Cancer can be treated. But if it is going to be treated fully, it must be detected in its early stages. This isn't always easy because of the silent period of tumor growth—the months or years when the malignant cells are quietly doubling again and again—before the cancer is big enough to detect. For a long time, there may be absolutely no indication that this process is going on.

So how do we discover that the tumor is there? Your own complaint may be the tip-off. Or your doctor might pick up on some clue that appears during a physical. Whatever sets off the search for cancer, the investigative process that leads to a definitive diagnosis follows a standard pattern. Suspicions are aroused. Questions are asked. Answers are found through examinations, tests, images of body organs, and analyses of tissues under a microscope.

**Symptoms**

When a lump has grown to a certain size, its presence is signaled in a number of ways:

- It presses on nearby tissues, which sometimes produces pain.
- It grows into nearby blood vessels, which may produce bleeding.
- It gets so large that it can be seen or felt.
- It causes a change in the way some organ works. Trouble swallowing (dysphagia), for example, might be the sign of a tumor partially obstructing the esophagus, the passage between the throat and stomach. Hoarseness or change of voice might indicate a tumor in the larynx, or voice box. These symptoms—pressure, bleeding, a mass, or interference with function—are reflected in the American Cancer Society's list of *seven early warning signals*:

1. Change in bowel or bladder habits.
2. A sore that does not heal.
3. Unusual bleeding or discharge.
4. Thickening or lump in breast or elsewhere.
5. Indigestion or difficulty in swallowing.
6. Obvious change in wart or mole.
7. Nagging cough or hoarseness.

Recognizing a symptom is the first critical step in the search for cancer. Unfortunately, many people don't pay any attention to these warning signals. They wait and wait, sometimes for months, before getting the medical attention that could save their lives.

The best chance of diagnosing cancer early depends on someone's thoughtful and perceptive awareness that something new has happened to his or her body—especially the appearance of one of these symptoms. Despite this, some cancers are silent until they grow to an advanced size, pointing out the need for sensitive tests for the early diagnosis of cancer.
The Physical Examination

The suspicion that a cancer is growing is often aroused during a routine physical examination, the major part of what should be a yearly checkup of your general health. The physical examination is a thorough, systematic, and progressive search throughout your body for signs of disease or abnormal function. To make sure that no significant area is missed, each physician generally develops his or her own standard pattern or sequence. Some start with the head and work down the body; others examine each organ system as a unit.

Whatever the pattern, a good physical examination with a view to detecting cancer involves a search of the entire body with a special emphasis on the parts that are most prone to malignancy.

- The nose and throat are examined. There is a quick and painless mirror examination of the larynx.
- The lymph-node-bearing areas—such as the neck above the collarbone, under the arms, and in the groin—are checked.
- Specific attention is paid to the breasts in women and the prostate gland in men.
- The abdomen is carefully pushed and probed to detect enlargement of any of the abdominal organs, especially the liver and spleen.
- Examination of the pelvic area in women, including a Pap smear, is essential to detect cancers of the cervix, uterus, and ovaries.
- A probing of the rectum with a gloved finger is an essential part of the physical for both men and women.

During the examination, your doctor will ask you many questions about various body functions. There will be specific questions about hoarseness, signs of gastrointestinal bleeding, constipation, swallowing problems, coughing up blood, and so on. A “yes” answer to any of these questions leads to more detailed questions, to more specific physical examinations, and possibly to blood tests, X-rays, or other studies.

You might also be asked questions about any family history of cancer, particularly among close relatives—parents, grandparents, aunts, uncles, brothers, and sisters. Detailed answers to these questions will help in the search for any cancers with a genetic basis, such as some breast and colon cancers.

Suspicious findings in any part of the physical examination will lead to further tests. An enlarged lymph node in the neck, for example, might indicate a cancer that has spread from somewhere else. This will set off a vigorous search for the primary site. Persistent coughing, especially with blood, might lead the doctor to look directly inside your lungs with a special instrument (a bronchoscope) to detect tumors (see “Endoscopy,” in this chapter).

Blood Tests

The next level of the diagnostic process involves a laboratory analysis of blood samples. Two categories of blood tests are used to help in the diagnosis of cancer:

Nonspecific Tests Most blood tests are nonspecific. This means they can reveal an abnormality in the blood that indicates some illness but not which one.

