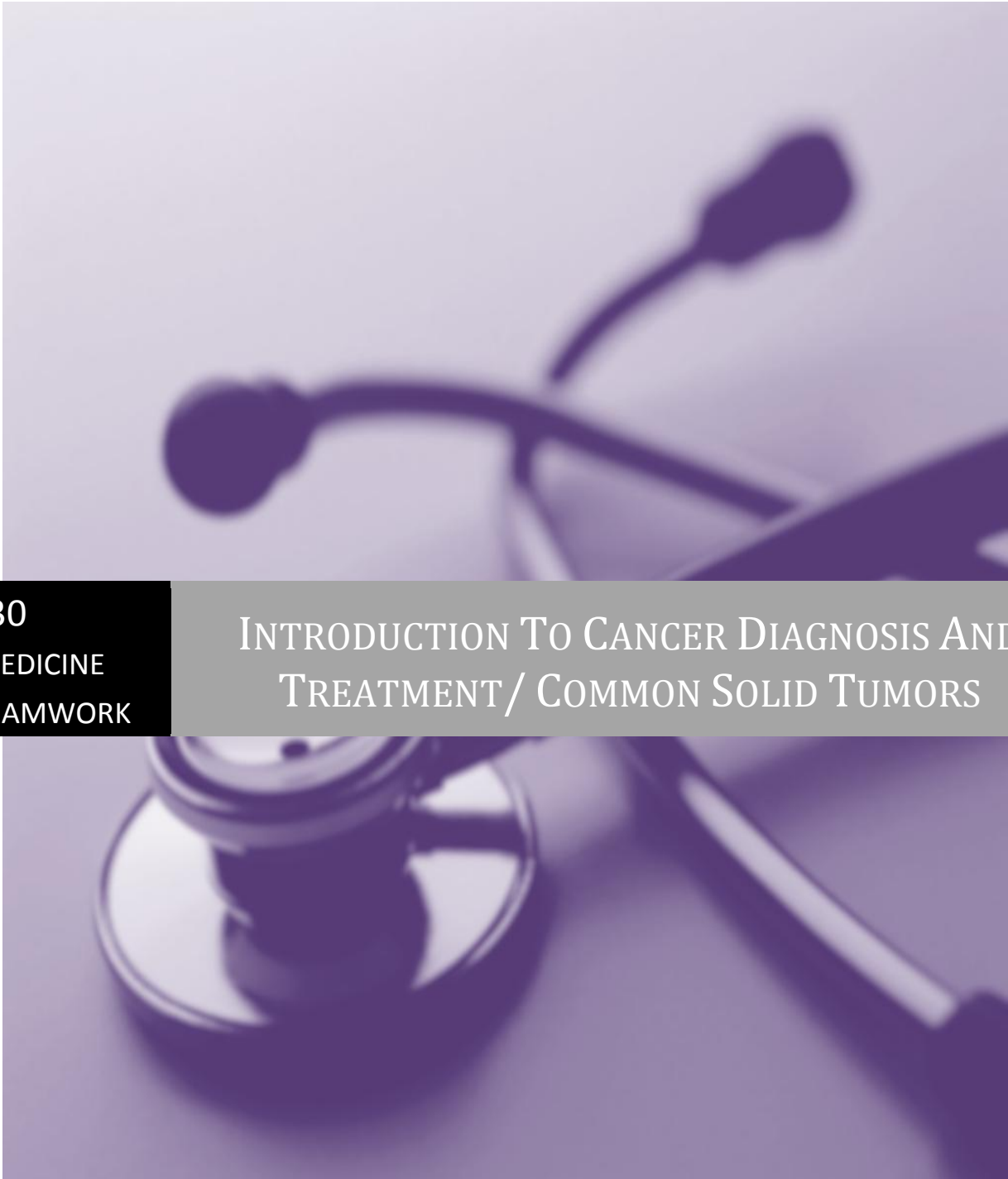


"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." – William Osler



430
MEDICINE
TEAMWORK

INTRODUCTION TO CANCER DIAGNOSIS AND TREATMENT/ COMMON SOLID TUMORS

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Introduction to oncology/Common Solid Tumors

Defining cancer:

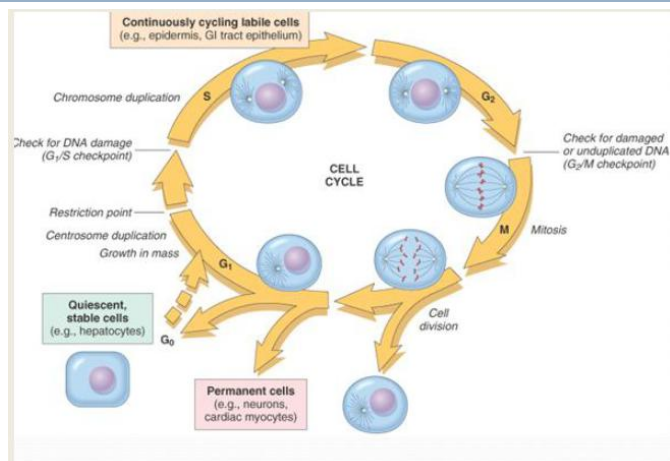
Cancer is a term used for diseases in which abnormal cells divide and escape the body control → depressed immunity

These cells are able to:

- 1-Invade surrounding tissues. = Malignant
- 2-Send distant metastases
- 3-Lose their functions

The cell cycle:

- Labile cells
- Permanent cells
- Stable cells
- Stem cells?



