

# Tumor Pathology: Definition, Development & Metastases

[See online here](#)

**Tumor malignancy is the second leading cause of death in the United States today with increasing incidence. Furthermore, the general public usually associates the term with disease leading to death. Not every diagnosis of a tumor, however, translates to a shortened lifespan in actuality. The following article will define the word 'tumor', will shed light on the mechanism of tumor development and detail means of classification with respect to treatment plans.**



## Definition of Tumor

Generally, a **tumor is a marked increase in the volume of a certain tissue** as a result of abnormal excessive cell divisions. More specifically, a newly developed (neoplastic) growth of abnormal tissue made up of degenerated cells may be termed a tumor. The growth displays the characteristics of being autonomous, progressive, invasive, and hyperproliferative. Tumors can be benign (non-cancerous) or malignant (cancerous).

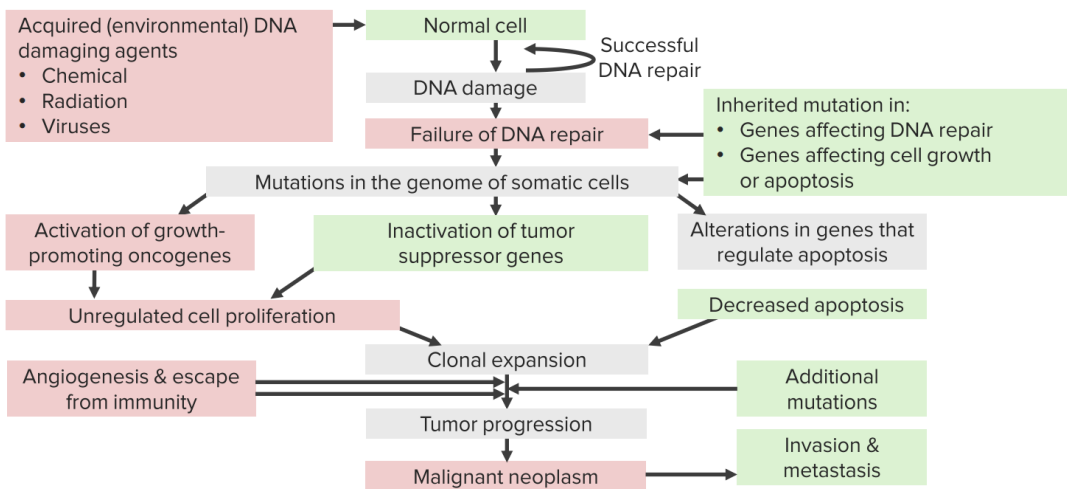
## Basics

- **Dysplasia** = disordered often reversible growth, but often leads to neoplasia
- **Neoplasia** = new irreversible growth
- **Tumor** = can be benign or malignant
- **Cancer** = malignant neoplasm

## Carcinogenesis

### Ames test: Screens for carcinogens

- Detects mutagenic effects on bacterial cells in culture
- Assumes that mutagenicity in vitro correlates with carcinogenicity in vivo



## Carcinogenic chemicals

**Nitrosamines:** Gastric adenocarcinoma

### Asbestos:

- Lung carcinoma (bronchogenic)
- Mesotheliomas
- Renal cell carcinoma

**Chromium and nickel:** Lung carcinoma

### Arsenic:

- Squamous cell carcinoma of the skin and lung
- Angiosarcoma of liver

**Vinyl chloride:** Angiosarcoma of liver

### Alkylating agents:

- Leukemia
- Lymphoma

### Naphthylamine:

- Bladder cancer

# Tumorigenesis

Cell death within regenerating tissue is constant while new cells are being formed. During this regeneration process, **tumorigenesis can cause DNA replication errors leading to genetic mutations**, potentially resulting in **hyperplasia and then metaplasia**. The effect is that cells may multiply uncontrollably.

**Finally, dysplasia occurs:** Disordered differentiation affects tissue formation, which is still reversible at this stage. An irreversible final differentiation of cells with marked loss of original structure and function is called anaplasia. Dysplasia is classified into:

- **Mild dysplasia:** Disordered tissue formation only observed in basal layer
- **Moderate dysplasia:** Disordered tissue formation reaches epithelial layer
- **Severe dysplasia:** Entire epithelium including surface is affected

**Dysplasia is a carcinoma occurring prior to the development of malignant tumors.** If there is a trigger caused by a genetic mutation, it is called a precancerous condition.

**Dysplasia can progress and spread to neoplasia** containing various tumor cell types. The most aggressive of the colonies may expand to spread beyond histological and anatomical margins. This **next stage is called *in situ carcinoma***. Hematogenous spread may lead to metastases (see below).

