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## About Cancer of Unknown Primary

Learn what cancer of unknown primary is and get the latest key statistics in the US.

### Overview and Types

If you have been diagnosed with a cancer of unknown primary or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- [What Is a Cancer of Unknown Primary?](#)

### Research and Statistics

See the latest estimates for new cases of cancers of unknown primary in the US and what research is currently being done.

- [Key Statistics for Cancers of Unknown Primary](#)
- [What's New in Cancer of Unknown Primary Research?](#)

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## What Is a Cancer of Unknown Primary?

Cancer starts when cells begin to grow out of control. Cells in nearly any part of the

spreads to the liver is still classified as lung cancer and not as liver cancer.

Sometimes it's not clear where a cancer may have started. When cancer is found in one or more metastatic sites but the primary site cannot be determined, it is called a **cancer of unknown primary (CUP)** or an **occult primary cancer**. This happens in a small portion of cancers.

- [Looking for the primary site](#)
- [General cancer types](#)
- [Broad categories of cancers of unknown primary](#)

## Looking for the primary site

Further tests may eventually find the primary site of some of these cancers. When this happens, they are no longer considered a cancer of unknown primary and are renamed and treated according to where they started.

As an example, a person has an enlarged lymph node on the side of their neck. When it is removed, cancer is found. But under the microscope it does not look like a cancer that normally starts in lymph nodes. At this point it might be considered a cancer of unknown primary. The way it looks under the microscope might suggest that the cancer started in the mouth, throat, or voice box (larynx). When this area is examined, a small cancer of the larynx might be found. From then on, the patient is said to have laryngeal cancer rather than a cancer of unknown primary and will get treated for that type of cancer.

In many cases, the source of the cancer is never determined. The most thorough search still might not find the primary site. Even when doctors do autopsies on people who have died of cancer of unknown primary, they are often still unable to find the site where the cancer started.

The main reason to look for the primary site of a CUP is to guide [treatment](#)<sup>1</sup>. Since a cancer that starts in one place needs the same treatments when it spreads, knowing where a cancer started tells the doctor what types of treatments to use. This is especially important for certain cancers that respond well to specific chemotherapy or hormone drugs. When the types of cancer that respond best to treatment have been ruled out by tests, it usually becomes less important to find the exact origin or cancer type.

But even if the primary site is not known, treatment can still be successful. How the cancer cells look under the microscope, the results of lab tests, and information about

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To learn more about how cancers start and spread, see [What Is Cancer?](#)

## General cancer types

Cancers are classified by their primary site. They can also be grouped by the types of cells in them, how the cancer cells look under the microscope, and on results of certain lab tests on the cells. Knowing the type of cell might give doctors a clue as to where the cancer started. When the cancer cells closely resemble normal cells of the organ where they start, the cancer is called **well differentiated**. When the cells do not look much like normal cells, the cancers are called **poorly differentiated**. Cancers of unknown primary are often poorly differentiated.

## Carcinomas

A carcinoma is a cancer that begins in the cells that line the inside or outside of a body organ. These cells are called **epithelial cells**. There are different types of carcinomas. lat oi 0 g a12 T



## Neuroendocrine carcinoma

These rare cancers start from cells of the diffuse neuroendocrine system. This system has cells that are like nerve cells in certain ways and like hormone-making endocrine cells in other ways. These cells do not form an actual organ like the adrenal or thyroid glands. Instead, they are scattered throughout other organs like the esophagus, stomach, pancreas, intestines, and lungs. These cancers account for a small number of CUP cases. (Some poorly differentiated cancers are found to be neuroendocrine carcinomas upon further testing.)

Even when doctors don't know where the cancer started, they do their best to classify the type of cancer. This can help them select the best treatment. Some cancers respond very well to specific treatments, so it is very important to classify the cancer as much as possible. This is best done by looking at the cancer under a microscope and doing special tests in the lab (see [Tests for a Cancer of Unknown Primary<sup>4</sup>](#)).

## Other types

Lymphoma often does not have a clear primary site, but it's not considered a CUP.

Although the primary site of a melanoma may not be clear, once a cancer is classified as a melanoma, it's no longer called a CUP.

