

# Team Medicine

## 7. Introduction to Cancer Diagnosis & Treatment

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## NEOPLASM:

Neo=New    -plasm=growth

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### Proliferative Capacities of Tissues

1- **Labile Cells**(continuously dividing)

Ex: Hematopoietic cells and skin.

2- **Stable cells**(only divides on demand)

Ex: Osteoblasts → when someone has a fracture, it heals with bone tissue, not fibrosis.

3- **permanent cells**(do not regenerate)

Ex: Cardiac muscles → when you have myocardial infarction what is the consequence? Fibrosis, the area will not contract anymore.

## (What controls the cell division? DNA)

**Malignancy and Cancer are diseases of the organ, of the cell, of the DNA. Whatever damaging the DNA can cause Malignancy and Cancer. Cancer is a disease of DNA (Important)**

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

These cells are able to:

- 1-Invade surrounding tissues
- 2-Send distant metastases.
- 3-Lost their functions

## Causes of Cancer:

**\*Suppressed immunity**(like in post organ transplantation, we give steroids to suppress immunity to decrease host rejection. In the same time, immune system is also suppressed not to catch mutated cells)

There is a category of tumors that are called post transplant tumors.

Transplant recipients have an increased risk of developing new cancers in general (one to two percent per year) and a 15-20 percent higher incidence of certain types of cancer.

**Skin cancer and lymphomas are the most prevalent types of cancer seen post transplantation.** The risk of cervical, breast cancer and colorectal cancer are also increased.

When it comes to skin cancer, post-transplant patients, in particular, have a significantly increased risk of developing squamous cell carcinomas, as well as increased risk for other types of skin cancers, such as melanoma.

**\*Disease** Ex: Inflammatory bowel disease increasing risk of Colon cancer

**\*Drugs** If you give cytotoxic drugs it will not just go to the abnormal cancer cells, it will also go to the normal cells and cause cell death ex; alopecia neutropenia, nail changes, thrombocytopenia...etc that's is why patients after chemotherapy experience hair loss.

**\*Infective agents** viruses use host cells to replicate. Viruses go inside the cells and imbed their genome in the DNA of host cell that control cell division. Therefore, Host cells will have abnormal signaling.

Ex: Viruses: Epstein Barr Virus (EBV) in Burkitts lymphoma, Human Papilloma Virus (HPV) in cervical cancer, and Hepatitis ( B and C ) in liver cancer

Bacterial: H.pylori in stomach cancer

Burkitts lymphoma is an uncommon type of Non-Hodgkin Lymphoma (NHL). Burkitt's lymphoma commonly affects children. It is a highly aggressive type of B-cell lymphoma that often starts and involves body parts other than lymph nodes.

**\*Genetic defects and DNA Mutations** genes that are responsible for cell divisions are called pro-oncogenes. When these genes are mutated they become oncogenes and incidence of cancer is now increased. Ex; Retinoblastoma.

These mutations are due to

- Environmental factors → Radiation, Tobacco, Alcohol, Radon, Asbestos..etc
- Random somatic mutations
- Inherited germ line mutations

Retinoblastoma (Rb) is a rapidly developing cancer that develops from the immature cells of a retina, the light-detecting tissue of the eye and is the most common malignant tumor of the eye in children.

The most common and obvious sign of retinoblastoma is an abnormal appearance of the pupil, leukocoria, also known as amaurotic cat's eye reflex

In children with the heritable genetic form of retinoblastoma there is a mutation on the RB1 gene



**Tumors can be :**

**- Primary Tumors**

Represent de novo tumors in their initial site

**Or**

**- Metastatic Tumors**

Originate from the distant growth of the primary tumors

**Hallmarks of cancer (Six changes for cancer) found in most if not all:**

- 1- Self-sufficiency in growth signals → they do not need growth signals to divide, they have their own growth factors.
- 2- Insensitivity to growth-inhibitory signals → body has no control over them
- 3- Absence of apoptosis → programmed cell death is lost in malignancy
- 4- Limitless proliferative capacity
- 5- Sustained angiogenesis
- 6- Tissue invasion and metastasis

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## **1- When to suspect cancer?**

### **Cancer Signs and Symptoms**

-Cancer gives most people **NO** symptoms or signs that **exclusively** indicate the disease. Unfortunately, every complaint or symptom of cancer can be explained by a harmless condition as well.

The problem is that there are no signs and symptoms exclusive for cancer, like for example IBD can present with diarrhea, bleeding per rectum, weight loss, and abdominal pain. Colon cancer can present in the same way as well.