## Benign vs. Malignant Tumors

Tumor classification is determined by whether it is benign or malignant and also by its cellular origin:

Origin	Benign Tumor	Malignant Tumor
Epithelial <ul style="list-style-type: none"><li>• Glandular tissue</li><li>• Squamous cells</li><li>• Urothelial cells</li></ul>	Adenoma Papilloma Papilloma	Adenocarcinoma Squamous cell carcinoma Urothelial carcinoma
Mesenchymal (Ex.) <ul style="list-style-type: none"><li>• Fatty tissue</li><li>• Connective tissue</li><li>• Osseous tissue</li><li>• Cartilage tissue</li></ul>	Lipoma Fibroma Osteoma Chondroma	<b>Sarcoma</b>

When a tumor grows invasively and destructively, but has not metastasized, it is termed a semi-malignancy.

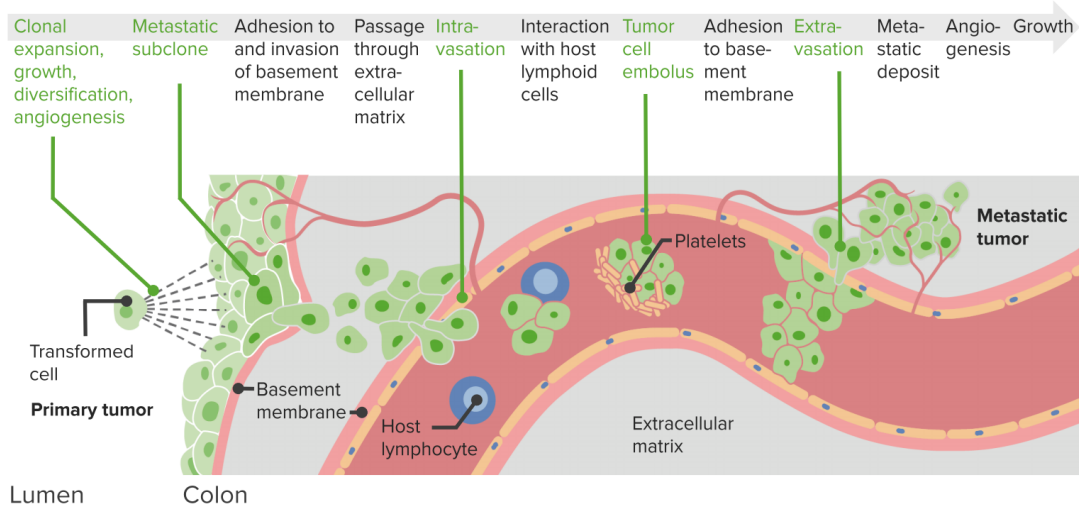
**Benign tumor does not grow destructively but rather slowly crowds healthy tissue.** It has a homogeneous consistency with smooth edges and is usually movable. Conversely, a **malignant tumor is marked by fast, invasive and destructive growth.** Often, metastases are formed. Visually, it displays a colorful heterogeneous morphology with irregular margins. When margins to neighboring structures are breached it leads to structural deformity and invasion.

Histologically, benign tumors display a low cell count with homogenous monomorphic nuclei. DNA content, chromatin, and nucleus are normal. No cellular abnormalities and a low mitotic index are also indicative of benign tumors.

By contrast, a malignant tumor displays a high cell count with different sizes of nuclei. The nucleus to plasma size ratio is increased. Nucleoli are prominent and lumped together. **Atypical mitotic index, heterochromia** (simultaneous existence of

eosinophil and basophil granules), **and aneuploidy** (numerical chromosome aberration, abnormal number of chromosomes) **are typical for malignant tumor cells.**

While a benign tumor can be removed surgically with a good prognosis, treatment of a malignant tumor typically includes surgery, if an option, followed by chemotherapy and radiation. However, depending on the type of tumor and on the possibility of recurrence, the prognosis may be poor.



## Grading and Staging

With a tissue sample biopsy, a pathologist determines histologically the grade and stage of malignancy for the tumor:

- **Atypical nucleus:** Is there evidence of heterochromatin, polymorpha and/or anisonucleosis?
- **Mitosis:** What is the mitotic index? Is it atypical?
- **Grade of differentiation:** How similar is the biopsy to originating tissue or cells?

Assessment:

- G1: Highly differentiated, only minimally malignant
- G2: Moderately differentiated, medium malignancy
- G3: Slightly differentiated, highly malignant
- G4: Completely undifferentiated, anaplastic

The level of differentiation decreases with increasing level of malignancy.

**Staging determines the extent and spread of the tumor.** This is described with the letters **T, N, and M**, which are followed by numbers that describe the criteria quantitatively.

T: Size of primary tumor	T1-3 = depending on size T4 = Infiltration observed Tis = Carcinoma in situ
N: Are there lymph node metastases?	N0 = none N1-3 = depending on number and location of affected lymph nodes
M: Are there hematogenous metastases?	M0 = none M1 = there is evidence of distant metastases

(pTNM means staging performed post-surgery)

This staging is expressed universally. Every tumor type has different definitions for the numbers which can be referenced. Grading describes histological assessment, while staging involves imaging and surgical procedures.