A blood count, for example, may show anemia. Why would you be anemic? There are many reasons, including cancer. But the anemia may not be related to a tumor unless you have a history of bleeding in the bowel and X-rays show a cancer of the colon. Similarly, there are tests for liver function that indicate abnormalities in that organ. But the problem might be caused by gallstones, hepatitis, tumors, or drug toxicity. Certain patterns in the test results will suggest tumors or some other cause of bile obstruction. Other
**Blood Tests Useful in Cancer Diagnosis**

### Nonspecific Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline phosphatase</td>
<td>Elevated in bone and liver disease</td>
</tr>
<tr>
<td>SGOT and SGPT</td>
<td>Elevated if there is liver damage</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Elevated in liver disease, especially with bile duct obstruction</td>
</tr>
<tr>
<td>LDH</td>
<td>Elevated in many diseases, including cancer</td>
</tr>
<tr>
<td>Uric acid</td>
<td>Elevated in gout, cancers of the blood and lymph nodes, and after cancer treatment</td>
</tr>
<tr>
<td>Creatinine and BUN</td>
<td>Elevated in kidney disease</td>
</tr>
<tr>
<td>Calcium</td>
<td>Elevated in cancer that has spread to the bone, with tumors that produce parathyroid hormone-like protein, and in multiple myeloma, as well as in some nonmalignant diseases</td>
</tr>
<tr>
<td>Electrolytes (sodium, potassium, carbon dioxide, chloride)</td>
<td>These levels are useful in metabolic and endocrine disease, and for monitoring both nutritional status and the effects of treatment</td>
</tr>
<tr>
<td>Amylase</td>
<td>Used to assess pancreatic disease</td>
</tr>
</tbody>
</table>

### Specific Tests and Markers

Not all cancers produce these markers.

<table>
<thead>
<tr>
<th>Test</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA (carcino-embryonic antigen)</td>
<td>Elevated in cancers of the colon, rectum, lung, breast, and pancreas</td>
</tr>
<tr>
<td>CA-125</td>
<td>Elevated in cancers of the ovary and uterus</td>
</tr>
<tr>
<td>CA 19-9</td>
<td>Elevated in cancers of the colon, pancreas, stomach, and liver</td>
</tr>
<tr>
<td>CA 15-3/CA 27-29</td>
<td>Elevated in breast cancer</td>
</tr>
<tr>
<td>Alpha-fetoprotein (AFP)</td>
<td>Elevated in primary liver cancer and some cancers of the testis</td>
</tr>
<tr>
<td>HCG (human chorionic gonadotropin)</td>
<td>Elevated in some cancers of the testis and ovary and some lung cancers; also elevated in pregnancy</td>
</tr>
<tr>
<td>Prostatic acid phosphatase (PAP)</td>
<td>Markedly elevated in some cases of prostate cancer</td>
</tr>
<tr>
<td>Prostate-specific antigen (PSA)</td>
<td>Helpful in diagnosing prostate cancer, in detecting recurrent disease, and in guiding treatment</td>
</tr>
<tr>
<td>Serum protein electrophoresis</td>
<td>Abnormal gamma globulin (monoclonal “spike”) is found in myeloma</td>
</tr>
<tr>
<td>Serum protein immuno-electrophoresis (IgG, IgA, IgM)</td>
<td>Similar to above, but can classify the type of abnormal gamma globulin present</td>
</tr>
</tbody>
</table>
patterns will suggest hepatitis. But essentially these patterns are only important clues. They are not solutions to diagnostic questions.

There are so many tests used to detect abnormalities in different organ systems that physicians usually obtain a whole panel of them—blood counts, tests of metabolism (including levels of minerals such as calcium), and tests for the liver, kidneys, or thyroid. The test results may suggest certain types of tumors, but no specific diagnosis can be made on the basis of these tests alone.

**Specific Tests** Other blood tests are fairly specific for particular kinds of cancer, often several kinds. These tests will be ordered if your doctor strongly suspects one of these cancers.

**Tumor Markers** The most important are tests for chemicals called tumor markers. These are produced by various types of tumors. Breast, lung, and bowel tumors, for example, produce a protein called the carcinoembryonic antigen (CEA). Some inflammatory diseases may produce low levels of this chemical, but some tumors in these areas produce very high levels. If a very high CEA level is found, then a tumor is assumed to be present until proved otherwise. Similarly, prostate cancers and many cancers of the testicles and ovaries produce known chemicals.