Extra Explanation

Proliferation of both normal cells and cancer cells is dependent on progression of the cell cycle, which consist of 4 phases.

*S phase and M phase >>the functional phases.

*G1 phase and G2 phase >> the preparatory phases (primarily synthesis of the materials needed for the subsequent phase).

-In the S phase >>DNA replication, doubling the number of chromosomes and producing sister chromatids. (The G1 phases precedes this phase)

-In the M phase >>the nucleus divides and the chromosomes separate into 2 daughter cells during the process of mitosis. (The G2 phase precedes this phase).

- G₀ phase >> some cells enter this phase after the division.

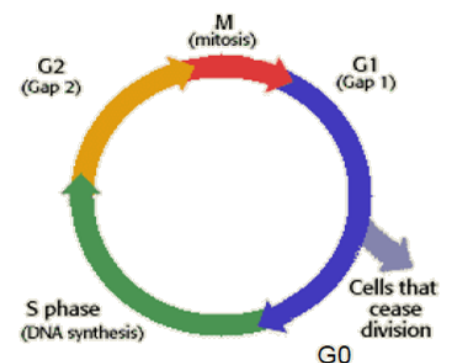
1*Constantly dividing cell (Labile cells):

1- Skin cells.

2- GIT.

3-blood cells in the bone marrow.

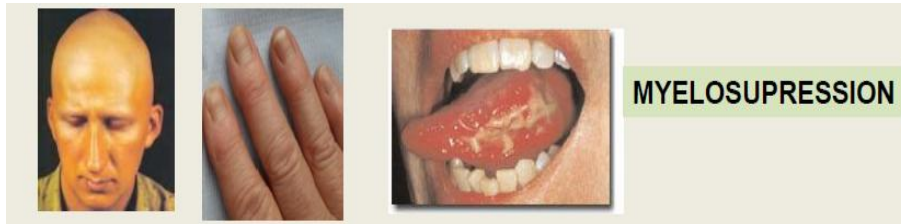
- Constantly dividing cells have a higher risk of becoming malignant and develop cancer, dividing uncontrollably.



Dividing cells in human body:

cytotoxic drugs, such as used in treatment of cancer, work by inhibiting the proliferation of dividing cells, the malignant cells as the desired target .

However, this has the adverse effect against the cells normally dividing in the body, and **Hair, skin, GI tract and bone marrow**.



MYELOSUPPRESSION

Myelosuppression: Bone marrow suppression or myelotoxicity .life-threatening infection, as the body cannot produce leukocytes in response to invading bacteria and viruses, as well as leading to anemia due to a lack of red blood cells and spontaneous severe bleeding due to deficiency of platelets.

2*Stable cells:

Multiply only when needed.

- Most of the time in the quiescent G_0 phase
- but can be stimulated to enter the cell cycle when needed.
- Examples include: **the liver**.

3* Permanent cells:

Do not have a division potential. Such as:

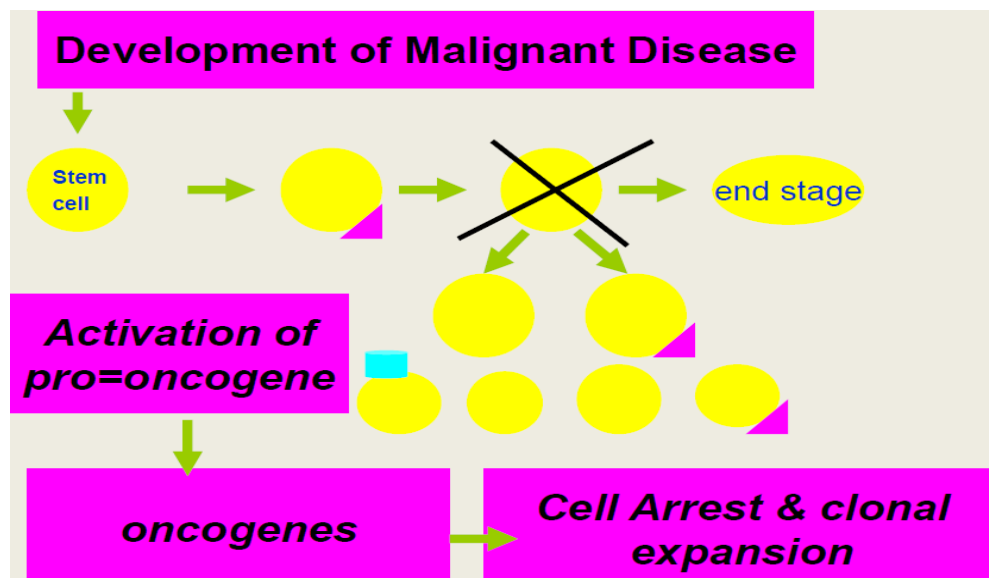
1-Neurons.

2-Muscle cells.

*When damaged (by radiotherapy) **they cannot be replaced**.

What causes cancer?

- Cell division is controlled by the genes which are formed of DNA
- Cancer arises from the **mutation** of a normal gene resulted from DNA defect.
- Mutated genes that cause cancer are activated pro-oncogene (genes related to cell division) called **oncogenes**.