Also other diseases are much more common than malignancies. If we say colon cancer is a common malignant disease, when you compare it to IBS or IBD it has a low occurrence, the ratio is about 10:100,000.

So what are the clues for cancer???????

**-Persistent** → patients with brain tumor come complain of headache. Patients with sinusitis will also come complain of headache. However, patients with sinusitis with symptomatic treatment will improve but brain tumor headaches will not. So symptoms that are persistent must be taken seriously.

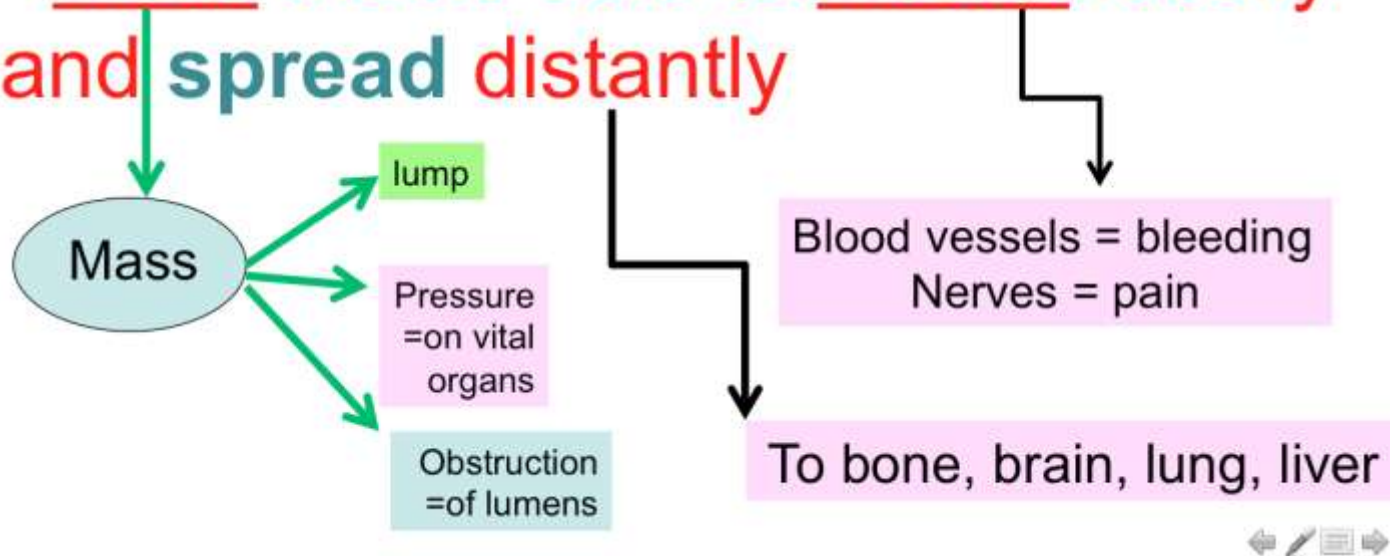
**-Progressive** → Ex: a mass increasing in size

**-Disabling** → patient cannot get out of bed or cannot go to work. The problem is disabling, changing the life of the patient

**- Symptoms & Signs changes according to the site of origin** → patient with lung cancer will present with hemoptysis but a patient with stomach cancer will present with hematemesis

**-Do not forget the constitutional symptoms** → Fatigue, fever, sweating, and weight loss

Think about the pathology and site:  
- Mass that is able to invade locally  
and spread distantly



### **\*A Mass:**

If it is on the outside

It is a lump → it is apparent and the patient present with a mass. Ex: enlarged lymph node, breast lump, and mass on femur.

If it is on the inside

Pressure symptoms

Or

Obstructive symptoms → Ex: dysphagia in esophageal cancer

**\*If the tumor invade:**

Blood vessels → bleeding

Nerves → pain

**\*The tumor can spread distantly to bone, brain, lung, liver**

## **2- How to diagnose cancer**

Cancer diagnosis is NOT a clinical diagnosis, NOT a radiological diagnosis, NOT a serological diagnosis.

**Cancer diagnosis is a PATHOLOGICAL DIAGNOSIS, it is a TISSUE DIAGNOSIS. (Important)**

In 99% of cancer cases we need tissue diagnosis...only 2-3 cases are exceptional  
"Ex;Choriocarcinoma" , and even in these exceptions it is better to have a tissue diagnosis.

