



## Benign tumor

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**Abstract:** A **benign tumor** is a mass of [cells \(tumor\)](#) that lacks the ability to either [invade neighboring tissue](#) or [metastasize](#) (spread throughout the body). When removed, benign tumors usually do not grow back, whereas [malignant tumors](#) sometimes do. Unlike most benign tumors elsewhere in the body, benign [brain tumors](#) can be life-threatening.<sup>[1]</sup> Benign tumors generally have a slower [growth rate](#) than malignant tumors and the tumor cells are usually more [differentiated](#) (cells have more normal features).<sup>[2][3][4]</sup> They are typically surrounded by an outer surface (fibrous sheath of [connective tissue](#)) or stay contained within the [epithelium](#).<sup>[5]</sup> Common examples of benign tumors include [moles](#) and [uterine fibroids](#).

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### Benign tumor

A **benign tumor** is a mass of [cells \(tumor\)](#) that lacks the ability to either [invade neighboring tissue](#) or [metastasize](#) (spread throughout the body). When removed, benign tumors usually do not grow back, whereas [malignant tumors](#) sometimes do. Unlike most benign tumors elsewhere in the body, benign [brain tumors](#) can be life-threatening.<sup>[1]</sup> Benign tumors generally have a slower [growth rate](#) than malignant tumors and the tumor cells are usually more [differentiated](#) (cells have more normal features).<sup>[2][3][4]</sup> They are typically surrounded by an outer surface (fibrous sheath of [connective tissue](#)) or stay contained within the [epithelium](#).<sup>[5]</sup> Common examples of benign tumors include [moles](#) and [uterine fibroids](#).

Although benign tumors will not metastasize or locally invade [tissues](#), some types may still produce negative health effects. The growth of benign tumors produces a "[mass effect](#)" that can compress tissues and may cause nerve damage, reduction of blood flow to an area of the body ([ischaemia](#)), tissue death ([necrosis](#)) and organ damage. The health effects of the tumor may be more prominent if the tumor is within an enclosed space such as the [cranium](#), [respiratory tract](#), [sinus](#) or inside bones. Tumors of [endocrine](#) tissues may overproduce certain [hormones](#). Examples include [thyroid adenomas](#) and [adrenocortical adenomas](#).<sup>[2]</sup>

Although most benign tumors are not life-threatening, many types of benign tumors have the

potential to become cancerous ([malignant](#)) through a process known as [tumor progression](#).<sup>[6]</sup> For this reason and other possible negative health effects, some benign tumors are removed by surgery.<sup>[7]</sup>

### Signs and symptoms

Benign tumors are very diverse; they may be asymptomatic or may cause specific symptoms, depending on their anatomic location and tissue type. They grow outward, producing large, rounded masses which can cause what is known as a "mass effect". This growth can cause compression of local tissues or organs, leading to many effects, such as blockage of ducts, reduced blood flow ([ischaemia](#)), tissue death ([necrosis](#)) and nerve pain or damage.<sup>[2]</sup> Some tumors also produce hormones that can lead to life-threatening situations. [Insulinomas](#) can produce large amounts of insulin, causing [hypoglycemia](#).<sup>[8][9]</sup> [Pituitary adenomas](#) can cause elevated levels of hormones such as [growth hormone](#) and [insulin-like growth factor-1](#), which cause [acromegaly](#); [prolactin](#); [ACTH](#) and [cortisol](#), which cause [Cushings disease](#); [TSH](#), which causes [hyperthyroidism](#); and [FSH](#) and [LH](#).<sup>[10]</sup> [Bowel intussusception](#) can occur with various benign colonic tumors.<sup>[11]</sup> Cosmetic effects can be caused by tumors, especially those of the skin, possibly causing psychological or social discomfort for the person with the tumor.<sup>[12]</sup> [Vascular tissue tumors](#) can bleed, in some cases leading to [anemia](#).<sup>[13]</sup>

## Causes

### PTEN hamartoma syndrome

PTEN hamartoma syndrome consists of four distinct [hamartomatous](#) disorders characterised by genetic mutations in the [PTEN](#) gene; [Cowden syndrome](#), [Bannayan-Riley-Ruvalcaba syndrome](#), [Proteus syndrome](#) and [Proteus-like syndrome](#). Although they all have distinct clinical features, the formation of hamartomas occurs in all four syndromes. PTEN is a [tumor suppressor](#) gene that is involved in [cellular signalling](#). Absent or dysfunctional PTEN protein allows cells to over-proliferate, causing hamartomas.<sup>[14]</sup>

