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Unknown Primary - Diagnosis [1]

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ON THIS PAGE: You will find a list of the common tests, procedures, and scans that doctors can use to find out what's wrong and identify the cause of the problem. To see other pages, use the menu on the side of your screen.

By definition, CUP is found after it has spread to another part of the body through a process known as metastasis. Therefore, doctors use many tests to try to find out where in the body the cancer begin, called the primary site. Some tests may also determine which treatments may be most effective.

This list describes options for diagnosing CUP and trying to find the primary site. Not all tests listed will be used for every person. Your doctor may consider these factors when choosing a diagnostic test:

- Age and medical condition
- Type of cancer suspected
- Signs and symptoms
- Previous test results

Biopsy

A biopsy is the removal of a small amount of tissue for examination under a microscope. Other tests can suggest that cancer is present, but only a biopsy can make a definite diagnosis. The sample removed during the biopsy is analyzed by a pathologist (see below). A pathologist is a doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease. Careful evaluation and testing of the tumor tissue removed during a biopsy can sometimes give clues to where the tumor began.

The type of biopsy a person has depends on the location of the cancer. Learn more about what to expect when having a biopsy [3].

Evaluation by a pathologist

A pathologist diagnoses cancer by looking at the sample of the tumor collected during a biopsy. The pathologist can sometimes predict the primary site of the tumor based on the microscopic appearance of the tumor biopsy or based on the results of special stains, known as immunohistochemical (IHC) stains, that are part of the standard pathologic evaluation. These results, which are often presented in a pathology report [4], give important information about the cancer and help doctors plan additional testing.

When such a prediction is not possible, an additional test called a molecular cancer classifier assay should be considered. For this test, the pathologist uses tumor tissue collected during the diagnostic biopsy. This new diagnostic test can accurately predict the site where the tumor began in many patients with CUP. It is frequently useful in directing treatment. Learn more about molecular tumor profiling in the Treatment Options [5] and Latest Research [6] sections.

Evaluation by an oncologist

Once CUP is diagnosed, an oncologist will do more tests to search for the primary site and find out how far the cancer has spread. This is called a clinical evaluation. An oncologist is a doctor who specializes in treating people with cancer.

For most people with CUP, the primary site is not found, even after extensive evaluation. For this reason, several diagnostic tests may be done to evaluate specific signs and symptoms, including:

- **Medical history.** The doctor will ask detailed questions about previous illnesses, surgeries, and medications. Doctors are able to help more if they also know as much information as possible about smoking history, drug use, previous moles or benign (noncancerous) tumors, and any exposure to radiation, asbestos, or other chemicals known to be dangerous. A complete family medical history [7] may also provide your doctor with important clues, especially if one or more siblings, parents, or grandparents have had breast, ovarian, or colorectal cancer.
- **Physical examination.** The doctor will do a thorough physical examination of the entire body, including the lymph nodes, pelvis, breasts, rectum, and genitals.

- **Urine and blood tests.** These tests can find certain tumor markers [8]and proteins that may help determine where the cancer began. Tumor markers are substances found at higher than normal levels in the blood, urine, or body tissues of some people with cancer. Tumor markers are made either by the tumor or by the body as a result of cancer or other conditions.

  For example, patients who have cancer in the neck lymph nodes and the Epstein-Barr virus

(EBV) may have nasopharyngeal cancer [9]. Also, high levels of the proteins human chorionic gonadotropin (HCG) and alpha-fetoprotein (AFP) may mean a young man with poorly differentiated carcinoma has a germ cell tumor [10].

- **X-ray.** An x-ray is a way to create a picture of the structures inside of the body using a small amount of radiation.
- **Computed tomography (CT or CAT) scan** [11] **of the chest and abdomen.** A CT scan creates a three-dimensional picture of the inside of the body with an x-ray machine. A computer then combines these images into a detailed, cross-sectional view that shows any abnormalities or tumors. For CUP, a CT scan can show cancer in the abdomen and chest. A CT scan can also be used to measure the tumor's size. Sometimes, a special dye called a contrast medium is given before the scan to provide better detail on the image. This dye can be injected into a patient's vein or given as a liquid to swallow.

- **Positron emission tomography (PET) scan** [12]**.** A PET scan is a way to create pictures of organs and tissues inside the body. A small amount of a radioactive sugar substance is injected into the patient's body. This sugar substance is taken up by cells that use the most energy. Because cancer tends to use energy actively, it absorbs more of the radioactive substance. A scanner then detects this substance to produce images of the inside of the body.

  PET scans have proven useful for finding a primary site in 20% to 30% of patients with CUP. However, in the single study that compared CT scans with PET scans, having a PET scan did not provide significantly more information than having a CT scan.

  Doctors do not usually recommended PET scans for people with CUP. However, a PET scan may provide valuable information in specific situations. For example, for patients who have one area of cancer where local treatment (surgery or radiation therapy) is being considered, a PET scan can make sure that no other parts of the body have cancer. For people with squamous cell carcinoma involving lymph nodes in the neck (see the Subtypes [13] section), a PET scan is often useful, in addition to CT scanning, to identify a primary site in the head and neck area. In these situations, using PET and CT scans together, called an integrated PET-CT scan [14], provides more detailed and specific information than either test alone.

- **Magnetic resonance imaging (MRI)** [15]**.** An MRI uses magnetic fields, not x-rays, to produce detailed images of the body. MRI can also be used to measure the tumor's size. A special dye called a contrast medium is given before the scan to create a clearer picture. This dye can be injected into a patient's vein or given as a liquid to swallow. In some parts of the body, especially the brain and spinal column, MRI provides more information than the CT scan. In addition, women with cancer in the axillary lymph nodes, located under the arm, should have a breast MRI [16], since this test can sometimes find a small breast cancer that cannot be seen on a mammogram (see below).

- **Endoscopy** [17]**.** This test allows the doctor to see inside the body with a thin, lighted, flexible tube called an endoscope. The person may be sedated as the tube is inserted through the mouth, down the esophagus, and into the stomach and small bowel. Sedation is giving medication to become more relaxed, calm, or sleepy.

  Similar procedures are named according to the part of the body being looked at. For example, a bronchoscopy allows doctors to look inside the bronchial tubes (lungs), and a colonoscopy [18] allows doctors to look inside the colon and rectum.

  Endoscopy is used for patients with CUP to evaluate specific symptoms. For example, patients with squamous cell carcinoma in the neck lymph nodes should always have a complete endoscopy of the nasopharynx, throat, and larynx (voice box) to search for a primary tumor.

- **Prostate-specific antigen (PSA) test** [19]**.** Prostate-specific antigen (PSA) is a substance released by prostate tissue. A PSA test detects higher than normal levels of PSA in a man's blood, which may mean a man has prostate cancer [20] or a noncancerous condition, such as benign prostatic hyperplasia (BPH) or prostatitis (inflammation of the prostate). Men with CUP should have their PSA level measured, since higher-than-normal levels usually identify the prostate as the primary site.
- **Mammography** [21]**.** Women may receive a mammogram, especially if they have cancer in the axillary lymph nodes; cancer in other areas that might suggest metastatic breast cancer [22], such as cancer in the bone; or fluid around the lungs.

After diagnostic tests are done, your doctor will review all of the results with you. These results may help determine the type of tumor and guide the development of your individual treatment plan.

The next section in this guide is Subtypes [13]*, and it describes the different CUP tumors that may be diagnosed. Or, use the menu on the side of your screen to choose another section to continue reading this guide.*

Links
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[3] http://www.cancer.net/node/24406
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