

We use the word to describe only neoplastic masses of tissue. In this block, we'll use the terms tumor and neoplasm interchangeably.

What does the term neoplasm describe?

What's the Difference Between Benign and Malignant Tumors?

There are two kinds of tumors:

- Benign tumors do not have the ability to metastasize (spread) to other tissues. In general, benign tumors tend to be smaller and grow more slowly than malignant tumors. Benign tumors are usually surrounded by a capsule, making them more surgically removable and leading to a better prognosis.
- Malignant tumors (cancerous tumors) are those that can invade tissues or spread to other parts of the body. The potential for metastasis is a characteristic feature of a malignant tumor. Malignant tumors usually ~~do not have a capsule and often have a worse prognosis~~.

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These are generalizations, but the core defining feature of a malignant tumor is that it can metastasize, while benign tumors do not metastasize. However, just because benign tumors do not metastasize, that does not mean that they cannot be life-threatening. For example, a meningioma is a benign tumor of the meninges that can compress brain tissue and cause neurological problems such as seizures, paralysis, and changes in vision. Benign brain tumors in particular are dangerous because of the limited space in the skull.

Table 1 summarizes tumor terminology.

Table 1

Term	Definition
Neoplasm/tumor	A new and abnormal growth of tissue in the body
Invasion	Local growth of a tumor into surrounding tissue
Metastasis	Spread of a tumor to distant sites in the body
Benign	Describes a localized tumor that does not metastasize
Malignant	Describes a tumor that may metastasize; may be resistant to treatment and recur after removal

They are pre-invasive: they have not broken through their basement membrane and penetrated the underlying tissue. CIS is the very earliest stage of cancer, also referred to as stage 0. Removal of a cancer at this stage is curative because the tumor has not metastasized.

STRUCTOR NOTE

This is an important concept

MARIA PLUMMER

How does metaplasia differ from dysplasia?

 CASE CONNECTION

Thinking back to TF, how do you explain these results to her?

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Your intent is to reassure TF quickly so you say, "It's benign." She responds, "I have no idea what that means. Is it cancer?" You explain that a uterine fibroid is the growth of uterine muscle but that it is not cancer. "Benign means that the growth is localized, in your case the growth of uterine smooth muscle cells, and that it will not spread or metastasize to other parts of the body." You explain that the fibroid can be removed for symptoms. Because of persistent pain and bleeding, TF opts for surgery, which she tolerates well without postoperative complications.

Summary

- The defining feature of a malignant tumor is its ability to metastasize, or spread to the rest of the body.
- Tumors range from well-differentiated to poorly differentiated to anaplastic.
- Well-differentiated tumors tend to grow slowly and have a better prognosis than poorly differentiated tumors.
- Histologic features of poorly differentiated tumors include pleomorphism, hyperchromatic nuclei, and a high nuclear-to-cytoplasmic ratio.
- Metaplasia is the replacement of one cell type by another.
- Metaplasia is often an adaption to some type of chronic damage to tissue, such as in Barrett esophagus.
- Dysplasia is the disordered growth of non-neoplastic epithelial cells characterized by morphologic changes such as pleomorphism and hyperchromatic nuclei.
- Both metaplasia and dysplasia are reversible but in some cases precede cancer.

Technically, a benign tumor of melanocytes should be called a melanoma, but for unknown reasons, the term melanoma is used for the malignant version of this tumor. So we're stuck with nevus.

What is the name for a benign tumor of blood vessels?

Malignant Tumors

Remember that the body is made up of two major classes of tissue: epithelial tissues and mesenchymal tissues. Epithelium consists of densely packed cells atop a basement membrane; this tissue covers various surfaces and lines cavities within the body.

Mesenchymal tissues are “soft” tissues, or connective tissues, that make up the bulk of the body (eg, muscle, bone, cartilage, fat, and connective tissue). These tissues are derived from mesenchyme, a gelatinous substance present during early embryogenesis. Mesenchyme arises from mesoderm, the germ cell layer sandwiched between the ectoderm and the endoderm.

endoderm.

When a malignant tumor is derived from epithelial tissue, “carcinoma” is added. For example:

- Malignant tumor of glandular cells = adeno (glandular cells) + carcinoma (glandular cells are epithelial) = adenocarcinoma
- Malignant tumor of squamous cells = squamous cell + carcinoma (squamous cells are epithelial) = squamous cell carcinoma

When a malignant tumor is derived from mesenchymal tissue, “sarcoma” is added. In Greek, sark or sark means flesh, so you can think of sarcomas as malignant tumors of fleshy tissues. For example: malignant tumor of smooth muscle = leiomyo (smooth muscle) + sarcoma (smooth muscle is mesenchymal) = leiomyosarcoma.

