

MEDICINE

432 Team

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Introduction to Cancer Diagnosis and Treatment



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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

1. Definition of cancer.
2. Etiology of cancer.
3. Staging of malignant diseases.
4. Principles of pathological classification of malignant diseases.
5. General symptoms and signs of malignancy.
6. Principles of cancer management.

Definition of Cancer

Cancer is a term used for diseases in which abnormal cells divide and escape the body's control.

These cells are able to:

- **Invade surrounding tissues.**
- **Send distant metastases.**
- **Lose their functions.**

Primary tumors vs. metastatic tumors:

Primary Tumors: represent de novo tumors in their initial site.

Metastatic Tumors: Originate from the distant growth of the primary tumors.

A Collection of Related Diseases ⁽¹⁾:

Cancer is the name given to a collection of related diseases. In all types of cancer, some of the body's cells begin to divide without stopping and spread into surrounding tissues. Cancer can start almost anywhere in the human body. Normally, human cells grow and divide to form new cells, as the body needs them. When cells grow old or become damaged, they die, and new cells take their place.

When cancer develops, however, this orderly process breaks down. As cells become more and more abnormal, old or damaged cells survive when they should die, and new cells form when they are not needed. These extra cells can divide without stopping and may form growths called tumors.

Cancerous tumors are malignant, which means they can spread into, or invade, nearby tissues. In addition, as these tumors grow, some cancer cells can break off and travel to distant places in the body through the blood or the lymph system and form new tumors far from the original tumor.

Unlike malignant tumors, benign tumors do not spread into, or invade, nearby tissues. Benign tumors can sometimes be quite large, however. When removed, they usually don't grow back, whereas malignant tumors sometimes do. Unlike most benign tumors elsewhere in the body, benign brain tumors can be life threatening.

Etiology of Cancer

Cancer arises from the mutation of a normal gene; mutated genes that cause cancer are called **oncogenes**.

1. DNA mutations:

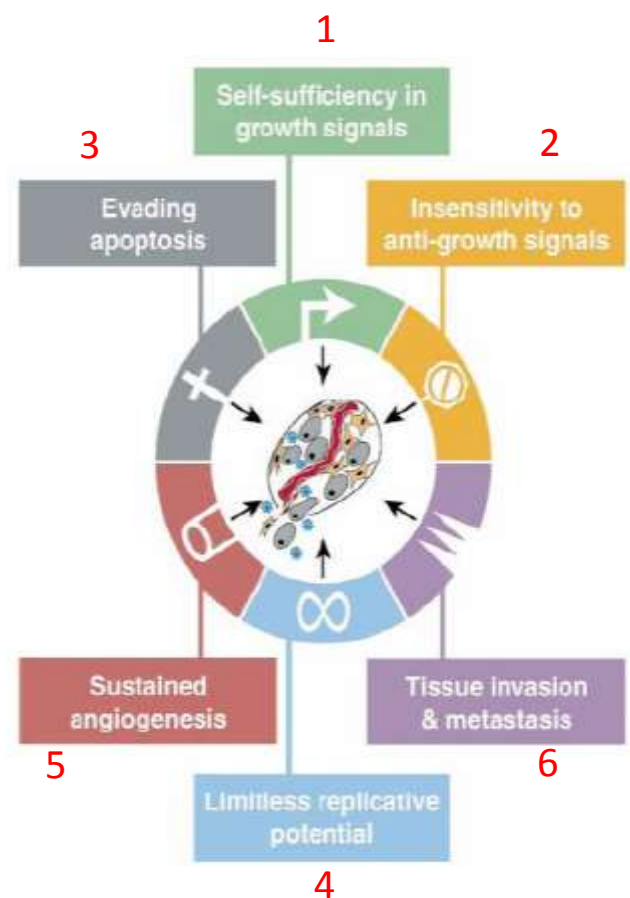
- **Radiation** and other environmental factors (tobacco, alcohol, radon, asbestos, etc.)
- **Random** somatic mutations.
- **Inherited** germ line mutations.

2. Genetic predisposition:

- Rb, p35, APC, CDKN2A, BRCA1, BRCA2.

3. Infectious agents:

- **Viral infections:**
- HPV – cervical cancer.
- Hepatitis – liver cancer.
- **Bacterial infections:**
- H.pylori – stomach cancer.
- EBV – lymphoma.



Hallmarks of cancer summarized by Hanahan and Weinberg (2000)

“Drivers” of Cancer ⁽¹⁾:

The genetic changes that contribute to cancer tend to affect three main types of genes—**proto-oncogenes, tumor suppressor genes, and DNA repair genes**. These changes are sometimes called **“drivers” of cancer**.