Some very exciting research is now being done to find more and more accurate markers for different types of cancer. We can now envision the day in the not-too-distant future when specific blood tests will identify most human cancers. But at the moment, the few tests we do have are invaluable. They not only help make the diagnosis but are especially useful for keeping track of the cancer after treatment. If the marker is elevated at the time of diagnosis, then successful treatment should result in the level falling or disappearing altogether. The reappearance of the marker often signals a relapse. If that happens, even if no other sign or symptom appears, there would be a search for a new tumor and consideration would be given to re-treatment. A problem with these tests, however, is that they can sometimes be elevated in the absence of cancer. Your doctor will need to evaluate these test results in the context of your individual condition.

**Other Blood Tests** When a cancer is in the blood cells themselves, tests of the blood and the blood-forming organs may be all that’s needed to make the diagnosis. Cancer of the white blood cells—leukemia—can often be diagnosed by looking at a sample of blood taken from the finger or arm. The diagnosis can be confirmed by examining cells from the bone marrow, where these cells are made. Bone marrow analysis will also diagnose multiple myeloma, which is basically a malignancy of plasma cells in the marrow.

**Tests of Fluids and Stools**

Our bodies produce wastes—urine and stool—that can reveal clues about disease. But there are also other fluids that can be analyzed to detect cancer cells.

- The most familiar test of body fluids is the urinalysis that is part of a regular checkup. Analyzing the urine’s composition can reveal all kinds of abnormalities. The presence of protein might indicate kidney disease. The level of sugar might indicate diabetes. Too many white blood cells can indicate an infection. Too many red blood cells could indicate bleeding, maybe because of a tumor, maybe from some other cause. If tumor cells are found, other tests will be done.

- A physical or X-ray examination may reveal the presence of fluid in the chest cavity, abdomen, or joints. A needle can be inserted into these areas and the fluid drawn out for examination.
• A lumbar puncture, also known as a spinal tap, is a special procedure to remove fluid from the spinal canal. It involves the insertion of a needle between the vertebrae, after you’ve been given a local anesthetic. Tests can identify any infection, inflammation, or cancer.

The Hidden Blood Stool Test Blood in the stool is always a sign of something going wrong in the digestive tract. Sometimes this blood can easily be seen in a bowel movement; most of the time, it’s all but invisible. One simple procedure to find out whether there is blood in the stool is called the occult (hidden) blood test. A small amount of stool is smeared on specially treated paper and then chemicals that reveal the presence of blood are added. If blood is found, the upper and/or lower bowel will be examined with scopes or barium X-rays.

Blood in the stool is often caused by hemorrhoids, but a benign or premalignant tumor (a polyp) or a hidden cancer is always a possibility.

Imaging Techniques
Any suspicious findings in the physical exam or the lab test results will make your doctor want to find out what is going on inside your body. He or she could just look inside directly, either with special instruments or by opening up some area. But the first step usually involves the use of one or more devices that produce images of suspicious areas.

These “imaging studies” may show a tumor in a specific organ, and the image will help your doctor assess its size and whether it has involved surrounding tissues.

If you complain of indigestion, for example, your doctor may suspect stomach cancer. This would lead to an X-ray or endoscopy of the upper gastrointestinal tract. Lower digestive tract complaints such as constipation or bleeding might lead to an X-ray or endoscopy to diagnose a possible carcinoma of the colon. Blood in the urine may lead to an X-ray of the kidneys to confirm a suspected tumor in the kidneys or bladder. And complaints of severe headaches, together with other symptoms of increased pressure in the head, may result in a CT scan of the head in search of a brain tumor.

In the past, radiography (X-ray) was the only imaging technique available. If X-rays couldn’t answer critical questions in the diagnostic investigation, then a surgeon would have to open up the body to take a direct look. But new techniques have revolutionized the art and science of diagnosis. Some of the new techniques involve the use of X-rays; others do not.

X-Rays This familiar imaging technique involves passing a small dose of ionizing radiation through a specific area of the body and onto a film. This produces a two-dimensional picture of the structures inside.

Bones and some other dense substances absorb more X-rays than other tissues, so they show up on the film as shadows that your doctor can interpret. But soft tissues can’t be seen very well on X-rays. It is impossible to see the inside of a stomach, for example, without adding a substance that will prevent the X-rays from penetrating.

If your stomach is going to be X-rayed, you will be asked to swallow a barium “meal.” The barium will improve the contrast and so produce a better picture. If your large bowel is going to be seen, you will be given a barium enema. If your kidneys are going to be examined, another type of contrast agent may be injected into a vein to fill the kidneys, which will allow them to be seen.

