cancers are widespread, they are not treatable by surgery.

If your liver is functioning well enough (Child-Pugh class A or B), the targeted therapy sorafenib may help control the growth of the cancer for a time and may help you live longer.

As with localized resectable liver cancer, clinical trials of targeted therapies, new approaches to chemotherapy (new drugs and regional chemotherapy), new forms of radiation therapy (with radiosensitizers or targeting via antibodies), and other new treatments (immunotherapy and gene therapy) may help you. These clinical trials are also important for improving the outlook for future patients.

Treatments such as radiation or chemotherapy may be used to help relieve pain and other symptoms. Please be sure to discuss any symptoms you have with your cancer team, so they may treat them effectively.

### **Recurrent liver cancer**

Cancer is called recurrent when it comes back after treatment. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the lungs or bone). Treatment of liver cancer that returns after initial therapy depends on many factors, including the site of the recurrence, the type of initial treatment, and how well the liver is functioning.

Patients with localized resectable disease that recurs in the same spot may be eligible for further surgery or local treatments like ablation or embolization. If the cancer is widespread, targeted therapy (sorafenib) or chemotherapy may be options. Patients may also wish to ask their doctor whether a clinical trial may be right for them.

Treatment may also be offered to relieve pain and other symptoms. Please be sure to discuss any symptoms you have with your cancer care team, so they may be treated effectively.

## **More treatment information**

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site ([www.nccn.org](http://www.nccn.org)).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site ([www.cancer.gov](http://www.cancer.gov)). Detailed guidelines intended for use by cancer care professionals are also available on [www.cancer.gov](http://www.cancer.gov).

## **What should you ask your doctor about liver cancer?**

As you cope with cancer and cancer treatment, we encourage you to have honest, open discussions with your doctor. Feel free to ask any question that's on your mind, no matter how small it might seem. Here are some questions you might want to ask. Be sure to add your own questions as you think of them. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions.

- What kind of liver cancer do I have? (There are different types of liver cancer. Also, there are certain subtypes of hepatocellular carcinoma such as the fibrolamellar variety that carry a better prognosis than others.)
- Has my cancer spread beyond my liver?
- What is the stage of my cancer, and what does that mean in my case?
- Are there other tests that need to be done before we can decide on treatment?
- Can my cancer be removed with surgery?

- How well is my liver functioning?
- What treatment choices do I have?
- What do you recommend and why?
- What risks or side effects are there to the treatments you suggest?
- What should I do to be ready for treatment?
- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect my daily activities?
- What are the chances my cancer will recur with these treatment plans?
- What would we do if the treatment doesn't work or if the cancer recurs?
- What type of follow-up would I need after treatment?

In addition to these sample questions, you might want to write down some of your own. For instance, you might want to ask about second opinions or about clinical trials for which you may qualify.

## **What happens after treatment for liver cancer?**

Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called *recurrence*.) This is a very common concern among those who have had cancer.

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. Even with no recurrences, people who have had cancer learn to live with uncertainty.

### **Follow-up care**

After your treatment is over, it is very important to go to all follow-up appointments. During these visits, your doctors will ask about symptoms, do physical exams, and may order blood tests (such as AFP levels or liver function tests) or imaging studies, such as ultrasound, CT, or MRI scans.

If you have been treated with a surgical resection or a liver transplant, most doctors recommend follow-up with imaging tests and blood tests every 3 to 6 months for the first 2 years, then tests every 6 to 12 months. Follow-up is needed to check for cancer recurrence or spread, as well as possible side effects of certain treatments.

This is the time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them effectively.

If cancer does recur, treatment will depend on the location of the cancer, what treatments you've had before, and your health and liver function. For more information on how recurrent cancer is treated, see the section "How is liver cancer treated?" For more general information on dealing with a recurrence, you may also want to see the American Cancer Society document, *When Your Cancer Comes Back: Cancer Recurrence*. You can get this document by calling 1-800-227-2345.

### **Anti-viral treatment**

If you have hepatitis B or C that may have contributed to your liver cancer, your doctor may want to put you on medicines to treat or help control the infection.