Proto-oncogenes are involved in normal cell growth and division. However, when these genes are altered in certain ways or are more active than normal, they may become cancer-causing genes (or oncogenes), allowing cells to grow and survive when they should not.

Tumor suppressor genes are also involved in controlling cell growth and division. Cells with certain alterations in tumor suppressor genes may divide in an uncontrolled manner.

DNA repair genes are involved in fixing damaged DNA. Cells with mutations in these genes tend to develop additional mutations in other genes. Together, these mutations may cause the cells to become cancerous.

How Cancer Starts ⁽²⁾:

Cancer starts when cells in a part of the body start to grow out of control. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells can't do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of DNA (deoxyribonucleic acid) damage. DNA is in every cell and it directs all its actions. In a normal cell, when DNA is damaged the cell either repairs the damage or dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, the cell goes on making new cells that the body doesn't need. These new cells all have the same damaged DNA as the first abnormal cell does.

Staging of Malignant Diseases (3)

Staging describes the severity of a person's cancer based on the size and/or extent (reach) of the original (primary) tumor and whether or not it has spread in the body.

All cancers are staged when they are first diagnosed. This stage classification, which is typically assigned before treatment, is **called the clinical stage**. A cancer may be further staged after surgery or biopsy, when the extent of the cancer is better known. This stage designation **called the pathologic stage** combines the results of the clinical staging with the surgical results.

TNM system: The TNM system is based on **the size and/or extent (reach) of the primary tumor (T)**, the amount of **spread to nearby lymph nodes (N)**, and the **presence of metastasis (M)** or secondary tumors formed by the spread of cancer cells to other parts of the body.

Primary Tumor (T)

TX: Primary tumor cannot be evaluated.

T0: No evidence of primary tumor.

Tis: Carcinoma in situ.

T1, T2, T3, T4: Size and/or extent of the primary tumor.

Regional Lymph Nodes (N)

NX: Regional lymph nodes cannot be evaluated.

N0: No regional lymph node involvement.

N1, N2, N3: Degree of regional lymph node involvement.

Distant Metastasis (M)

MX: Distant metastasis cannot be evaluated

M0: No distant metastasis

M1: Distant metastasis is present

What types of tests are used to determine stage?

- ✓ **Physical exam:** the physical exam may show the location and size of the tumor(s) and the spread of the cancer to the lymph nodes and/or to the tissues and organs.
- ✓ **Imaging studies:** x-rays, CT scans, and MRI scans can show the location of the cancer, the size of the tumor, and whether the cancer has spread.
- ✓ **Laboratory tests.**
- ✓ **Pathology reports:** provides information about the size of the tumor, the growth of the tumor into other tissues and organs, the type of cancer cells, and the grade. These information could be provided by a biopsy.
- ✓ **Surgical reports.**

What is tumor grade? ⁽⁴⁾

Tumor grade is the description of a tumor based on how abnormal the tumor cells and the tumor tissue look under a microscope. It is an indicator of how quickly a tumor is likely to grow and spread.

If the cells of the tumor and the organization of the tumor's tissue are close to those of normal cells and tissue, the tumor is called "**well-differentiated.**" These tumors tend to grow and spread at a slower rate than tumors that are "**undifferentiated**" or "**poorly differentiated,**" which have abnormal-looking cells and may lack normal tissue structures. The factors used to determine tumor grade can vary between different types of cancer.

Tumor grading:

- Grade X: grade cannot be assessed
- Grade I: Well differentiated
- Grade II: moderately differentiated
- Grade III: poorly differentiated
- Grade IV: undifferentiated

Principles of Pathological Classification of Malignant Disease

Categories of Malignant Disorders:

- Liquid malignancies:
 - **Myeloproliferative disorders:** myeloid leukemia
 - **Lymphoproliferative disorders:** Lymphoblastic leukemia
- Solid malignancies:
 - **Epithelial tissues:** surface tissues or glandular = **Carcinoma**
 - **Connective tissues:** bone or soft = **Sarcoma**

General Signs and Symptoms of Malignancy

Cancer gives most people **no symptoms or signs that exclusively indicate the disease.**

Unfortunately, every complaint or symptom of cancer can be explained by harmless condition as well. **The clues are: persistent, progressive, and disabling signs and symptoms.**

They change according to the site of origin, so you should think about the pathology and site: e.g. mass that is able to invade locally and spread distantly.

Constitutional symptoms: **fatigue, fever, sweating, and weight loss.**

Principles of Cancer Management

The aim of cancer treatment is to cure cancer if possible, control the symptoms and improve the patient's survival if not curable ⁽⁵⁾.