What is the name for a malignant tumor of fat cells?

Exceptions to the Rule

Please let me know if you have any further questions." SN thanks you for your prompt reply. In his follow-up visit, you jointly decide to repeat the colonoscopy in 5 years.

Summary

- Neoplasia is the unregulated, monoclonal proliferation of cells; a neoplasm can be benign or malignant.
- Benign tumors remain localized and do not metastasize, while malignant tumors are capable of metastasizing; "cancer" refers to malignant tumors.
- In general, tumor names have two parts: the first part refers to the tumor's tissue of origin, and the second part includes the suffix -oma.
- Benign tumors are named by adding -oma to the tumor's tissue of origin (eg, adenoma).
- Malignant tumors are named by adding "carcinoma" (if the tumor is derived from epithelial cells) or "sarcoma" (if the tumor is derived from mesenchymal cells) to the tumor's tissue of origin (eg, adenocarcinoma).
- There are many exceptions to the general rules for tumor nomenclature; it's important to become familiar with the most common ones to avoid confusion.

Review Questions

1. A patient receives a diagnosis of squamous cell carcinoma of the lung. According to the standard rules of tumor nomenclature, which of the

following is true about this lesion?

- A. It can also be called a papilloma
- B. It can invade locally and spread to distant anatomic sites
- C. It is a benign tumor
- D. It is not cancer
- E. The tissue of origin is mesenchymal

Explanation (requires correct answer)

2. A man is told he has a fibroma. According to the standard rules of tumor nomenclature, which of the following is true about this lesion?

- A. It is a benign tumor
- B. It is cancer
- C. It is derived from muscle cells
- D. It has the potential to metastasize
- E. It will contain many areas of necrosis

Explanation (requires correct answer)

What Are Tumor Markers?

INSTRUCTOR NOTE

Discussed in Intro to Neoplasia, part 2

MARIA PLUMMER

A tumor marker is a compound that can be measured in the serum or urine that is elevated in the presence of cancer. These markers are usually substances that are produced by the tumors, resulting in levels higher than is otherwise normal. Common examples include:

- CA19-9, a marker for pancreatic cancer
- Alpha-fetoprotein (AFP), a marker for hepatocellular carcinoma (HCC)
- Chromogranin, a marker for neuroendocrine tumors
- Prostate-specific antigen (PSA), a marker for prostate cancer
- CA-125, a marker for ovarian cancer

CLINICAL CORRELATION

Prostate cancer is the most common cancer in men, and breast cancer is the most common cancer in women. Lung cancer is the second most common cancer in both men and women, and it is the most common cancer killer in both men and women as well. A better way to state this is to say that lung cancer has the greatest mortality across both men and women, while breast

cancer has the greatest morbidity for women and prostate cancer has the greatest morbidity for men.

Tumor markers should not be used as a primary tool for diagnosing or screening for cancer. Levels can vary from patient to patient and can be affected by specific patient characteristics, so they are not a reliable tool for diagnosis. (For example, PSA levels change as men age, so the threshold for elevated PSA levels is different for men of different ages. Therefore, PSA has low sensitivity and specificity for detecting prostate cancer.)

However, after a cancer diagnosis is established, tumor markers can be very useful. A physician can measure the baseline levels of a tumor marker and track the changes over time. A decrease usually signifies a positive response to treatment, while an increase suggests minimal response; this can influence prognosis. Markers can also be used to monitor patients after treatment. Once a patient's baseline level is established after treatment, an increasing tumor marker level later might suggest cancer recurrence.

Remember that PSA stands for **Prostate-Specific Antigen** to recall it is the tumor marker for prostate cancer.

CASE CONNECTION

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Thinking back to PF, how do you explain the summary to him? What is his prognosis?

You explain to PF that the abbreviation is a way of reporting the staging of his lung cancer. Staging describes the size of the tumor (T), whether or not it has spread to the lymph nodes (N), and whether there is distant spread of the cancer or metastases (M). You explain that his tumor is between 4 and 5 cm in size, and there is no spread to either the lymph nodes or distant sites.

"With this information, we can give you some numbers about your prognosis. Your 5-year survival is 31%," you tell him.

Summary

- Prognosis is a forecast of the likely course and outcome of a patient's disease. Having a prognosis helps inform patients and providers on the best steps in management.
- Numerous outcome measures are used when giving a prognosis. Because each type of cancer has a range of possible prognoses, each patient must be individually evaluated to determine an accurate prognosis.
- There are many factors involved in determining the prognosis for a patient with a particular type of cancer (eg, lung or breast cancer). In

general, the most important of these is the stage of the cancer (eg, stage 2 or stage 4).