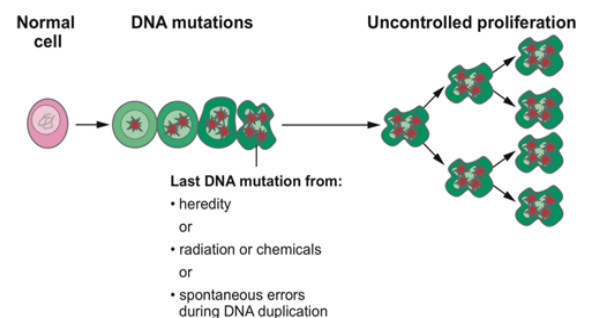
Such mutation starts at the activation of a Pro-oncogene which may be either at the level of the stem cell itself or at a stage after the supposedly apoptosis. Such activation leads to a Genetic Mutation which in turn results in cell arrest and clonal expansion.

Causes of Cancer:

DNA Mutations :

- A variety of genes are involved in the control of cell growth and division.
- The cell cycle is the cell's way of replicating itself in an organized, step-by-step fashion.
- Tight regulation of this process ensures that a dividing cell's DNA is copied properly, any errors in the DNA are repaired, and each daughter cell receives a full set of chromosomes.
- The cycle has checkpoints (also called restriction points), which allow certain genes to check for mistakes and halt the cycle for repairs if something goes wrong.
- If a cell has an error in its DNA that cannot be repaired, it may undergo programmed cell death (apoptosis)
- Apoptosis is a common process throughout life that helps the body get rid of cells it doesn't need.
- Cells that undergo apoptosis break apart and are recycled by a type of white blood cell called a macrophage.
- Apoptosis protects the body by removing genetically damaged cells that could lead to cancer, and it plays an important role in the development of the embryo and the maintenance of adult tissues.

Cancer Arises From DNA Mutations in Cells



DNA mutations can occur due to:

- Radiation – and other environmental factors (Tobacco, Alcohol, Radon, Asbestos, etc)
- Random somatic mutations
- Inherited germ line mutations

Infectious agents

Viral

- HPV – cervical cancer
- Hepatitis – liver cancer

Bacterial

- H. pylori – stomach cancer
- EBV - Lymphoma

Genetic Predisposition:

A predisposition to certain cancers can be inherited via altered genes such as:

- BRCA1 and BRCA2 for breast and ovarian cancer.
- RB for a childhood ocular tumor, retinoblastoma.
- P53 Tumor Suppressor gene, plays a central role in cell cycle control, apoptosis and maintenance of genetic stability.
- APC Tumor suppressor gene, for risk of colorectal cancer.
- CDKN2A gene is involved in the growth of neuroblastoma cells and its expression is associated with prognosis of neuroblastoma patients.

What should you know as an oncologist?

•1-When to suspect cancer?

Cancer mostly gives **no** specific symptoms that might give us an **exclusive** clue about it. Unfortunately, every complaint or symptom of cancer can be explained by a harmless condition as well. However, clues may be given. Cancer is known as Progressive, Persistent and disabling in most circumstances. Overall, such symptoms and signs change according site of origin.

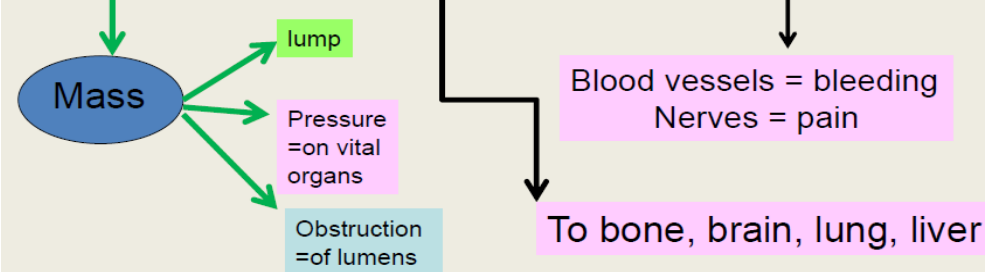
Cancer Signs and Symptoms **What are the clues?**

- Persistent P
- Progressive P
- Disabling D

Cancer Signs and Symptoms

Think about the pathology and site:

- Mass that is able to invade locally and spread distantly



•2-How to diagnose cancer?

Clinical examination might give us a clue, same about radiological and serological examination. On the other hand, cancer is only diagnosed Pathologically and by Tissue Diagnosis.

- Cancer diagnosis
- It is **not** a clinical diagnosis.
- It is **not** a radiological diagnosis.
- It is **not** serological diagnosis.
- It is a **pathological** diagnosis.
- It is a **tissue diagnosis**.