Anticancer therapy ⁽⁶⁾ may be either **curative** (to cure the disease) or **palliative** (control symptoms and improve survival) and this distinction influences the approach to management of individual patients.

- **Palliation:** the aim of palliative chemotherapy is to produce and improvement is quality of life with a minimized impact of toxicity on the patient; there may be a small increase in survival.

The therapy is simple, short term, acute, and less toxic. Curative therapy is aggressive, expensive, and complex and has long-term toxicity.

- **Adjuvant treatment:** administered after surgery and its aim is to increase the disease-free and overall survival.
- **Neoadjuvant treatment:** patients receive chemotherapy, radiotherapy, or hormonal therapy before surgery.

Overall Approach to Cancer Management ⁽⁵⁾:

Three main questions to consider are:

1. What is the type of cancer?

In most cases, this requires a tissue diagnosis. In modern oncology, it is unusual or inappropriate to start treatment based on clinical diagnosis alone without tissue diagnosis. Tissue diagnosis is also important to perform molecular studies to select appropriate targeted therapies.

2. What is the extent of the spread of the cancer?

This is answered by staging scans including CT scans, bone scans and PET scans.

3. Is it curable or not curable?

This depends on the type of cancer and the presence or absence of and the extent of metastasis.

For curable cancers, rate of cure is determined by prognostic factors (for example: tumor size and nodal status in breast cancer).

For incurable cancers, duration of survival is expressed in median survival rather than in absolute time frame ⁽⁵⁾.

Different Treatment Modalities:

- Local Therapy: surgery and radiotherapy.
- Systemic Therapy: chemotherapy, hormonal therapy, and biological therapy.

What is the patient's prognosis?

The prognosis depends on:

1. The cancer type and extent (**stage**).
2. The patient factors (**age, sex, comorbidities**)
3. The available tools.

Tumors can be cured

- Lymphomas, leukemia, and early solid tumors.

Tumors can have prolonged survival

- Locally advanced and some of the metastatic tumors.

Tumors can be palliated

- Metastatic solid tumors.

SUMMARY

1. Cancer is a disease in which the body's cells undergo abnormal division
2. It is caused by DNA mutations. The mutated genes are called **oncogenes**
3. The disease is staged using the **TNM system**:
 - a. **T**: size of primary tumor
 - b. **N**: regional lymph node involvement
 - c. **M**: Presence of metastasis
4. **Tumor Grade**: describes the tumor cell's abnormality (how well it is differentiated)
5. **Signs and Symptoms**: there are no specific signs for cancer however, there are vague and persistent symptoms such as fever, fatigue and weight loss
6. **Malignant disorders** are categorized into:
 - a. **Liquid malignancies**: Myeloproliferative & Lymphoproliferative disorders
 - b. **Solid malignancies**: Epithelial and Connective tissue malignancies
7. **Management** can either be curative (to cure) or palliative (relieve symptoms and improve survival).
8. **Treatment** can either be local (surgery and radiotherapy) or systemic (chemotherapy and hormonal therapy)
9. **Prognosis** depends on the type of cancer, it's stage, patient factor's and the available treatment options

IMPORTANT NOTES FROM EXTERNAL RESOURCES

Notes

- (1) <http://www.cancer.gov/cancertopics/what-is-cancer>
- (2) <http://www.cancer.org/cancer/cancerbasics/what-is-cancer>
- (3) <http://www.cancer.gov/cancertopics/factsheet/detection/staging>
- (4) <http://www.cancer.gov/cancertopics/diagnosis-staging/prognosis/tumor-grade-fact-sheet>
- (5) http://wiki.cancer.org.au/oncologyformedicalstudents/Principles_of_cancer_management
- (6) Davidson's Principles and Practice of Medicine 21st Edition, Oncology Chapter.

Note: we have not put an approach because each cancer has its own one, so if you guys have any doubt just go through Approach to Internal Medicine contact us if you need any help with that.

Questions

- 1) Which of the following therapies is administered to improve the patient's quality of life?
 - a. Adjuvant therapy
 - b. Neo-adjuvant therapy
 - c. Palliative therap
 - d. Curative therapy

- 2) Which of the following is not an oncogene?
 - a. BRCA2
 - b. CDKN2A
 - c. BRCA1
 - d. P45

- 3) Which of the following is not a carcinogenic?
 - a. H. Pylori
 - b. Human Papilloma Virus
 - c. Asbestos
 - d. Measles Virus

432 Medicine Team Leaders

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Answers:

1st Questions: c

2nd Questions: d

3rd Questions: c