Categories of malignant disorders

- Liquid malignancies:
    - 1-Myeloproliferative disorders= leukemia
    - 2-lymphoproliferative disorders= leukemia
  - Solid malignancies: (Classified according to origin)
    - 1- Epithelial tissues → carcinomas
    - 2- Connective tissue → sarcomas
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### 3- What is the essential work up for staging?

T= tumor

N= Node

M= Metastases

There is radiological staging, and there is surgical staging.

We need staging to decide type of management.

Ex: adenocarcinoma.

If it is localized, stage 1 or 2 → can be resected

If it is stage 3 → need chemotherapy

If it has metastasized → need palliation and chemotherapy

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### 4- How to treat cancer?

Before that you should determine whether the cancer diagnosis is suspected or established ...

Established cancer diagnosis :

Answer the following questions:

1-Does the patient have cancer?

2-What type of cancer?

3-What stage of cancer?

Answering the previous Qs will let you know how to treat cancer.

ManagementMultidisciplinary:

- 1- Surgery
- 2- Radiation
- 3- Medical ONC ( Chemotherapy )

Other Disciplines:

Radiology, Pathology, Lab

-Combined clinics

-Tumor board

There are two types of management :

1- curative : the cancer is really cured

2- palliative : the goal is to relieve the annoying symptoms ( BUT does not cure cancer )



## A- Curative :

Therapy : Aggressive, expensive, recent, updated, and complex.

Toxicity: long term and irreversible.

## B- Palliative:

Therapy : Simplest, avoid hospitalization availability, least toxic

Toxicity: short term, acute, quality of life.

Local therapy : surgery and radiotherapy

Systemic therapy : Chemotherapy

Categories of malignant disorders

Liquid malignancies: **Treated by Systemic therapy**

1- Myeloproliferative disorders= leukemia

2- lymphoproliferative disorders= leukemia

• Solid malignancies: **Treated by local therapy**

4- Epithelial tissues → carcinomas

5- Connective tissue → sarcomas

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## 5-What is the prognosis of your patient?

What can medicine offer the cancer patient?

1- The cancer type & extent ( stage)

2- The host factors (age , sex , co morbidities)

3- The available tools

1- Tumors that can be cured:

lymphomas, leukemia, early solid tumors

2- Tumors that can have prolonged survival:

Locally advanced and some of the metastatic tumors

3- Tumors that can be palliated:

Metastatic solid tumors

**\*The doctor did not mention anything about how to treat and manage cancer and the prognosis so we did not include them here (original lecture slides 30 to 43 are not included in the teamwork)**

## Summary:

1- Cancer is a disease of **DNA**.

2- Cancer is a term used for diseases in **which abnormal cells divide and escape the body control**. These cells are able to **Invade surrounding tissues, Send distant metastases&lost their functions**.

3-Causes of Cancer:

A-Suppressed immunity such as in case of **transplantation (Skin cancer and lymphomas are the most prevalent types of cancer seen post transplantation)**

B- Disease: IBD "Ulcerative colitis" increasing risk of Colon cancer.

C- Infective agents:

-Viruses: Epstein Barr Virus (EBV) in Burkitts lymphoma, Human Papilloma Virus (HPV) in cervical cancer, and Hepatitis (B and C) in liver cancer

-Bacterial: H.pylori in stomach cancer.

- Parasite: schistosomiasis in *Transitional Cell Carcinoma*.

D-Genetic defects and DNA Mutations:**Retinoblastoma**

4- Hallmarks of cancer (**Six changes for cancer**) found in most if not all:

**Self-sufficiency in growth signals**, **Insensitivity to growth-inhibitory signals**, **Absence of apoptosis**, **Limitless proliferative capacity**, sustained angiogenesis and **Tissue invasion and metastasis**.

5-Cancer diagnosis is a **PATHOLOGICAL DIAGNOSIS**, it is a **TISSUE DIAGNOSIS**.

**6-Exceptions that could be diagnosed without tissue:**

A-Hepatocellular carcinoma with AFP (Alpha-fetoprotein) or MRI.

B-prostatic cancer with very high PSA (*Prostate-specific antigen*).

C-Choriocarcinoma with very high HCG (*human chorionic gonadotropin*).

## MCQs

1-A 64-year-old man complains of cough, increasing shortness of breath, and headache for the past 3 weeks. He has mild hypertension for which he takes hydrochlorothiazide; he has smoked one pack of cigarettes a day for 40 years. On exam you notice facial plethora and jugular venous distension to the angle of the jaw. He has prominent veins over the anterior chest and a firm to hard right supraclavicular lymph node. Cardiac exam is normal and lungs are without rales. What is the most likely cause of his condition?