### Other syndromes

[Cowden syndrome](#) is an [autosomal dominant genetic disorder](#) characterised by multiple benign [hamartomas](#) ([trichilemmomas](#) and mucocutaneous papillomatous papules) as well as a predisposition for cancers of multiple organs including the breast and thyroid.<sup>[15][16]</sup> [Bannayan-Riley-Ruvalcaba syndrome](#) is a [congenital disorder](#) characterised by hamartomatous intestinal polyposis, [macrocephaly](#), [lipomatosis](#), [hemangiomas](#) and [glans penis macules](#).<sup>[14][17]</sup> [Proteus syndrome](#) is characterised by [nevi](#), asymmetric overgrowth of various body parts, adipose tissue dysregulation, [cystadenomas](#), [adenomas](#), vascular malformation.<sup>[18][19]</sup>

### Familial adenomatous polyposis [\[edit\]](#)

[Familial adenomatous polyposis](#) (FAP) is a familial [cancer syndrome](#) caused by mutations in the [APC](#) gene. In this disorder [adenomatous](#) polyps are present in the [colon](#) that will progress into [colon cancer](#) unless removed.<sup>[20]</sup> The APC gene is a [tumor suppressor](#); its protein product is involved in many cellular processes. Inactivation of the APC gene leads to the buildup of a protein called [β-catenin](#), which activates two [transcription factors](#): [T-cell factor](#) (TCF) and [lymphoid enhancer factor](#) (LEF). These cause the upregulation of many genes involved in cell [proliferation](#), [differentiation](#), [migration](#) and [apoptosis](#) (programmed cell death), causing the growth of benign tumors.<sup>[21]</sup>

### Tuberous sclerosis complex

[Tuberous sclerosis complex](#) (TSC) is an autosomal dominant genetic disorder caused by mutations in the genes [TSC1](#) and [TSC2](#), which produce the proteins [hamartin](#) and [tuberin](#), respectively. This disorder presents with many benign hamartomatous tumors including [angiofibromas](#), renal [angiomyolipomas](#), pulmonary [lymphangiomyomatosis](#). Tuberin and hamartin inhibit the [mTOR](#) protein in normal cellular physiology and the inactivation of the TSC tumor suppressors causes an increase in mTOR

activity. This leads to the activation of genes and the production of proteins that increase cell growth.<sup>[22][23][24]</sup>

### Von Hippel-Lindau disease

[Von Hippel-Lindau disease](#) is a dominantly-inherited cancer syndrome that significantly increases the risk of various tumors including benign [hemangioblastomas](#) and malignant [pheochromocytomas](#), [renal cell carcinomas](#), [pancreatic endocrine tumors](#) and [endolymphatic sac tumors](#). It is caused by genetic mutations in the [Von Hippel-Lindau tumor suppressor](#) gene. The VHL protein (pVHL) is involved in cellular signalling in oxygen starved ([hypoxic](#)) cells. One role of pVHL is to cause the cellular degradation of another protein, [HIF1α](#). Dysfunctional pVHL leads to accumulation of HIF1α, which activates several genes responsible for the production of substances involved in cell growth and blood vessel production: [VEGF](#), [PDGFβ](#), [TGFα](#) and [erythropoietin](#).<sup>[25]</sup>

## Mechanism

### Benign vs malignant

One of the most important factors in classifying a tumor as benign or malignant is its invasive potential. If a tumor lacks the ability to invade adjacent [tissues](#) or spread to distant sites by metastasizing then it is benign, whereas invasive or metastatic tumors are malignant.<sup>[2]</sup> For this reason, benign tumors are not classed as cancer.<sup>[3]</sup> Benign tumors will grow in a contained area usually encapsulated in a fibrous [connective tissue](#) capsule. The growth rates of benign and malignant tumors also differ; benign tumors generally grow more slowly than malignant tumors. Although benign tumors pose a lower health risk than malignant tumors, they both can be life-threatening in certain situations. There are many general characteristics which apply to either benign or malignant tumors, but sometimes one type may show characteristics of the other. For example, benign tumors are mostly well differentiated and malignant tumors are often undifferentiated. However, undifferentiated benign tumors and differentiated malignant tumors can occur.<sup>[26][27]</sup> Although benign tumors generally grow slowly, cases of fast-growing benign tumors have also been documented.<sup>[28]</sup> Some malignant tumors are mostly non-metastatic such as in the case of [basal cell carcinoma](#).<sup>[4]</sup> CT and chest radiography can be a useful diagnostic exam in visualizing a benign tumor and differentiating it from a malignant tumor. The smaller the tumor on a radiograph the more likely it is to be benign as 80% of lung nodules less than 2 cm in diameter are benign. Most benign nodules are smoothed radiopaque densities with clear margins but these are not exclusive