### **Seeing a new doctor**

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report(s) from any biopsy or surgery
- if you had surgery, a copy of your operative report(s)
- if you were hospitalized, a copy of the discharge summary that doctors must prepare when patients are sent home
- if you had radiation therapy, a summary of the type and dose of radiation and when and where it was given
- if you had chemotherapy or targeted therapies, a list of your drugs, drug doses, and when you took them

It is also important to keep your health insurance. Even though no one wants to think of their cancer coming back, it is always a possibility. If it happens, the last thing you want is to have to worry about paying for treatment.

## **Lifestyle changes to consider during and after treatment**

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even begin this process during cancer treatment.

### **Make healthier choices**

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn't exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes today that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society's Quitline<sup>®</sup> tobacco cessation program at 1-800-227-2345.

### **Diet and nutrition**

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to put healthy eating habits into place. You will be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Try to eat 5 or more servings of vegetables and fruits each

day. Choose whole grain foods instead of white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

### **Rest, fatigue, work, and exercise**

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a "bone-weary" exhaustion that doesn't get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline some. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired. For more detailed information, see our document *Fatigue in People With Cancer*.

Any program of physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household.

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.

- It helps you feel better about yourself.

And long term, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that adults take part in at least 30 minutes of moderate to vigorous physical activity, above usual activities, on 5 or more days of the week; 45 to 60 minutes of intentional physical activity are preferable. Children and teens are encouraged to try for at least 60 minutes a day of energetic physical activity on at least 5 days a week.

## **How about your emotional health?**

Once your treatment ends, you may find yourself overwhelmed by emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through your treatment.

Now you may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide not to include them. Let them in -- and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-ACS-2345 and we can put you in touch with an appropriate group or resource.

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life, making healthy choices and feeling as well as possible, physically and emotionally.

## **What happens if treatment is no longer working?**

If cancer continues to grow after one kind of treatment, or if it returns, it is often possible to try another treatment plan that might still cure the cancer, or at least shrink the tumors enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it's important to weigh the possible limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it's just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called *palliative treatment*.

Palliative treatment helps relieve these symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this is given at home. Your cancer may be causing symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. It just means that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. In a way, pausing at this time in your cancer treatment is an

opportunity to refocus on the most important things in your life. This is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do.

## What's new in liver cancer research and treatment?

Because there are only a few effective ways to prevent or treat liver cancer at this time, there is always a great deal of research going on in the area of liver cancer. Scientists are looking for causes and ways to prevent liver cancer, and doctors are working to improve treatments.

### Prevention

The most effective way to reduce the worldwide burden of liver cancer is to prevent it from happening in the first place. Some scientists believe that vaccinations and improved treatments for hepatitis could prevent about half of liver cancer cases worldwide. Researchers are studying ways to prevent or treat hepatitis infections before they cause liver cancers. Research into developing a vaccine to prevent hepatitis C is ongoing. Progress is being made in treating chronic hepatitis with drugs that boost the patient's immune system.

### Screening

Several new blood tests are being studied to see if they can pick up liver cancer earlier than using AFP and ultrasound. So far, none of these has proved more helpful than what is already being used.

### Surgery

Newer techniques are being developed to make both partial hepatectomy and liver transplants safer and more effective.

#### **Adding other treatments to surgery**

Doctors are studying ways to make more liver cancers resectable by trying to shrink them before surgery. Studies are now looking at different types of *neoadjuvant* therapies (therapies given before surgery), including chemotherapy, immunotherapy, embolization, and radiation therapy. Early results have been promising but have only looked at small numbers of patients.

Another active area of research uses *adjuvant* therapies -- those given right after surgery -- to try to reduce the chances that the cancer will return. Unfortunately, most of the studies using chemotherapy or chemoembolization after surgery have not shown that they help people live

longer. Some promising results have been seen with radioembolization, but these need to be confirmed in larger studies.

### **Laparoscopic surgery**

Doctors are also beginning to study a technique called laparoscopic surgery. In this procedure, several small incisions are made in the abdomen, through which specially designed instruments are inserted to view and cut out the diseased portion of the liver. It does not require a large incision in the abdomen, which means there is less blood loss, less pain after surgery, and a quicker recovery. At this time, laparoscopy is still considered an experimental form of treatment for liver cancer. It is being studied mainly in patients with small tumors in certain parts of the liver that can be easily reached through the laparoscope.

### **Determining recurrence risk after surgery**

After a partial hepatectomy, one of the biggest concerns is that the cancer will come back (recur). Knowing someone's risk for recurrence after surgery might give doctors a better idea of how best to follow up with them, and may someday help determine who needs additional treatment to lower this risk.