## Hyperlinks

1. [www.cancer.org/cancer/types/cancer-unknown-primary/treating.html](http://www.cancer.org/cancer/types/cancer-unknown-primary/treating.html)
2. [www.cancer.org/cancer/understanding-cancer/what-is-cancer.html](http://www.cancer.org/cancer/understanding-cancer/what-is-cancer.html)
3. [www.cancer.org/cancer.html](http://www.cancer.org/cancer.html)
4. [www.cancer.org/cancer/types/cancer-unknown-primary/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/types/cancer-unknown-primary/detection-diagnosis-staging/how-diagnosed.html)

## References

<sup>5</sup>Greco FA, Hainsworth JD. Carcinoma of Unknown Primary In: DeVita VT, L1n knowancer.html

*Treatment*. 07/25/2015. Accessed at: <https://www.cancer.gov/types/unknown-primary/hp/unknown-primary-treatment-pdq> on February 9, 2018.

Varadhachary GR, Lenzi R, Raber MN, Abbruzzese JL. Carcinoma of Unknown Primary In: Neiderhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5<sup>th</sup> ed. Philadelphia, PA. Elsevier: 2014:1792-1803.

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## Key Statistics for Cancers of Unknown Primary

- [How common are cancers of unknown primary?](#)

### How common are cancers of unknown primary?

The exact number of cancers of unknown primary (CUP) diagnosed each year is unknown, because some cancers start out being diagnosed as unknown primary, but the primary site is found later. Still, the American Cancer Society estimates that about 37,370 cases of cancer of unknown primary will be diagnosed in 2025 in the United States. This number represents about 2% of all cancers. As more sophisticated lab tests become available to determine where a cancer started, the number of cancers of unknown primary may go down.

Visit the [American Cancer Society's Cancer Statistics Center](#)<sup>1</sup> for more key statistics.

### Hyperlinks

1. [cancerstatisticscenter.cancer.org/](http://cancerstatisticscenter.cancer.org/)

### References

American Cancer Society. *Facts & Figures 2025*. American Cancer Society. Atlanta. 2025.

Bochtler T, Löffler H, Krämer A. Diagnosis and management of metastatic neoplasms with unknown primary. *Semin Diagn Pathol*. 2018 May;35(3):199-206. doi: 10.1053/j.semdp.2017.11.013. Epub 2017 Nov 26. PMID: 29203116.

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## **What's New in Cancer of Unknown Primary Research?**

## Diagnosis

It's important for doctors to be able to identify the origin of cancers of unknown primary so that the most effective treatments can be used. Immunohistochemistry and [tumor genomic profiling](#)<sup>1</sup> (also known as **next generation sequencing** of the tumor) can be very helpful in this regard, but they are not yet able to tell where all cancers of unknown primary (CUPs) have started. Newer lab tests now becoming available, and others being studied, will help classify CUP more precisely and predict a patient's prognosis and response to treatment.

Hopefully at some point in the future, the number of cancers of unknown primary will drop dramatically, as doctors will be able to test tumor samples and determine what types of cancer they are.

## Treatment

Because CUP represents a number of different types of cancer, it's unlikely that a single treatment breakthrough will benefit all people with CUP. Still, progress in treating some of the more common types of cancer is likely to benefit people with CUP as well, especially if the cancers can be classified more accurately.

As researchers have come to understand the genetic changes that cause these tumors, they've been able to use newer treatments to target these changes.

As targeted treatments are found for more of the specific molecular changes in cancer cells, knowing the origin of a cancer may become less important. Instead, detailed information about changes in the cancer cells' DNA and RNA may become more important in choosing the treatments most likely to help individual patients.

In addition to identifying "targetable mutations" in the DNA of cancer cells, testing for the cancer cell's PD-L1 expression and tumor mutational burden may also be important. These results can be used when making decisions about the risks and benefits of



therapy. Because CUP is many types of cancers, progress is likely to depend on continued progress toward understanding the molecular basis of all cancers.

## Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/treatment-types/precision-medicine.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/precision-medicine.html)
2. [www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html](http://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html)
3. [www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html)

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Greco FA, Hainsworth JD. Carcinoma of Unknown Primary In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Wilkins 2015: 1719-1736.

National Cancer Institute. Physician Data Query (PDQ). Cancer of Unknown Primary Treatment. 05/6/2024. Accessed at: <https://www.cancer.gov/types/unknown-primary/hp/unknown-primary-treatment-pdq> on May 20, 2024. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Occult Primary. v.2.2024. Accessed at <https://www.nccn.org> on May 20, 2024.

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