A fluoroscope might also be used. This lets the doctor see a continuous, moving image. In this procedure, the X-ray beam strikes a small fluorescent
screen and the image is amplified through a video system.

**Nuclear Scans** Radioactive isotopes that emit gamma rays can produce an image on photographic film or on a scintillation detector. Some of these isotopes, generally given by injection, are organ specific, which means that they concentrate in that part of the body suspected of harboring cancer.

Different organs react to the isotopes in different ways. The isotopes used for liver scanning concentrate in normal tissues but are not taken up by cancer cells. So the image shows “cold spots” that may be cancerous areas. The isotopes used for bone scans, however, work in the opposite way. Cancer cells make the bone react to the isotope to a greater degree than normal bone, so “hot spots” light up the image of the skeleton. Hot spots can be produced by diseases other than cancer, however, such as bone injury or arthritis, and can represent healing bone.

**Angiography** This is a useful way to study the blood vessels in a specific area of the body. Angiography is sometimes used to diagnose and precisely locate tumors in the pancreas, liver, and brain, especially when surgery is being considered.

Angiography is also used in some chemotherapy treatments, when a small plastic tube (catheter) is placed in an artery to deliver anticancer drugs to the tumor. It is especially important in those cases to know the exact size of the tumor to make sure all of it is treated. It makes no sense to insert the catheter and then miss a portion of the tumor not supplied by the blood vessel being used. Angiograms safeguard against this problem by defining the blood vessels within the tumor, which have a different quality and appearance from the arteries next to the tumor.

**CT Scans** Computerized tomography (CT) scans are highly sensitive examinations that use small amounts of X-rays to see parts of the body that are difficult or impossible to view any other way. The images produced are far superior to those obtained by traditional X-rays. And the images are even clearer if you drink a contrast agent or get an injection before the scan is done.

The CT machine scans the area being investigated—chest, brain, abdomen, or any other part of the body—by taking X-rays of one thin layer of tissue after another. A computer puts the images together to create a cross section of the area. Looking at a set of CT images is the same idea as looking at a loaf of bread, with each slice laid out side by side in a row.

Although there is higher X-ray exposure with CT scans than with some conventional X-rays, such as chest X-rays, not undergoing the procedure is much riskier if cancer is strongly suspected. For example, the information from the scan is not only useful for diagnosis but very helpful in planning treatment. Today, some CT scans can be reconstructed with three-dimensional images. In some cases, these images can replace more invasive tests, such as colonoscopy.

**Magnetic Resonance Imaging (MRI)** The MRI scan can complement or even replace the CT scan in some cases. The images look similar to CT scan images, but there are no X-rays involved. The MRI scanner uses a powerful magnetic field to make certain particles in the body vibrate. Extremely sophisticated computer equipment measures the reaction and produces the images. Cross sections can be obtained not only across the body, as in CT scanning, but also from front to back and from left to right. This lets your doctor see your body from all three directions. In some cases, the images are superior to and provide more information than those obtained by CT scans. This is especially true for images of the central
nervous system and the spine. In some other cases, CT scanning is more useful than MRI scanning.

MRI is not suitable under certain conditions. An implanted metallic device such as a pacemaker, clip, or pump can be affected by the strong magnetic field.

Ultrasound This is a harmless and painless imaging technique. It is noninvasive, meaning that nothing enters your body except sound waves.

The technique involves spreading a thin coating of jelly over a particular area of the skin, then bouncing high-frequency sound waves through the skin onto internal organs. It works basically on the same principle as the sonar used by the navy to detect submarines, where sound waves are sent through the water and the “ping” of the sound bouncing back is analyzed. In a similar way, the complex ultrasound scanning apparatus draws a picture of whatever organ the sound waves are bouncing off. This picture can reveal a lot of information.

Many people are aware of ultrasound as a safe way to examine a fetus to search for abnormalities. But it is also useful for detecting possibly malignant masses or lumps without the need for X-rays.

Ultrasound is used to examine the neck for tumors of the thyroid gland or of the parathyroids. It is the standard method to diagnose gallstones, since the sound waves bounce quite nicely off the stones. And it is often used in the pelvis to study possible enlargement of the prostate or an ovary. Benign ovarian cysts are common, and other ways of examining this part of the body are not very precise. It has also been adapted to be used with endoscopes to help stage rectal and esophageal cancers. Ultrasound is helpful to distinguish cysts from solid breast tumors.