Researchers may have found a way to do this by testing the cells in the surgery sample. In a recent study, they looked at the pattern of genes in liver cells near the tumor (not the tumor cells themselves) and were able to predict which patients were at higher risk for recurrence. This is an early finding that will need to be confirmed in other studies before it is widely used.

### **Radiation therapy**

The major problem with using radiation therapy against liver cancer is that it also damages healthy liver tissue. Researchers are now working on ways to focus radiation therapy more narrowly on the cancer, sparing the nearby normal liver tissue. Several new approaches to radiation therapy are being tried, including using radiosensitizers (drugs that make cancers more vulnerable to radiation).

### **Targeted therapy**

New drugs are being developed that work differently from standard chemotherapy drugs. These newer drugs target specific parts of cancer cells or their surrounding environments.

Tumor blood vessels are the target of several newer drugs. Liver tumors need new blood vessels to grow beyond a certain size. The drug sorafenib (Nexavar<sup>®</sup>), which is already used for some liver cancers that can't be removed surgically, works in part by hindering new blood vessel growth (angiogenesis). Bevacizumab (Avastin<sup>®</sup>) also works to block new blood vessel

growth. It has shown promising results against liver cancer both alone and in combination with the drug erlotinib (see below).

Other new drugs have different targets. For example, a drug called erlotinib (Tarceva<sup>®</sup>), which targets a protein called EGFR on cancer cells, has shown some benefit in people with advanced liver cancer in early studies. Several other targeted drugs are now being studied as well.

## **Chemotherapy**

New forms of systemic and regional chemotherapy combined with other treatments are being tested in clinical trials. A small number of tumors respond to chemotherapy, although it has not yet been shown to prolong survival.

Newer chemotherapy agents, such as oxaliplatin, capecitabine, gemcitabine, and docetaxel, are being tested against liver cancer in clinical trials. The drug oxaliplatin has shown promising results when given in combination with doxorubicin and also when given with gemcitabine and the targeted therapy drug cetuximab (Erbix<sup>®</sup>).

## **Gene therapy**

Scientists are learning more about many of the genes that are damaged when normal liver cells become cancerous. They are hoping to be able to use this information to develop gene therapies to replace these defective DNA sequences.

The p53 gene is a tumor suppressor gene that is often altered in liver cancers. In normal liver cells, it prevents excessive growth, helps cells repair damage to their DNA, and promotes the death of cells when DNA damage becomes too much to be repaired. Restoring normal p53 DNA to liver cancer cells might suppress tumor growth and cause the cancer cells to die. Clinical trials are being done to study the effectiveness of this type of therapy, including possible short and long-term side effects.

## **Additional resources**

### **More information from your American Cancer Society**

The following information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Caring for the Patient with Cancer at Home (available in Spanish as "Home Care for the Person With Cancer")

Imaging (Radiology) Tests

Pain Control: A Guide for People With Cancer and Their Families (also available in Spanish)

Surgery (also available in Spanish)

Understanding Chemotherapy (also available in Spanish)

Understanding Radiation Therapy (also available in Spanish)

When Your Cancer Comes Back: Cancer Recurrence

The following books are available from the American Cancer Society. Call us at 1-800-ACS-2345 to ask about costs or to place your order.

*American Cancer Society's Guide to Pain Control, Second Edition*

*Cancer in the Family: Helping Children Cope with a Parent's Illness*

*Caregiving: A Step-By-Step Resource for Caring for the Person With Cancer at Home*

*What Helped Me Get Through: Cancer Patients Share Wisdom and Hope*

*What to Eat During Cancer Treatment*

## **National organizations and Web sites\***

In addition to the American Cancer Society, other sources of patient information and support include:

### **American Liver Foundation**

Toll-free number: 1-800-GO-LIVER (1-800-465-4837)

Web site: [www.liverfoundation.org](http://www.liverfoundation.org)

### **National Cancer Institute**

Toll-free number: 1-800-4-CANCER (1-800-422-6237)

Web site: [www.cancer.gov](http://www.cancer.gov)

## United Network for Organ Sharing

Toll-free number: 1-888-894-6361

Web site: [www.unos.org](http://www.unos.org)

*\*Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit [www.cancer.org](http://www.cancer.org).

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