Do not forget the constitutional symptoms:

- Fatigue
- Fever
- Sweating
- Wt. loss

Categories of malignant disorders

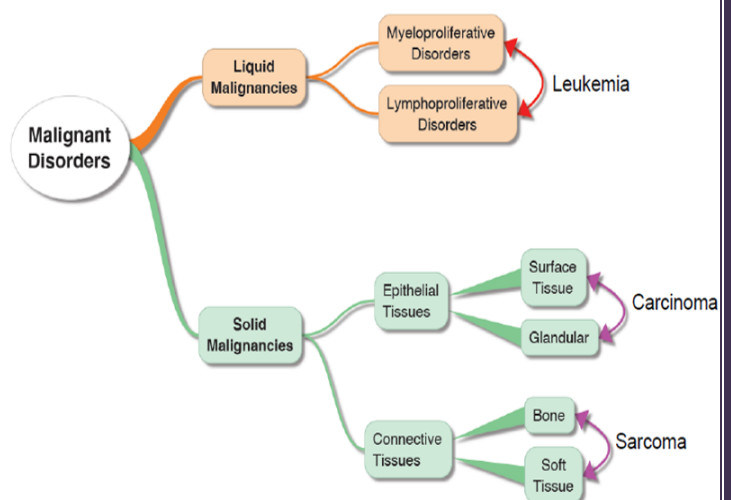
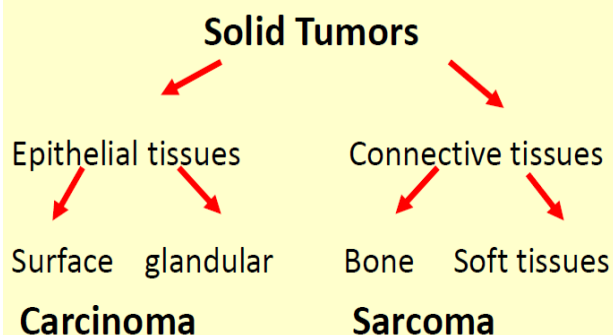
*Liquid malignancies.

1-Myeloproliferative disorders= leukemia

2-lymphoproliferative disorders= leukemia

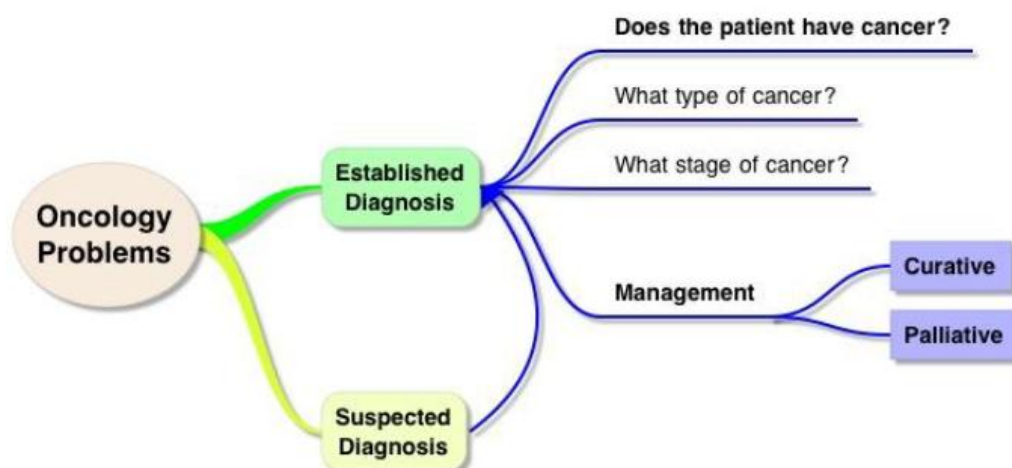
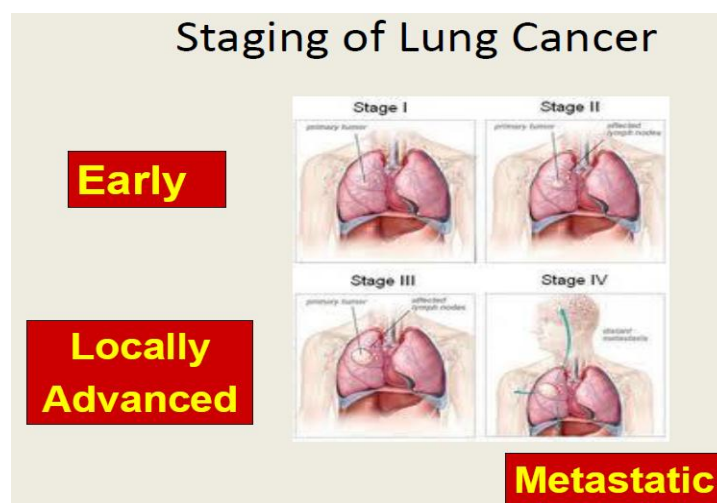
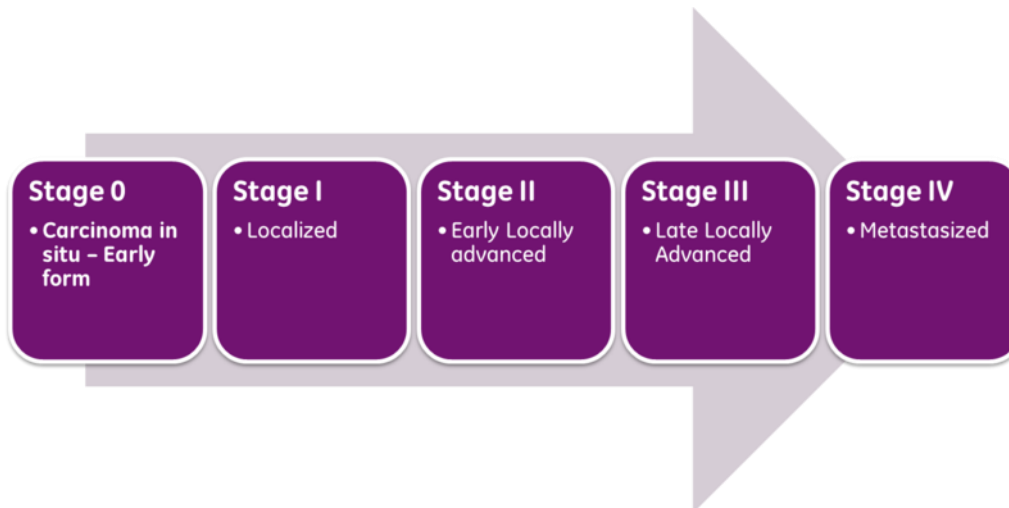
*Solid malignancies.