Positron-Emission Tomography (PET) This noninvasive scanning technique is becoming a valuable aid in finding hidden cancers. In contrast to other types of scans (CT, MRI) that show that “something is taking up space” in a certain area, PET scans “light up” areas of growing tissue. These scans depend on differences in metabolic activity (rate of growth), since tumors grow faster than normal tissue. Thus, this scan might distinguish living cancer from dead cancer tissue or blood clots or scar tissue. For those who appreciate details, PET is an accurate way to detect cancer invasion and help stage cancer. This comprehensive assessment is
helpful both in initial staging of newly diagnosed patients and for follow-up staging after treatment for the extent of disease. PET has thus helped physicians in making more accurate and rational decisions, and will likely be used more and more in the future.

PET uses an imaging agent, radioactive tracer F-18 fluorodeoxyglucose (FDG). It was developed in the late 1960s, and with greater availability of FDG and new technology, it provides an improved imaging technique by being able to image active cancer processes. Images are in three dimensions. Most malignant tumors use a lot of glucose and will “light up” on a PET scan. Then the PET scan can be compared or integrated with a CAT or MRI scan. PET scans can be viewed in three dimensions on a computer screen, and the image can be “rotated” to see the mass from any angle. Both cancer and some benign processes can be seen on PET scans but cannot be distinguished. Tissue biopsies are sometimes required for a cancer diagnosis.

It is now common to use PET scans for staging of lung cancer and melanoma. For example, in lung cancer, the PET has 85 percent accuracy versus 52 percent for CT scans. PET detects accurately 83 to 94 percent of metastatic lymph nodes versus 63 to 73 percent accuracy for CT scans. PET detects metastases outside the chest in up to 30 percent of patients with lung cancer. In one study, 41 percent of patients had a change in treatment management based on PET scans.

Three technologies are required for PET scanning to be possible:

1. A source for the FDG radioisotope. FDG is produced in a cyclotron and can be purchased from a radiopharmacy.
2. A scanner that can record the location of the FDG in the body, to localize tissue with active metabolism—especially cancer.
3. A powerful computer to reconstruct the signals into the three-dimensional images of the body, for the radiologist to interpret.

Newer techniques merging CT/MRI and PET have improved the efficiency of our ability to diagnose cancer and assess the effectiveness of its therapy. PET scanning is likely to become even more useful, and in fact frequently necessary, in the diagnosis and management of cancer.

Endoscopy

Sometimes images are not enough. The use of direct visualization has become more and more important in recent years, not only for diagnosing malignancies but in some cases as an aid in treatment (see chapter 10, “Laser Therapy”).

Rigid, thin telescopes have been used for years to look inside body cavities with natural openings. A bronchoscope inserted into the mouth or nose and through the windpipe (trachea) can be used to look inside the lungs. A cystoscope inserted into the urethra can be used to examine the bladder. Sometimes mirrors are used with these rigid scopes to examine, for example, the nasal passage and the back of the mouth (nasopharyngoscope) and the larynx (laryngoscope).

Flexible Scopes Flexible fiber-optic “telescopes” have come into widespread use, as they are more versatile and comfortable than rigid telescopes. These scopes use bundles of glass fibers that can bend around corners and form perfect pictures of the tissues at their far ends. Doctors looking through one end of the scope can look into many areas of the body safely, often with a minimum of sedation or local anesthetic. Not only can your doctor see exactly what’s going on in these areas, but he or she can also take photographs or remove cell samples.

The inside of the lung passages can be examined easily and quickly with the fiber-optic bronchoscope. A diagnosis of
lung cancer can often be made by this method alone, without resorting to the surgical procedures that used to be necessary.

Usually as an outpatient procedure, the nose and throat are sprayed with a local anesthetic and a thin flexible tube is passed into the lung area. Specialized fiber optics allow the doctor to “see” inside the lungs, look for areas that appear abnormal, and do small biopsies to see if cancer is present.

Similar instruments have revolutionized the diagnosis of tumors in the stomach and bowel. With a flexible gastroscope or colonoscope, the entire stomach or colon can clearly be seen and pieces of tissue can be collected. Similar specialized instruments for other body cavities have made diagnostic procedures much safer. And the procedures can be repeated after treatment to see how effective the treatment has been.

