

Cancer of Unknown Primary Origin

Key Points

- Cancer of unknown primary (CUP) origin is the diagnosis when metastatic cancer is found but the place where the cancer began (the primary site) cannot be determined.
- About 2 to 4 percent of all cancer patients have a cancer whose primary site is never identified.
- Treatment for CUP depends on many factors, including where the metastatic cancer is found, what the cancer cells look like under a microscope, and the patient's age and general health.
- Recent advances in diagnostic techniques have improved doctors' ability to eventually find the primary site, even when the original diagnosis is CUP.

Cancer can begin in any organ or tissue of the body. The primary, or original, tumor is usually named for the part of the body or the type of tissue in which the cancer begins. The disease can spread (metastasize) from the primary tumor and form metastatic tumors in other parts of the body. For example, breast cancer cells can metastasize to the lungs and cause the growth of a new tumor. When this happens, the tumor in the lung is called metastatic breast cancer because it is composed of breast cancer cells, not lung cancer cells.

Each year in the United States, several thousand people are diagnosed with metastatic cancer whose primary cancer site is not known. When the primary site cannot be identified, this disease may be called carcinoma of unknown primary (CUP). Most often, the metastatic cancer is first found in the lymph nodes, liver, lung, or bone.

In recent years, microscopic and other diagnostic techniques have improved dramatically. For this reason, doctors can now determine the primary site in about four out of five cases first diagnosed as CUP. In some cases, the part of the body where cancer cells are first found helps the doctor decide which diagnostic tests will be most helpful. Doctors also have other clues that help them find the primary site:

- The pattern of spread may suggest the location of the primary site. When the metastatic cancer is found in the upper part of the body, the original site is likely to be above the diaphragm (the thin muscle under the lungs that separates the chest from the abdomen) at sites such as the lung and breast. If the metastatic cancer appears first in the lower part of the body, the primary cancer is likely to be at sites below the diaphragm, such as the pancreas and liver.
- The type of cell found in the metastatic cancer can also provide clues about the hidden primary site.



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Most patients with an unidentified primary tumor have a cell type called adenocarcinoma. The term adenocarcinoma refers to cancer that begins in the cells in glandular structures in the lining or covering of certain organs in the body. Common primary sites for adenocarcinomas include the lung, pancreas, breast, prostate, stomach, liver, and colon.

When the cancer cells are poorly differentiated (that is, they look very different from normal cells when viewed under a microscope), the cancer may be either a lymphoma or a germ cell tumor. Lymphomas begin in the lymphatic system (a grouping of lymph glands and lymph vessels found throughout the body that participates in the defense against attack from bacteria, viruses, or other agents); germ cell tumors usually begin in the ovaries and testes.

In patients in whom the primary cancer is eventually found, the lung and pancreas are the most common primary cancer sites. CUP also may be traced to the breast, prostate, colon, or rectum as the primary site.

Sometimes, however, even when doctors use very sophisticated methods to try to identify the primary site, the part of the body the cancer cells came from cannot be determined. About 2 to 4 percent of all cancer patients have a cancer whose primary site is never found.

Identifying the primary tumor site is important because knowing its location and type often helps doctors plan the best treatment. Treatment that is specific to the suspected type of cancer is likely to be more effective. Still, when diagnostic tests have not identified the primary site, doctors must decide whether the potential benefits of more extensive testing outweigh a patient's discomfort and the financial costs.

CUP is a term that refers to many different cancers. For that reason, treatment depends on where the cancer is found, what the cancer cells look like under a microscope, and the patient's age and overall physical condition. No method is standard, but chemotherapy, radiation therapy, hormone therapy, and surgery may be used alone or in combination to treat patients who have CUP. Even when the cancer is unlikely to be cured, treatment may help the patient live longer or improve the patient's quality of life. However, the potential side effects of the treatment must be considered along with the potential benefits.

The National Cancer Institute is currently supporting clinical trials (research studies) of new treatments for CUP. Information about ongoing studies is available on the NCI's Cancer.gov Web site at <http://www.cancer.gov/clinicaltrials> or from the Cancer Information Service (see below).

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 6.7, *Cancer: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Sites-Types/general>)
- National Cancer Institute Fact Sheet 6.20, *Metastatic Cancer: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Sites-Types/metastatic>)
- *What You Need To Know About™ Cancer* (<http://www.cancer.gov/cancertopics/wyntk/cancer>)

How can we help?

We offer comprehensive research-based information for patients and their families, health professionals, cancer researchers, advocates, and the public.

- **Call** NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237)
- **Visit** us at <http://www.cancer.gov> or <http://www.cancer.gov/espanol>
- **Chat** using LiveHelp, NCI's instant messaging service, at <http://www.cancer.gov/livehelp>
- **E-mail** us at cancergovstaff@mail.nih.gov
- **Order** publications at <http://www.cancer.gov/publications> or by calling 1-800-4-CANCER
- **Get help** with quitting smoking at 1-877-44U-QUIT (1-877-448-7848)

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