Cancer of Unknown Primary: Diagnosis

How is cancer of unknown primary diagnosed?

Cancer of unknown primary (CUP) is cancer that's found after it has spread (metastasized) to another part of the body. If your healthcare provider thinks you might have CUP, you'll need certain exams and tests to be sure. These tests will be used to try to find the primary site. This is the place the cancer first started.

Diagnosing CUP starts with your provider asking you questions. You'll be asked about your health history, symptoms, risk factors, and family history of disease. A physical exam will also be done.

What tests might I need?

Tests help your healthcare providers learn more about the cancer. They're used to try to find out where the cancer first started (called the primary site). They can also show where the cancer has spread in your body. The results help your providers decide the best ways to treat the cancer.

The tests you get depend on where the CUP is found.

You may have 1 or more of these tests to look for the primary site and spread of CUP:

- Urine and blood tests
- Imaging tests
- Biopsy and tissue tests

Urine and blood tests

Some cancers make and release certain substances in your blood and urine. These substances are called tumor markers. If you have certain markers, your healthcare provider may be able to tell what kind of cancer you have. For instance, if someone has high prostate-specific antigen (PSA) levels in their blood, it might mean the cancer started in the prostate gland.

A complete blood count (CBC) and blood chemistry test can show signs that may be linked with certain types of cancer. They also give an idea of your overall health and how well your organs are working. These tests may be used to see if cancer has spread to your bones or bone marrow, too.

Imaging tests

Chest X-rays

A chest X-ray might be done to look for changes in your lungs. It might show a tumor in your lungs or chest. It might show enlarged lymph nodes in your chest, too. An X-ray takes a few minutes and doesn’t hurt.

CT scans

CT scans use a series of X-rays and a computer to make detailed 3-D images of the inside of your body. During the test, you lie still on a narrow table as it slides into a ring-shaped CT scanner. A CT scan doesn't hurt. You may be asked to hold your breath a few times during the scan.

You may need to drink a contrast dye 4 to 6 hours before the scan. The dye helps certain parts of your body show up more clearly. It will pass through your body and come out in your bowel movements. A dye might also be put into your blood through a vein. When the dye is injected, you may have a warm flush feeling spread through your body.

Tell your healthcare provider if you've ever had any reaction to contrast dye. This includes hives, trouble breathing, or becoming suddenly hot. You might need to take medicines before the test to help prevent a reaction.

PET (positron emission tomography) scans

PET scans can look for cancer cells all over your entire body. For this test, a mildly radioactive form of sugar (glucose) is put into your blood through a vein in your arm or hand. The PET scan will show where in your body the glucose is being used the most. This helps find active cells that are dividing quickly, like cancer cells.

You'll lie still on a table that slides into the rings of the PET scanner. It will rotate around you and take pictures. Other than the injection, a PET scan is painless. Some people are sensitive to the sugar used. This may cause nausea, a headache, or vomiting. Some newer machines can do PET and CT scans at the same time. This way, the areas that show up on the PET scan can be compared with the more detailed CT scan images.

MRI

An MRI uses radio waves, large magnets, and a computer to make detailed images of your insides. An MRI can show if cancer has spread to your spine or brain.

During the test, you'll lie still on a narrow table that slides into a long, tubelike scanner. If you're claustrophobic, you may need a sedative before the test. This test may last an hour or more. An MRI test is painless, but it's noisy. You may be offered earphones or earplugs.

Bone scans

Bone scans use a radioactive dye that's put into your blood through a vein. The dye will travel to and be taken up by your bones. Cancer cells in bone take up the dye differently than normal bone. These spots can be seen on the scan.

Endoscopy

Endoscopy is when a long, narrow tube with a light and a camera on the end is used to look inside your body. This tube may be put into a natural body opening, like your mouth, to look at your stomach, breathing tubes, or lungs. Or it may be put in through your anus to look at your rectum and colon.

Mammogram

A mammogram is an X-ray done to look for tumors or other changes in your breasts. It may be used if cancer is found in lymph nodes in your armpit.

Biopsy

A biopsy is a test to take tiny pieces of tissue, called samples, from your body. If fluid has collected where it shouldn't, like in the space around your lung, it can be taken out, too. A pathologist tests the tissue or fluid for signs of cancer. The way the cells look and the lab test results can help healthcare providers tell where the cancer started. Special stains done on the tissue can sometimes help, too.

During a biopsy, your provider removes tissue or fluid samples from areas that might be cancer, such as swollen lymph nodes or tumors. There are several types of biopsies that can be used. Many times, a biopsy is the only way to know if a person has cancer. It's also an important part of figuring out where the cancer started.

Fine needle aspiration

A very thin needle is used to remove some fluid or a small amount of tissue from the tumor.

Core needle biopsy

More tissue can be taken out in this test. The needle is wider than the needle used in a fine needle aspiration.

Paracentesis or thoracentesis

For paracentesis, a long, thin needle is used to take out fluid from your belly (abdomen). For thoracentesis, a needle is used to remove fluid that's built up around your lungs. Ultrasound may be used to guide the needle to the right place.

Bone marrow aspiration/biopsy

A special needle is used to take out a small amount of thick liquid bone marrow (aspiration) and a piece of bone tissue (biopsy). It’s normally taken from the back of your pelvis bone.

Excisional biopsy

In this case, the whole tumor is taken out in 1 piece. Lymph nodes that could contain cancer may also be removed.

Incisional biopsy

Only a part of the tumor is taken out for this type of biopsy. This method is used if the tumor is so big that removing the whole thing may cause problems.

Tissue tests

The samples taken out during a biopsy are sent to a lab for testing. A pathologist is a healthcare provider with extra training in looking at and testing tissues to diagnose diseases like cancer. The pathologist uses many different lab tests to look for signs of cancer and find out where it first started. Sometimes the tissue samples are stained with special dyes to find tumors. These include sarcomas, melanomas, and lymphomas. Other stains help find tumors or cells that may have come from the testicle, prostate, breast, thyroid gland, or colon.

The pathologist may also look at the sample under an electron microscope. This can show more details that give clues about what kind of cells the cancer started in.

Molecular tests will also be done. These tests look for certain genes and gene changes (mutations) in the cells. Different gene mutations are linked to different kinds of cancers.

Other tests may be used, too. It depends on the symptoms you have and the results of the previous lab tests.

Getting your test results

When your healthcare provider has the results of your tests and biopsy, they will contact you. Ask how you can expect to find out your results. Will it be a phone call, or do you need to make an appointment?

If the primary site, or the place the cancer started, can't be found after many tests, you may be diagnosed with cancer of unknown primary. A pathologist will review your biopsy samples. They will then classify the cancer as 1 of these 5 most common types:

- Squamous cell carcinoma
- Adenocarcinoma
- Poorly differentiated carcinoma
- Neuroendocrine carcinoma
- Poorly differentiated malignant neoplasm

This classification will help your provider decide on a treatment plan, even if the primary site of the cancer isn't known.

Your provider may repeat a physical exam and some tests. A second pathologist might look at the biopsy samples, too. Sometimes, as time passes, a small hidden primary tumor may grow large enough to be found. This can help the providers reclassify the CUP and decide which treatment is best.

Working with your healthcare provider

Your provider will talk with you about which tests you'll have. Make sure to follow their advice to get ready for the tests. Ask questions so you know what to expect and talk about any concerns you have.