- Cancer staging describes the size and spread of a tumor. We use the TNM system to establish the stage of a cancer. M refers to the distant metastasis of cancer, and it is the most important prognostic factor; lymph node involvement (N) is the second most important.
- The higher the cancer stage, the worse the prognosis.
- The grade of a cancer describes its histologic features.
- Grading also contributes to prognosis, with a high grade conferring a worse prognosis. However, grading is not as important a factor as staging.
- Tumor markers are measurable compounds that are useful for measuring response to cancer treatment, prognosis, or the recurrence of disease. They are generally not useful for diagnosis.

Review Questions

1. Which of the following patients carries the worst prognosis?

- A. A 25-year-old man with stage 3 Hodgkin lymphoma
- B. A 50-year-old man with stage 2 colon cancer
- C. A 65-year-old woman with stage 3 estrogen receptor-positive breast cancer
- D. A 70-year-old man with stage 4 lung cancer
- E. A 75-year-old woman with stage 3 lung cancer

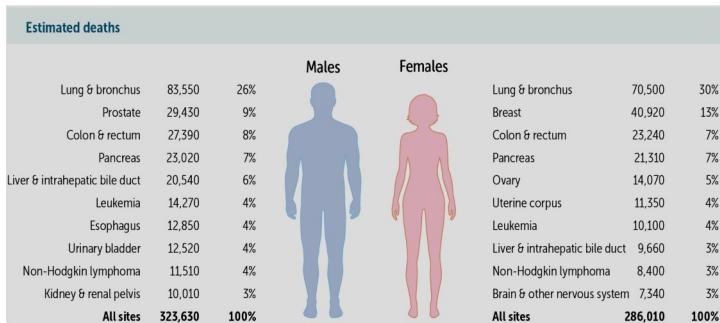


Figure 1

There are many different types of cancer, and each has its own prognosis. Some types of cancer, like thyroid cancer, are almost always curable. Others, like pancreatic cancer, are almost always rapidly fatal. This is why the lists of the most common cancers and the cancers causing the most deaths look different!

For example, take a look at the most common cancers in men (prostate) and women (breast) in Figure 1. Although these cancers can be fatal, their overall prognosis is relatively good compared with lung cancer, which has a terrible prognosis. That's why so many more women die of lung cancer than breast cancer, even though the incidence of breast cancer is more than double the incidence of lung cancer. Thyroid cancer is fairly common, especially in women—but its prognosis is so good that it doesn't even make it onto the list of cancers causing the most deaths in women. Pancreatic cancer is uncommon, yet it causes almost as many deaths as does colon cancer.

What type of cancer causes the most deaths in both men and women in the United States?

How Have Cervical, Colorectal, and Breast Cancers Changed in Incidence?

Let's take a detailed look at three cancers—cervical, colorectal, and breast—which incidences have changed in the past century. A common theme you will see is the development of screening tools for these cancers and how their use has affected the statistics.

STRUCTOR NOTE

Please note, you do not need to know the specifics of these cancers at this time. Rather, these are being used as examples to incorporate the concepts. You will learn about these cancers in their respective systems. However, it is important to realize that many environment factors may cause cancers including infectious agents like HPV which may lead to squamous cell carcinoma of the cervix (see further below).

Occupational Agents

Several carcinogens are encountered primarily in occupational settings. A wide range of fields, from agriculture to construction to manufacturing, use specific agents that are known to cause cancer:

- Asbestos (in construction materials) is linked to several cancers, including mesothelioma.
- Benzene (in printing, paint, and light oil) is linked to acute myeloid leukemia.
- Radon (in underground mines and also in residential properties) is linked to lung cancer.
- Vinyl chloride (in refrigerants and adhesives) is linked to hepatic angiosarcoma.

As we can see, carcinogens are both diverse and widespread, and a solid awareness of them is critical to successfully preventing many cancers.

What type of cancer is linked to benzene exposure?

What Are the Genetic Risk Factors for Cancer?

Because cancer arises from mutations in DNA, it is not surprising that heredity plays a role in cancer. This brings up the distinction of cancers that are inherited vs sporadic, ie, arising de novo. Sporadic cancers can be further classified as spontaneous cancers, which arise without carcinogen exposure, and induced cancers, which are the result of carcinogen exposure. Figure 3 illustrates this breakdown with several examples.