Look here for more information about [staging and grading](#).

## Metastases–How does a Tumor Spread?

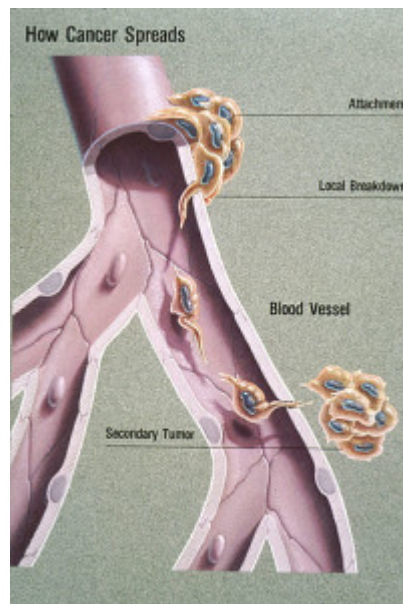


Image: "Metastasis Illustration" by National Cancer Institute. License: Public Domain

The spread of a tumor from beyond its primary site is called metastasis. Metastasis occurs through infiltration to adjacent healthy tissues with lymph vessel/node and/or blood vessel dissemination. When a tumor grows in an infiltrating manner, it can enter the lymphatic and vascular systems. Invasion is facilitated through proteases and hyaluronidases. **Malignant cells transported through the lymph and blood vessels** can attach to distant parts of the body. Depending on the means of dissemination, the appropriate terminology is **lymphogenic or hematogenous metastases**.

**Within the blood circulatory system, malignant cells interact with the immune system.** A tumor cell embolism is formed which can attach to the basal membrane of the vessel. Cells invade other tissues and organs through extravasation. Initially, they are dormant and excrete signal complexes which stimulate angiogenesis. Blood vessels will grow towards the metastasis and deliver nutrients. This enables an increase in tumor size.

Different types of primary tumors have different distinct and specific routes of metastasis depending on the location and blood flow.

Primary lung cancer metastasizes via systemic circulation. Primary liver cancer spreads via the hepatic vein and inferior vena cava to the lungs. Likewise, tumors in the drainage area of the venae cavae will metastasize via the [heart](#) to the [lungs](#). The tumor may spread via the portal vein first into the [liver](#) and finally into the lungs.

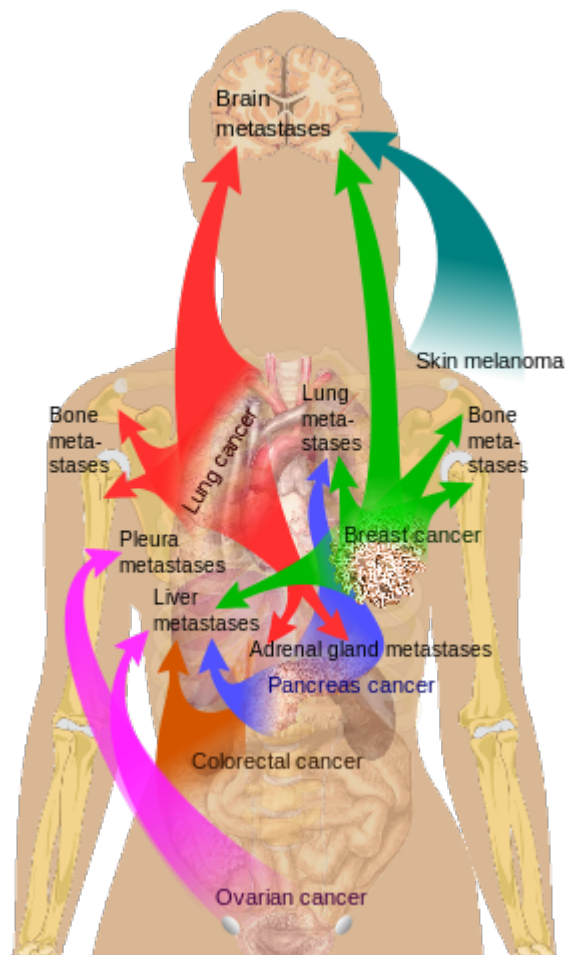


Image: "Main sites of metastases for common cancer types" by Mikael Häggström. License: Public Domain

## Tumor Resection

Tumors are often removed surgically, possibly in combination with chemotherapy or radiation therapy. To judge the result of resection, the following classification has been established.

Resection grade	Definition
R0	Margins of resected tissue are pathologically proven to be free of tumor tissue.
R1	Tumor tissue can be shown microscopically to exist within resection margins.
R2	Tumor tissue macroscopically shown within resection margins.

## Prognosis of metastatic tumors

Metastasis of tumors is difficult to control. Most metastatic tumors are untreatable. The aim of treatment is to stop tumor growth and to relieve the symptoms caused by it. The prognosis of the primary tumor itself is determined by its metastasis. Prognosis is worse if the primary tumor metastasizes to other anatomical sites.

# References

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