**Endoscopic-Ultrasound-Guided Fine Needle Aspiration** An ultrasound probe can be integrated into an endoscope, allowing images of masses close to the esophagus, stomach, or bowel to be visualized and sampled with a thin needle. The ultrasound device makes it possible to watch the needle tip moving into the mass and collect a small sample for microscopic analysis and diagnosis. A general description of fine needle aspiration can be found below under “Cytological Studies.” Masses in the pancreas, the esophagus, the stomach and the bowel walls as well as a subset of lymph nodes and other structures in the abdomen and the mediastinum can be visualized, reached, and sampled with this technique.

**ERCP** Clever adaptations of these endoscopic methods and tools are sometimes used for specialized diagnosis and therapy. In a procedure called endoscopic retrograde cholangiopancreatography (ERCP), for example, a doctor can pass a flexible fiber-optic telescope into your stomach, visualize the opening of the ducts draining bile from the liver, and insert a tube (stem) into these ducts from inside the

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*Lung cancer can often be diagnosed and biopsied through a bronchoscope.*
stomach either to provide drainage or to take pictures showing the exact location of tumors in the bile ducts and exactly how involved the ducts are.

**Cytological Studies**

Cytology is simply the study of cells. In cancer diagnosis, the term *cytological studies* means the examination of cellular material removed from the body. The cells might be removed by natural means, such as coughing up sputum (phlegm). They might also be removed by washing a body cavity with a salt solution—the inside of the abdomen after abdominal surgery, for example—or by scraping the surface of an organ or a suspected cancer.

The best-known cytology test is the one developed by George Papanicolaou—the Pap smear. The cervix is scraped and brushed to remove for analysis cells that could be abnormal or cancerous. In the same way, the tongue, the esophagus, the stomach, or the lung’s air passages can easily be scraped using a small brush through a scope.

**Fine Needle Aspiration (FNA) Biopsy.** This is another type of cytological test, used primarily to find out if a lump (for example, in the breast, thyroid, lung, lymph node, etc.) is benign or malignant. In most cases, it is also possible to find out exactly what type of benign or malignant process is causing the lump. In order to collect the cell sample for analysis, a very thin needle (thinner than a needle that is used to draw blood) is placed inside the lump, and over a duration of ten to twenty seconds, a small amount of cellular material is withdrawn for analysis. Usually at least two samples are collected. The discomfort experienced is usually comparable to a blood test, and the only common side effect is a limited local bruise with accompanying soreness lasting a few days.

The removed cells are put on slides, stained with dyes, and examined under a microscope. The cytotechnologist will screen the slide for the characteristic appearance of malignant or premalignant cells. A pathologist will subsequently examine the slides and may either diagnose cancer or report a strong suspicion of cancer. In some cases, a conventional surgical biopsy may be done to confirm the diagnosis.

FNA, when performed by well-trained practitioners, is suitable for definitive diagnosis of most types of cancer, including the majority of cancers involving lymph glands. For the latter, conventional microscopic interpretation is complemented by analysis of specialized stains highlighting markers on the surface of the tumor cells. This may be done by the flow cytometry method and/or by examination of the stained cells using a microscope.

Generally, specialized physicians who perform a large number of FNAs are more likely to provide a definitive diagnosis and a high rate of diagnostic accuracy. All diagnostic procedures carry a slight possibility of error (in the range of 1 to a few percent). If you are facing extensive treatment for cancer, you may want to consider obtaining a second opinion to confirm the diagnosis. Many institutions provide this by presentation at regularly scheduled multidisciplinary conferences, often called tumor boards, where experts from all aspects of cancer diagnosis and care come together to review diagnosis and treatment options for patients.

**Tumor Tests** Several other techniques for cell analysis, in addition to the usual examination under a microscope, are available. These techniques improve doctors’ ability to diagnose cancer, help determine the likely clinical course, and help guide the choice of treatment options.

- **Special Stains** There are now a large number of special ways to stain cancer tissue in the laboratory. These stains are often of great help in determining the
type of cancer when there is some uncertainty. They also provide helpful information about prognosis and treatment. Examples are hormone receptor analysis in breast cancer, Her-2/neu (c-erb B2), various cytokeratins, etc.

- **Flow Cytometry** This technique can analyze a tumor’s DNA content to find out whether the cancer cells contain the normal number of chromosomes (diploid) or an abnormal amount (aneuploid). Aneuploid tumors tend to be poorly differentiated and aggressive.