Classification Of Solid Tumors

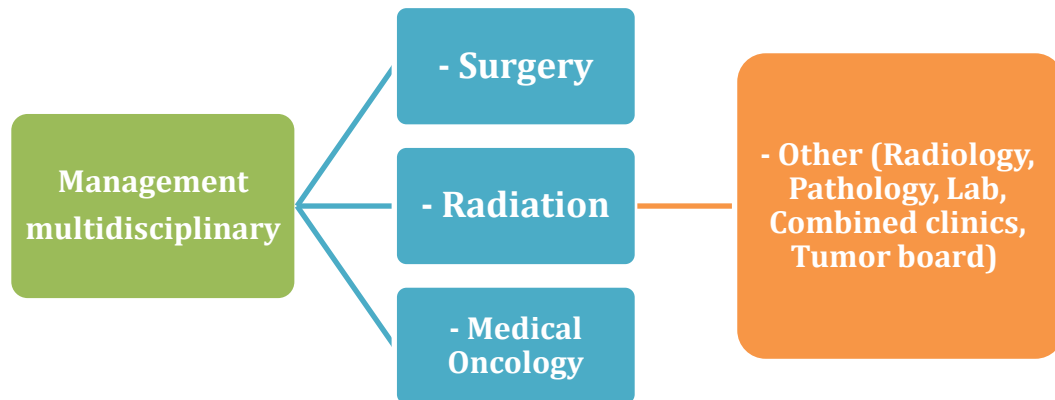


•3-What the essential work up for staging?

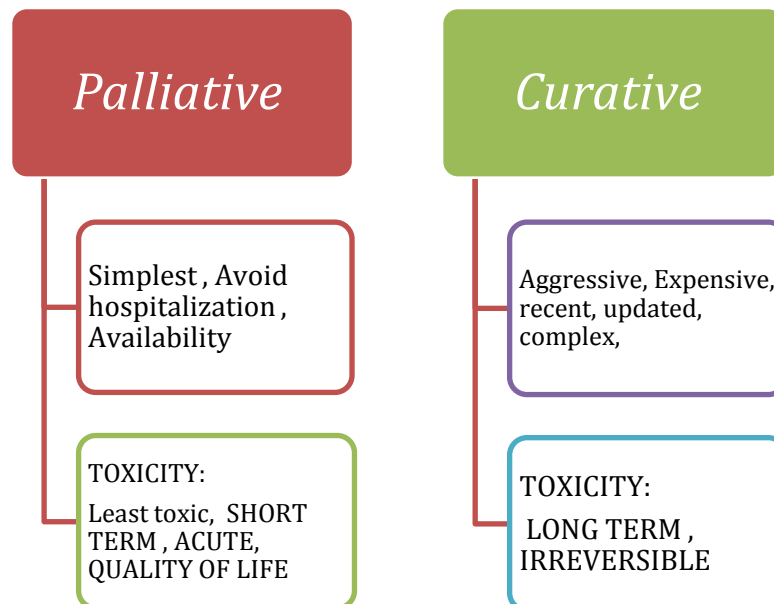
- Cancer staging can be divided into a clinical stage and a pathologic stage.
- In the TNM (Tumor, Node, Metastasis) system, clinical stage and pathologic stage are denoted by a small "c" or "p" before the stage (e.g., cT3N1M0 or pT2N0).
- Clinical stage is based on all of the available information obtained before a surgery to remove the tumor. Thus, it may include information about the tumor obtained by physical examination, radiologic examination, and endoscopy.
- Pathologic stage adds additional information gained by examination of the tumor microscopically by a pathologist.
- Radiology staging is usually through X-ray, MRI, CT and US.



4-How to treat cancer



Treatment modalities



Different Treatment Modalities

- Local therapy: **Surgery & RTH** (radiotherapy) .
- Systemic therapy: **Cth** (chemotherapy), **Hormone**, **Biological**.

Categories of malignant disorders

-Liquid malignancies

- 1-Myeloproliferative disorders= leukemia
- 2-lymphoproliferative disorders= lymphoma

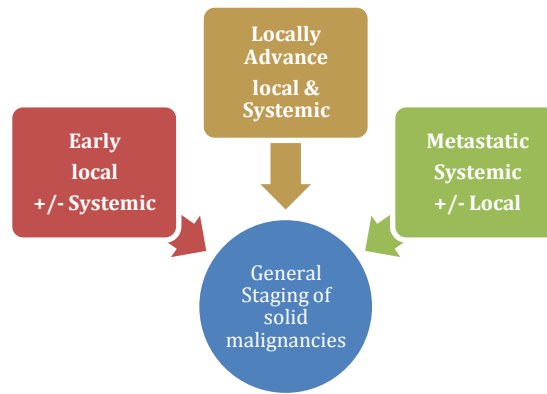


Systemic therapy

- Solid malignancies



According to stage



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

Cancers are classified by the Type of cell that the tumor cells presumed to be originating from.