signs of benign tumors.<sup>[29]</sup>

### Multistage carcinogenesis

Tumors are formed by [carcinogenesis](#), a process in which cellular alterations lead to the formation of cancer. Multistage carcinogenesis involves the sequential [genetic](#) or [epigenetic](#) changes to a cell's [DNA](#), where each step produces a more advanced tumor. It is often broken down into three stages; initiation, promotion and progression, and several mutations may occur at each stage. Initiation is where the first genetic mutation occurs in a cell. Promotion is the clonal expansion (repeated division) of this transformed cell into a visible tumor that is usually benign. Following promotion, progression may take place where more genetic mutations are acquired in a sub-population of tumor cells. Progression changes the benign tumor into a malignant tumor.<sup>[6][30]</sup> A prominent and well studied example of this phenomenon is the tubular adenoma, a common type of [colon polyp](#) which is an important precursor to colon cancer. The cells in tubular adenomas, like most tumors that frequently progress to cancer, show certain abnormalities of cell maturation and appearance collectively known as [dysplasia](#). These cellular abnormalities are not seen in benign tumors that rarely or never turn cancerous, but are seen in other pre-cancerous tissue abnormalities which do not form discrete masses, such as [pre-cancerous lesions of the uterine cervix](#).

### Diagnosis

#### Classification

Benign [neoplasms](#) are typically but not always composed of cells which bear a strong resemblance to a normal cell type in their organ of origin. These tumors are named for the cell or tissue type from which they originate, followed by the suffix "-oma" (but not -carcinoma, -sarcoma, or -blastoma, which are generally cancers). For example, a [lipoma](#) is a common benign tumor of fat cells ([lipocytes](#)), and a [chondroma](#) is a benign tumor of cartilage-forming cells ([chondrocytes](#)). [Adenomas](#) are benign tumors of gland-forming cells, and are usually specified further by their cell or organ of origin, as in [hepatic adenoma](#) (a benign tumor of [hepatocytes](#), or [liver](#) cells). [Teratomas](#) contain many cell types such as skin, nerve, brain and thyroid, among others, because they are derived from germ cells.<sup>[4]</sup> [Hamartomas](#) are a group of benign tumors that have relatively normal [cellular differentiation](#) but the architecture of the tissue is disorganised.<sup>[22]</sup> There are a few cancers with 'benign-sounding' names which have been retained for historical reasons, including [melanoma](#) (a cancer of pigmented skin cells, or [melanocytes](#)) and [seminoma](#) (a cancer of male reproductive cells).<sup>[32]</sup> Skin tags,

vocal chord polyps and hyperplastic polyps of the colon are often referred to as benign but they are actually overgrowths of normal tissue rather than neoplasms.<sup>[4]</sup>

### Treatment

Some benign tumors need no treatment; others may be removed if they cause problems such as seizures, discomfort or cosmetic concerns. [Surgery](#) is usually the most effective approach and is used to treat most benign tumors. In some case other treatments may be of use. Adenomas of the [rectum](#) may be treated with [sclerotherapy](#), a treatment in which chemicals are used to shrink blood vessels in order to cut off the blood supply.<sup>[13]</sup> Most benign tumors do not respond to [chemotherapy](#) or [radiation therapy](#), although there are exceptions; benign intracranial tumors are sometimes treated with radiation therapy and chemotherapy under certain circumstances.<sup>[33][34]</sup> Radiation can also be used to treat hemangiomas in the rectum.<sup>[13]</sup> Benign skin tumors are usually surgically resected but other treatments such as [cryotherapy](#), [curettage](#), [electrodesiccation](#), [laser therapy](#), [dermabrasion](#), [chemical peels](#) and [topical medication](#) are used.<sup>[35][36]</sup>

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