- Long-standing hypertension
- Gastric carcinoma
- Emphysema
- Lung cancer
- Nephrotic syndrome

2- A 67-year-old male presents with hemoptysis 1 week in duration. He has smoked 11/2 packs of cigarettes per day for 50 years and has been unable to quit smoking despite nicotine replacement therapy and bupropion. He has mild COPD for which he uses an ipratropium inhaler. Chest x-ray reveals a 3-cm perihilar mass. Which of the following is the most likely cause of this patient's hemoptysis?

- Adenocarcinoma of the lung
- Squamous cell carcinoma of the lung
- Bronchoalveolar cell carcinoma
- Bronchial adenoma



3-A 52-year-old man with cirrhosis due to chronic hepatitis C presents with increasing right upper quadrant pain, anorexia, and 15-lb weight loss. The patient is mildly icteric and has moderate ascites. A friction rub is heard over the liver. Abdominal paracentesis reveals blood-tinged fluid, and CT scan shows a 4-cm solid mass in the right lobe of the liver. Which of the following is the most important initial diagnostic study?

- a. Serum  $\alpha$ -fetoprotein level
- b. Percutaneous liver biopsy
- c. Measurement of hepatitis C viral RNA
- d. Upper GI endoscopy
- e. Positron emission tomography scans

4-A 40-year-old male complains of hematuria and an aching pain in his right flank. Laboratory data show normal BUN, creatinine, and electrolytes. Hemoglobin is elevated at 18 g/dL and serum calcium is 11 mg/dL. A solid renal mass is found by ultrasound. Which of the following is the most likely diagnosis?

- a. Polycystic kidney disease
- b. Renal carcinoma
- c. Adrenal adenoma
- d. Urolithiasis

5- A patient complains of fatigue and night sweats associated with itching for 2 months. On physical exam, there is diffuse nontender lymphadenopathy, including small supraclavicular, epitrochlear, and scalene nodes. A chest x-ray shows hilar lymphadenopathy. Which of the following is the best next step in evaluation?

- a. Excisional lymph node biopsy
- b. Monospot test
- c. Toxoplasmosis IgG
- d. Serum angiotensin converting enzyme level

6- A 19-year-old woman presents for evaluation of a nontender left axillary lymph node. She is asymptomatic and denies weight loss or night sweats. Exam reveals three rubbery firm nontender nodes in the axilla, the largest 3 cm in diameter. No other lymphadenopathy is noted; the spleen is not enlarged. Lymph node biopsy, however, reveals mixed-cellularity Hodgkin's lymphoma. Liver function tests are normal. Which of the following is the best next step in evaluation?

- a. CT scan of chest, abdomen, and pelvis
- b. Liver biopsy
- c. Staging laparotomy
- d. Erythrocyte sedimentation rate

7-A 62-year-old African American man presents with fatigue, decreased urine stream, and low back pain. The physical examination shows a hard, nodular left prostatic lobe and percussion tenderness in the lumbar vertebral bodies and left seventh rib. Which of the following is the best next step in evaluation?

- a. Bone scan
- b. Biopsy of prostate
- c. CT scan
- d. Bone marrow biopsy

## Answers

1-The answer is d. This patient presents with the superior vena cava syndrome. Such patients have jugular venous distension but no other signs of right-sided heart failure. They have prominent facial (especially periorbital) puffiness and may complain of headache, dizziness, or lethargy. SVC syndrome is due to a malignant tumor 90% of the time. Lung cancer and lymphoma, both of which are often associated with bulky mediastinal lymphadenopathy, predominate. Gastric cancer often metastasizes to the supraclavicular nodes (most often on the left, the so-called Virchow's node) but does not usually affect the mediastinal nodes to this degree. Prompt diagnosis is necessary to prevent CNS complications or laryngeal edema. Sensitive tumors (lymphoma, small cell lung cancer) may be treated with chemotherapy, while most other cell types are treated with radiation therapy.

2-The answer is b. Cigarette smokers have a 15- to 25-fold increased incidence of both squamous cell carcinoma and small cell undifferentiated carcinoma of the lung. Both of these neoplasms tend to be central (i.e., perihilar); the presence of obstructive lung disease increases the risk of lung cancer over and above the smoking history. Of the choices given, squamous cell carcinoma is the likeliest explanation for this patient's hemoptysis. Bronchoscopy would likely show the lesion and allow a tissue diagnosis to be made. Adenocarcinoma of the lung is the commonest lung cancer seen in nonsmokers, women, and younger patients.