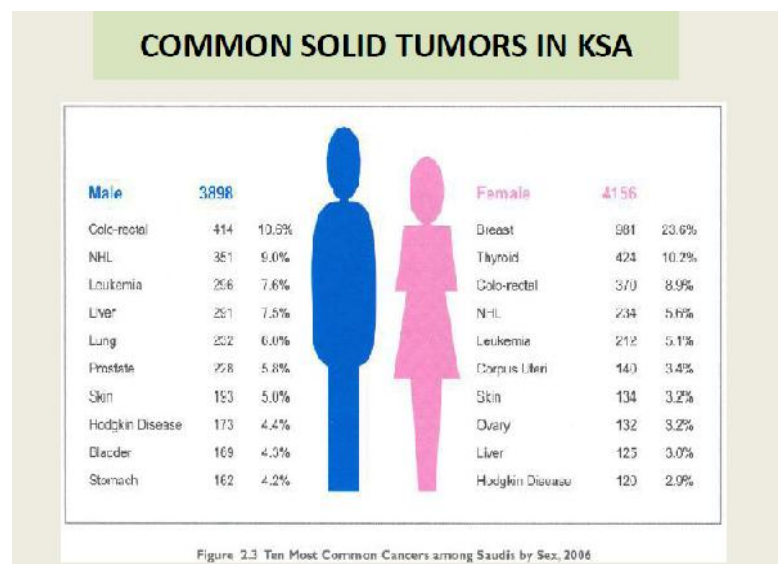
- Carcinoma: Cancers derived from epithelial cells. This is the most common cancers, breast, prostate, lung, pancreas, and colon.
- Sarcoma: Cancers arising from connective tissue (i.e. bone, cartilage, fat, nerve), each of which develop from cells originating in mesenchymal cells outside the bone marrow.

Other Tumor Types

- Germ cell tumor: Cancers derived from pluripotent cells, in the testicle or the ovary (seminoma and dysgerminoma, respectively).
- Blastoma: Cancers derived from immature "precursor" cells or embryonic tissue.
 - Most common in children.
 - *blastoma* as a suffix, with the Latin or Greek word for the organ or tissue of origin as the root. hepatoblastoma,

Common Solid Tumors:

- In the US, the three most common cancers:
 - Men: Prostate, lung, colorectal.
 - Women: Breast, colorectal, lung
- In KSA, the three most common cancers:
 - Men: Colorectal, Lymphoma, Leukemia
 - Women: Breast, Thyroid, Colorectal



Breast Cancer

Breast Cancer Facts:

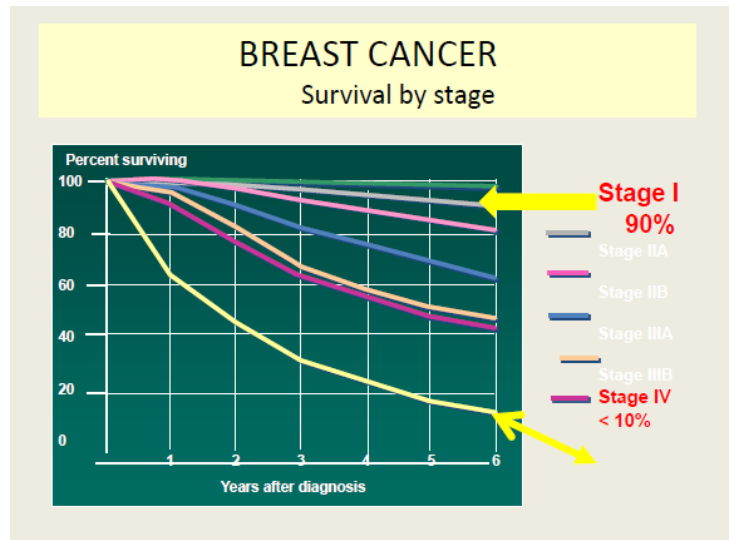
- 1st most common cancer in females
- 2nd leading cause of death

We Need Early Detection

- Late presentation + Advanced stage = Poor Outcome
- Early Presentation + Early Stage = Good Outcome

A good health plan

- Mammograms
- Self Awareness (Monthly self exams)



Remember:

- Breast cancer: -
 - Most common cancer in females.
 - Wide age range 20 - +70y.
 - Breast cancer can occur during pregnancy ,during lactation.
 - Breast cancer can occur in pre, peri and post menopausal females.