Figure 3

Hereditary cancers are caused by gene mutations that are passed on from the parent to child. Well known among these are mutations in the *BRCA* gene (hereditary breast and ovarian cancer syndrome) and in mismatch repair genes (Lynch syndrome). Lynch syndrome carries an increased risk of endometrial cancer and colorectal cancer.

Sporadic cancers do not come from inherited genetic mutations. Instead, at some point in the individual's life, he or she acquires a mutation in a somatic cell, which then leads to cancer. Because the somatic cell line is not passed onto the next generation, the individual's cancer is considered sporadic. Lung and bladder cancers are examples of sporadic cancers due to carcinogen exposure.

Hereditary cancers tend to manifest earlier and act more aggressively than their sporadic counterparts. For example, colon cancer can be either sporadic or hereditary. Sporadic cases usually appear after age 50 years and if detected early typically have a relatively good prognosis. In contrast, hereditary forms of colon cancer, such as those that develop in patients with Lynch syndrome, can occur as early as age 20 years and typically have a poor prognosis.

Retinoblastoma, the most common intraocular malignancy in children, is another cancer that has both hereditary and sporadic forms. This rapidly progressive cancer of the eye usually appears in childhood and is caused by inactivating mutations in the *RB* (retinoblastoma) gene. The *RB* gene is a tumor-suppressor gene, which means that in normal cells it encodes a product that puts the brakes on cell division. If just one of the two *RB* alleles is mutated, retinoblastoma does not develop because the remaining normal *RB* allele is able to compensate adequately. However, if both *RB* alleles are mutated in such a way that they don't work, then it's like having

the brakes go out in your car: there's nothing to stop the cell from dividing and proliferating, and as a result, retinoblastoma develops.

About 40% of cases of retinoblastoma are **hereditary** in nature. Patients with hereditary retinoblastoma inherit one normal *RB* allele and one mutated, inactive *RB* allele. The mutated *RB* allele is inherited in an **autosomal dominant** fashion. But because one mutated *RB* allele is not enough to cause retinoblastoma, the patient is said to be a carrier of the retinoblastoma trait. Without a second *RB* mutation, the patient will not develop retinoblastoma.

This doesn't sound so bad at first. How likely can it be that the patient would just spontaneously develop a mutation in the second *RB* allele? Unfortunately, very likely. In fact, carriers of the retinoblastoma trait are 10,000 times more likely to develop retinoblastoma as compared with noncarriers, often in both eyes. In addition, they have a very high risk of developing other aggressive malignancies, such as **osteosarcoma**.

The remaining 60% of cases of retinoblastoma are **spontaneous**, which means that the patient inherits two normal *RB* alleles and then at some point develops mutations in both alleles. The chances of this happening are pretty low. Patients who do develop spontaneous retinoblastoma do not have an increased risk of developing other cancers.

The explanation for these two patterns of retinoblastoma is known as the **"two-hit" hypothesis**. This hypothesis states that to develop retinoblastoma, two hits (mutations) are required: one in each *RB* allele. In hereditary cases, patients inherit one mutated *RB* allele, and the other allele undergoes mutation on its own. In spontaneous cases, the patient inherits two normal *RB* alleles, both of which undergo spontaneous mutation.

In hereditary retinoblastoma, what is the Mendelian mode of inheritance?

CASE CONNECTION

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Thinking back to FH, how do you respond to his comment?

You begin your discussion by explaining that factors other than family history contribute to a person's risk of cancer. In fact, you say that environmental factors and exposures actually play a bigger role than genetics. "Your tobacco and alcohol use are strong risk factors for cancer of the mouth, and I am concerned about the non-healing ulcer you have." FH agrees to a biopsy, and the results reveal squamous cell carcinoma.

Summary

- Earlier detection of cancer has changed cancer mortality and prevalence.

- The most common cancers in men and women are prostate and breast cancer, respectively.
- The cancer that causes the most deaths in both men and women is lung cancer.
- Cervical cancer has decreased in prevalence in the United States largely due to the introduction of the Pap smear.
- Eighty percent of cervical cancers occur outside the United States in developing countries, where access to Pap smears is limited.
- Colorectal cancer is increasing in prevalence in developing countries but is decreasing in prevalence in the United States due to improved screening.
- Environmental factors, such as dietary choices and smoking, play a major role in the development of many types of cancer.
- Cancers may be sporadic or hereditary; hereditary cases appear at younger ages and act more aggressively than their sporadic counterparts.

Review Questions

1. Which of the following is not a cancer screening tool?

- A. Colonoscopy
- B. Mammography
- C. Pap smear
- D. Urinalysis