Its incidence is increased in smokers (probably twofold), but not to the degree seen with squamous cell carcinoma and small cell undifferentiated carcinoma. Adenocarcinoma is typically peripheral with pleural involvement (rather than the central involvement seen in this case). Bronchoalveolar cell carcinoma arises from alveolar epithelium, is typically peripheral, and may resemble a nonhealing pneumonia (it may even have air bronchograms like a pneumonia). Bronchial adenomas (carcinoid being the commonest type) are often central but are usually smaller and are less common than squamous cell carcinomas. Their incidence is not increased by cigarette smoking.

3-The answer is a. This patient has probably developed hepatocellular carcinoma as a complication of her macronodular cirrhosis. HCC is a feared complication of patients with cirrhosis due to hepatitis B, hepatitis C, and hemochromatosis (although it occurs with modestly increased frequency in patients with alcoholic cirrhosis as well). The incidence in high-risk patients is 3% per year. An  $\alpha$ -fetoprotein (AFP) level greater than 500 mcg/L is suggestive, and greater than 1000 mcg/L virtually diagnostic, of this tumor. Most patients will die within 6 months if untreated; resection of the tumor is often difficult due to the underlying liver disease. Liver transplantation can be curative in selected patients.

4-The answer is b. Renal carcinoma is twice as common in men as women and tends to occur in the 50- to 70-year age group. Many patients present with a hematuria or flank pain, but the classic triad of hematuria, flank pain, and a palpable flank mass occurs in only 10 to 20% of patients. Paraneoplastic syndromes such as erythrocytosis, hypercalcemia, hepatic dysfunction, and fever of unknown origin are common. Surgery is the only potentially curable therapy; the results of treatment with chemotherapy or radiation therapy for nonresectable disease have been disappointing. Interferon  $\alpha$  and interleukin 2 produce responses (but no cures) in 10 to 20% of patients. The prognosis for metastatic renal cell carcinoma is dismal.

5- The answer is a, the long-term nature of these symptoms, the fact that the nodes are nontender, and their location (including scalene and supraclavicular) all suggest the likelihood of malignancy. Although infectious mononucleosis and toxoplasmosis can cause diffuse lymphadenopathy, these infections are usually associated with other evidence of infection such as pharyngitis, fever, and atypical lymphocytosis in the peripheral blood. It would be unusual for the lymphadenopathy associated with these infections to persist for 2 months. Serum angiotensin-converting enzyme level is a nonspecific test for sarcoidosis but is also elevated in other granulomatous diseases and is not sensitive or specific enough to be used as an initial diagnostic test. Lymphadenopathy associated with sarcoidosis requires a biopsy for diagnosis. In this patient, an excisional biopsy is necessary primarily to rule out the malignancy, particularly lymphoma.

6- The answer is a. The staging of Hodgkin's disease is important so that proper treatment can be planned. Stage I (single lymph node bearing area) or stage II (more than one lymph node site on the same side of the diaphragm) patients who have good prognostic features may be treated with radiation therapy. Those with stage III (affected lymph nodes on both sides of the diaphragm) or stage IV (extranodal disease) are treated with combination chemotherapy. A CT scan or an MRI of the abdomen and pelvis will show evidence of lymph node involvement below the diaphragm. Staging laparotomy with splenectomy, formerly done to provide pathology of the periaortic nodes and spleen, is rarely done today. Gallium scans can be useful in difficult cases. Bone marrow biopsy is usually performed to exclude bone marrow disease, which would imply stage IV.

7-The answer is b. A prostate biopsy is necessary to confirm the diagnosis of prostatic carcinoma. A metastatic workup, including bone scan, would then follow. Bone scan is a very sensitive test for metastatic prostate carcinoma, which tends to spread through the venous plexus surrounding the prostate to the sacrum and lower lumbar vertebrae. Since prostate cancer stimulates osteoblastic activity of the bone, and since osteoblasts (rather than osteoclasts) take up the tracer used in bone scanning, the test is very reliable. Pure osteolytic metastases (typically seen in myeloma, occasionally in thyroid or renal carcinoma) will not produce hot spots on bone scans. MRI scanning of pelvic nodes is occasionally used to assess resectability. If this patient has bony metastases, however, systemic rather than local therapy will be necessary.