STAGES:

- T1 <1cm
- T2 <5 cm
- T3 >5 cm
- T4 = metastasis

Risk factors

- History of breast cancer
- Family history of breast cancer, especially in first-degree relatives
- Benign breast diseases / atypical hyperplasia
- Early menarche, late menopause
- Late first pregnancy/no pregnancy
- Exogenous estrogens
- Radiation (High Dose)

If you suspect Breast Cancer

- Do not just reassure the patient
- Do not give hormonal therapy
- Do not give antibiotics

Warning signs and symptoms:

- Painless lump or thickening (can be painful)
- Thickening or swelling that persist
- Nipple pain or retraction
- Nipple discharge
- Breast skin irritation or dimpling

Warning signs and symptoms:

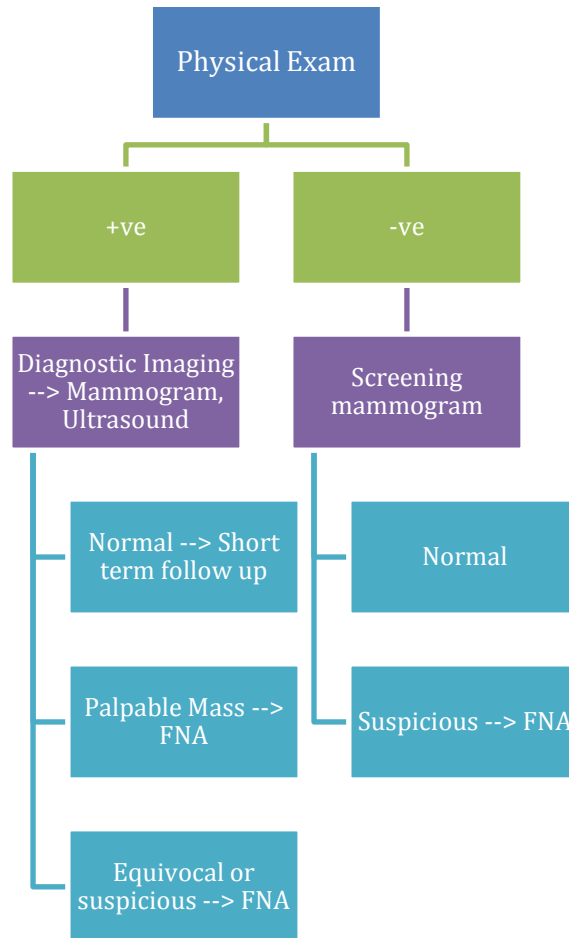
- Painless lump or thickening (can be painful)
- Thickening or swelling that persistent
- Nipple pain or retraction
- Nipple discharge
- -Breast skin irritation

What to do:

- Careful Hx & physical
- Bilateral mammogram + U/S +/- FNA

MOST AGGRESSIVE

is invasive ductal carcinoma



Treatment:

- Local Therapy
 - Surgery
 - Radiotherapy
- Systemic Therapy
 - Chemotherapy
 - Hormonal Therapy
 - Biological Therapy

Treatment: (Extra)

1980: Mastectomy

• 1987: Proper medical oncology

• 2010

- Very early breast cancer (T2): remove the tumor and the area around it, **WLE (wide local excision)**
- Practice guidelines
 - CT of lung, abdomen, liver
 - Bone scan
 - Locally advanced disease (T3, T4): Neo-adjuvant chemotherapy (chemo or radiotherapy **BEFORE** surgery)
 - Anti estrogen, anti progesterone, and anti herceptin
 - If **>60 y/o**, consider hormonal treatment before chemotherapy
 - If pre-menopausal, chemotherapy +/- hormonal therapy

Colon Cancer:

Colon cancer is the second leading cause of cancer deaths

Risk factors of colon cancer

- **Older age.** About 90 percent of people diagnosed with colon cancer are older than 50. Colon cancer can occur in younger people, but it occurs much less frequently.
- **A personal history of colorectal cancer or polyps.** If you've already had colon cancer or adenomatous polyps, you have a greater risk of colon cancer in the future.
- **Inflammatory intestinal conditions.** ulcerative colitis and Crohn's disease,
- **Inherited syndromes that increase colon cancer risk..** familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer, which is also known as Lynch syndrome.
- **Family history of colon cancer and colon polyps.** a parent, sibling or child with the disease.
- **Low-fiber, high-fat diet.**
- **A sedentary lifestyle.**
- **Diabetes.** insulin resistance may have an increased risk of colon cancer.
- **Obesity.**
- **Smoking.** People who smoke cigarettes may have an increased risk of colon cancer.
- **Alcohol.** Heavy use of alcohol may increase your risk of colon cancer.
- **Radiation therapy for cancer**

Constipation:

Why is constipation a risk factor?