- **S-Phase Testing** This technique measures how fast a tumor is growing. In the S-phase of a cell’s growth cycle, new DNA is synthesized to prepare for the division of one cell into two. A tumor that is growing slowly may have less than 7 percent of cells in the S-phase. A more rapidly growing tumor has 8 percent or more. Tumors with higher rates of growth have a poorer prognosis and may need more aggressive treatment.

**Biopsies**

Ultimately the diagnosis of cancer depends on examining a small bit of tissue to see if it has the characteristic patterns and cell types defined as cancer. The definitive way to diagnose a suspicious area may be by cytology, by core biopsy, or by performing a surgical biopsy. Sometimes this is done even before doing other tests.

This microscopic examination is carried out by a pathologist who is an expert in distinguishing the very exact criteria that separate malignant cells from normal or benign ones. It is essential to obtain a specimen of tissue to do this examination. The biopsy is the procedure for obtaining the tissue.

There are two types:

- An incisional biopsy involves cutting into a portion of the tumor, then stitching the area closed.
- An excisional biopsy involves removing the entire tumor.

The excisional biopsy is often done with small tumors that are easily accessible and relatively small, such as those involving the skin, the mouth or nasal cavity, lymph nodes, or a woman’s reproductive system.

Biopsies are often done during the surgery that may be needed to expose the tumor. In such cases, it’s customary to take tissue samples not only from the apparent
site of the tumor but also from the lymph nodes or other tissues in the neighborhood. This will help measure the tumor’s potential or actual spread. This defines the stage of the cancer, so the staging process may be carried out at the same time as the diagnostic process. Of course, the surgeon may also try to carry out the most appropriate therapy at the same time by removing all the visible tumor.

Core Needle Biopsies  These may be used to collect a slender piece of tissue from a palpable mass or an abnormal area seen on a radiological imaging study. If the mass is not palpable, then imaging guidance is necessary in order to correctly position the needle for sampling. Depending on the nature of the mass and the location in the body, ultrasound, CT (computerized tomography), or MRI (magnetic resonance imaging) may be used to guide the needle into the mass. The diameter of the needle varies from $\frac{1}{10}$ to $\frac{1}{6}$ of an inch.

Fine Needle Aspiration (FNA)  Described earlier under the heading “Cytological Studies,” fine needle aspiration can be utilized in a manner similar to core needle biopsies. The FNA needles are considerably smaller in diameter (25 to 22 gauge—smaller than a venipuncture needle). When FNA is utilized for deep-seated masses, requiring image guidance of the needle, it is common to have a cytologist present during sampling to examine a part of the material during the procedure in order to judge when enough material suitable for diagnosis has been collected.

What to Expect  Local anesthetic is routinely used for all core needle biopsies and for deep-seated fine needle aspiration biopsies. Sedation is typically not needed. Local bruising is an expected side effect following both core needle biopsies and fine needle aspiration biopsies. The thinner needles usually cause less bleeding and accompanying soreness after the procedure.

When sampling deep-seated masses in the abdomen and chest, bleeding can be more severe and very rarely life-threatening. Therefore a blood test, checking factors important for normal coagulation (clotting), is carried out before deep-seated sampling. In addition, patients are usually asked to temporarily stop taking “blood-thinning” medicines (aspirin, a variety of nonsteroidal anti-inflammatory drugs, heparin, Coumadin, etc.). If you are being scheduled for a procedure, make sure your provider knows what drugs you are on. Also ask when you should stop taking a particular drug. Several blood-thinning drugs take a number of days to clear from your body.

Very rare complications from needle biopsy include nerve damage and leakage of bile fluid or pancreatic juice that may cause serious peritonitis (inflammation in your abdomen). The risk of leakage is less with thinner needles and nerve damage has not been reported after using fine needle aspiration biopsy.

In order to limit bleeding after sampling of superficial masses, local pressure is applied for a few minutes (similar to a blood test). After deep-seated biopsies, patients are usually observed in the clinic/hospital for a few hours before release.

The Next Step  Once the biopsy is performed and the diagnosis confirmed, the medical evaluation should rapidly be completed. At this point, treatment planning can begin.

Bone Marrow Examination

Bone marrow is analyzed to diagnose blood or bone marrow cancers and to find out if a malignancy from somewhere else has spread to the bone marrow.