- Waste stagnation → Bacterial action → Carcinogens

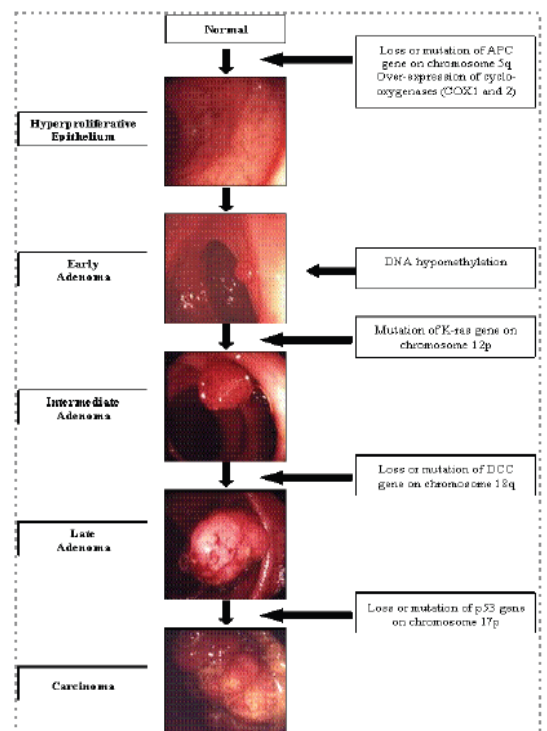
Colon Cancer Pathogenesis

- It starts with a simple cell the mutates and grows into a polyps
- If a polyp is allowed to remain in the colon it can grow into a cancerous tumor that can invade other organs.
- Colon cancer is the second leading cause of cancer deaths
- If a polyp is allowed to remain in the colon it can grow into a cancerous tumor that can invade other organs.

Signs & Symptoms

It can occur at any age but mostly if you're of 45 years of age

- Change in bowel habits
- Blood in Stool
 - Bright red
 - Very dark red
 - Black/Tarry Stool
- Diarrhea
- Constipation
- Does your bowel feel like it emptied completely?
- General abdominal discomfort
 - Gas pains
 - Bloating
 - Fullness
 - Cramps
- Weight loss w/ no explained reason
- Constant tiredness
- Vomiting (coffee grounds)
- Unexplained Fatigue and Unexplained iron deficiency anemia



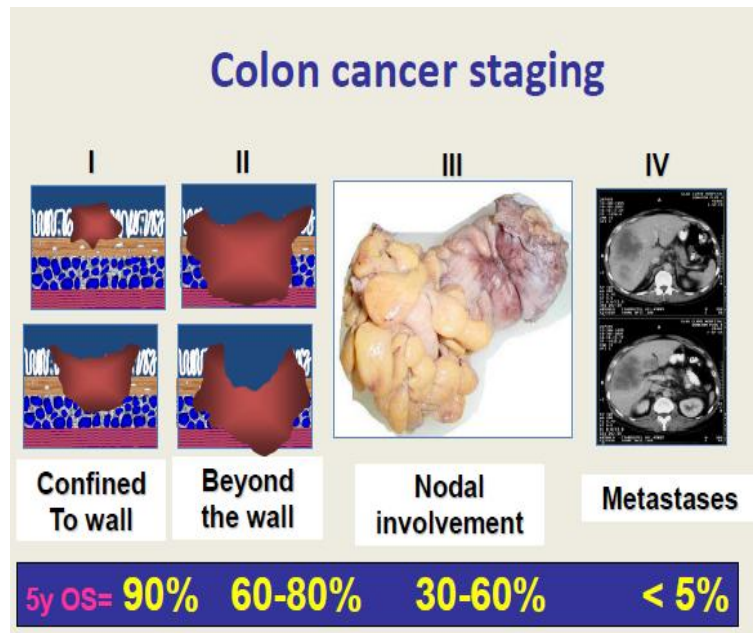
Early detection:

Why does this contribute to a better survival?

- Early detection → Early stage → Better survival
- Occult blood in stools
- Colonoscopy
- Better imaging,
- Better public and physician awareness.

Management of Colon Cancer:

- Early → Surgery
- Locally Advanced → Surgery + Adjuvant Chemotherapy
- Metastatic → Chemotherapy + Surgery
- The most imp tumor marker is **CEA**
- Colon cancer → **SURGERY** is the treatment of choice, then give chemo after surgery to increase the survival rate
- Rectal cancer → Best treatment is **CHEMO + RADIOTHERAPY** for 1 month, then rest for 42 days & then surgery.



Prevention

- Passive prevention → Identify etiological factors → Avoid these factors eg. Smoking, asbestos
 - General health maintenance
 - Eat a healthy diet
 - Don't smoke
 - Don't drink too much
 - Exercise/ maintain optimal weight
 - Try to avoid Breast Cancer risk factors
 - Weight gain
 - Estrogen and progestin use
 - Alcohol use
- Active Prevention → Discover pre-malignant lesions → Get rid of them before developing invasive cancer eg: Colonic polyps and DCIS
 - Eliminate or prevent pre-invasive disease before invasion develops
 - Chemoprevention
 - Surgery

It is not an easy task. Why?

- Social change is difficult and takes a long time
- Not good enough in high risk people

MCQs

- 1- Which of the following tests will provide the best evaluation of the patient with colorectal cancer?
 - A. CA 19 – 9
 - B. CA 125
 - C. CEA (carcinoembryonic antigen)**
 - D. AFP (alpha-foetoprotein)
 - E. HCG (human chorionic gonadotropin)

 - 2- Which factor is prominent for the development of breast cancer?
 - A. High level of estrogen**
 - B. Smoking
 - C. Obesity
 - D. Pollution of environment
 - E. Using of contraception

 3. The man 59-year-old, was admitted to the hospital with suspect colorectal cancer. Which method of examination is the best?
 - A. Computed tomography scan of abdomen
 - B. Colonoscopy with biopsy**
 - C. X-Ray examination of colon with contrast medium
 - D. Laparoscopy with biopsy
 - E. Ultrasonography
-

References:

- 1- Lecture slides.
- 2- Davidsons Principle and Practice of Medicine 21st Edition.
- 3- 429's Medicine Team.