The procedure is simple and brief. It can be done in a doctor’s office using a local
anesthetic similar to the one used by your dentist. In much the same way as blood is taken from your arm, a needle is inserted into either the breastbone or the pelvic bone, both of which are just under the skin and are easily entered. A small amount of liquid bone marrow is drawn into a syringe, placed on slides, and examined under a microscope for evidence of leukemia, lymphoma, or any other cancer cells. Sometimes a bone marrow biopsy may be done. A special cutting needle can be put into an anesthetized area of the pelvic bone and tiny bone chips (like pencil lead) can be removed. This procedure may be necessary for several reasons—to diagnose certain types of blood and bone marrow malignancies, to see if other cancers involve the marrow, or as part of the staging process.

Red marrow, which constitutes about 50 percent of an adult’s marrow, actively produces red blood cells, white cells, and platelets. Yellow marrow contains fat cells and connective tissue and is inactive, but it can become active in response to the body’s needs.

Bone marrow biopsies are helpful in staging using immunocytochemistry (cytokeratin) to detect micrometastases. One-third of women with breast cancer with negative lymph nodes had micrometastases. This ultrasensitive test is an independent prognostic predictor for relapse or death.

The Most Important Questions You Can Ask

Why is this test done?
A bone marrow biopsy may be done for the following reasons:

- To help the doctor diagnose blood diseases and anemias
- To diagnose primary and cancerous tumors
- To determine the cause of infection
- To help the doctor evaluate the stage of a cancer such as Hodgkin’s disease
- To evaluate the effectiveness of chemotherapy and other treatments

What should you know before the test?
- The biopsy usually takes only five to ten minutes. Test results are generally available in one week.
- More than one bone marrow specimen may be required and a blood sample will be collected before biopsy for lab testing.
- The nurse will ask you to sign a consent form.
- You’ll be told which biopsy site will be used (usually the breastbone [sternum] or the hip [iliac crest], but sometimes other places are used).
- You’ll be given a local anesthetic but will feel pressure on insertion of the biopsy needle and a brief, pulling pain on removal of the marrow.

What happens during the test?
- The nurse or doctor has you lie down and urges you to remain as still as possible.
- The nurse or doctor may talk quietly to you during the procedure, describing what’s being done and answering any questions.
- After the skin over the biopsy site is prepared and the area is draped, the doctor will inject the local anesthetic.
- After allowing time for the anesthetic to work, the doctor will then insert a needle into the bone and withdraw a bone marrow sample and then may do a needle biopsy.
- Immediate analysis is done on the sample taken from the bone marrow cavity by a hematologist, oncologist, or pathologist.

In a needle biopsy, a specimen is taken from the marrow cavity and sent to the lab.

What happens after the test?
- The nurse will apply pressure to the site for five minutes or so, then put on a bandage.
• If an adequate marrow specimen hasn’t been obtained on the first attempt at aspiration, while your skin is still numb, the needle may be repositioned within the marrow cavity or may be removed and reinserted in another site within the anesthetized area. A needle biopsy may follow the aspiration biopsy.

**Does the test have risks?**
• Bone marrow biopsy isn’t used in people with severe bleeding disorders, but bone marrow aspiration is still possible.
• Very rarely, bleeding and infection may be caused by bone marrow biopsy, which is why the nurse applies pressure to the site at the end of the procedure and why you are instructed to refrain from showering for twenty-four hours following the procedure and to leave the original dressing on for that duration. Problems or complications are very unusual, however.

**What are the normal results?**
Yellow marrow contains the fat cells and connective tissue. Red marrow contains various types of blood-making cells, fat cells, and connective tissue. An adult has a large blood-making capacity. An infant’s marrow is mainly red, reflecting a small capacity.

**What do abnormal results mean?**
Microscopic examination of a bone marrow specimen can be used to detect scar tissue (myelofibrosis), inflammation (granulomas), or cancer, such as lymphoma and leukemias. Blood analysis, including cell counts, can alert the doctor to a wide range of blood disorders. Examples are iron deficiency, anemias of various types, infectious mononucleosis, and various kinds of leukemias and lymphomas. Rarely, cancer cells have spread to the bone marrow.
Bone marrow examinations are also sometimes done to check for infections, follow up the effectiveness of treatment, or discover how well the bone marrow could produce blood cells if really aggressive chemotherapy were to be given, which would require the bone marrow to work “extra hard” to produce new blood cells.

Bone marrow examinations, if needed, can greatly assist your physician in his or her search for the most complete and helpful information to use for diagnosis and treatment planning.