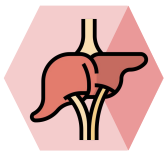
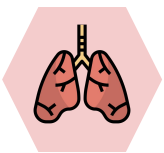
Medicine TEAM 437

MED437 KING SAUD UNIVERSITY

Introduction To Cancer

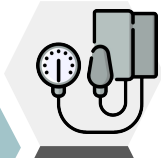
Diagnosis & Treatment



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 (curative Vs palliative concept)
7. Principles of immuno- oncology




Worked on this lecture :

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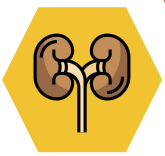
Revised by: Yazeed Al-Dossare

Resources :

Doctors Slides + Notes: Prof Ahmed Abd El-Warith
Books:
Videos:




Cancer

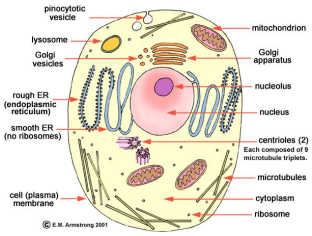
A term used for diseases in which abnormal cells divide and escape the body control. These cells are able to:

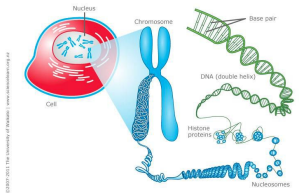
1. Invade surrounding tissues
2. Send distant metastases.
3. Lose their functions

Defining Cancer:

- Primary Tumors
  - Represent de novo tumors in their initial site When we say Breast cancer → primary in the Breast
- Metastatic Tumors
  - Originate from the distant growth of the primary tumors E.g Colon cancer that metastasized to liver
- Unknown primary
  - When you have a metastatic tumor without identifying a primary after the basic work up.

What causes cancer?





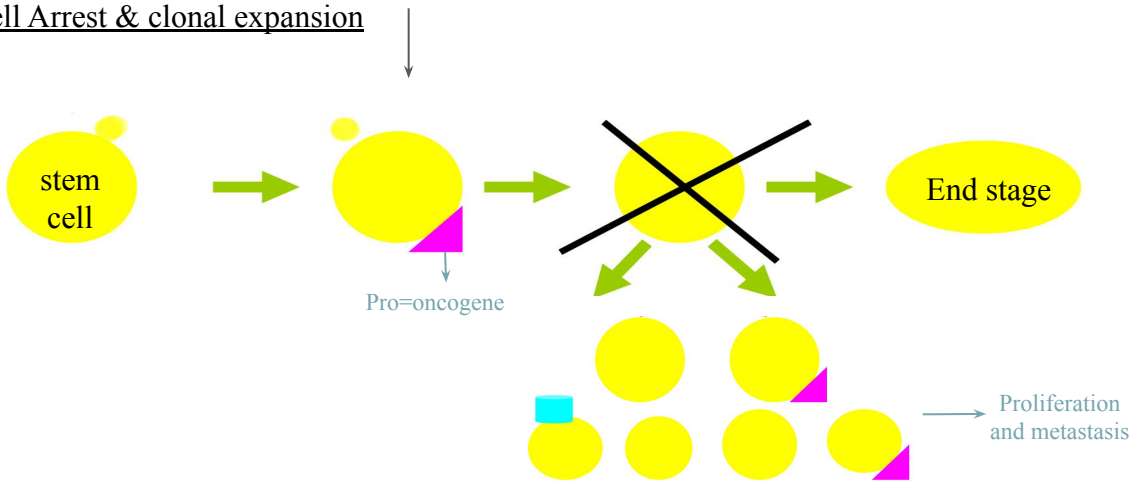
The body is made of different systems
The systems are made of organs
The organs are made of tissues
The tissues are made of cells
The cell is made of cytoplasm + nucleus

- The nucleus has chromosomes which are carrying the genes which are made of **DNA**
  - **DNA controls cell functions → Cell division**
    When there's a problem in the normal mechanism of DNA it can lead to cancer, In cancer there's uncontrolled cell division and loss of apoptosis

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

Development of Malignant Disease

Starts at the stem cell → Activation of pro=oncogene → Genetic mutation → Cell Arrest & clonal expansion



Causes of Cancer:

DNA Mutations:

- Radiation – and other environmental factors
  - Tobacco, Alcohol, Radon, Asbestos, etc..
- Random somatic mutations
- Inherited germline mutations

Genetic predisposition

- Rb, p53 li fraumeni syndrome → Sarcoma, APC, CDKN2A familial melanoma, glioblastoma and pancreatic cancer, BRCA1, BRCA2 Breast & ovarian cancer.

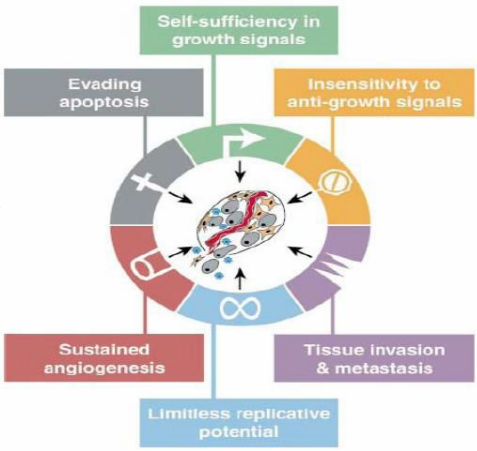
Infectious agents

- Viral:
  - HPV → cervical cancer
  - Hepatitis → liver cancer
  - EBV and HIV → Lymphoma
- Bacterial:
  - H. pylori → stomach cancer MALT Lymphoma

Hallmarks of Cancer:

Summarized by Hanahan and Weinberg (2000) Six changes for cancer found in most, if not all:

1. Self-sufficiency in growth signals ↑Growth
2. Insensitivity to growth inhibitory signals ↓Inhibition
3. Absence of apoptosis
4. Limitless proliferative capacity
5. Sustained angiogenesis formation of new blood vessels
6. Tissue invasion and metastasis



If you decided to be an oncologist what should you know?

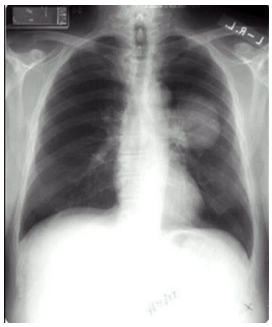
1. When to suspect cancer?
2. How to diagnose cancer?
3. What the essential work up for staging?
4. How to treat cancer?
5. What is the prognosis of your patient?

1- When to suspect cancer?

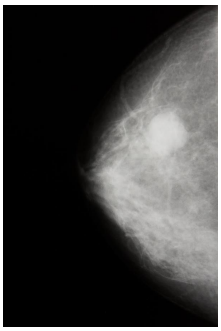
- Cancer Signs and Symptoms No specific sign or symptom But there are some clues
  - Cancer gives most people no symptoms or signs that exclusively indicate the disease.Unfortunately, every complaint or symptom of cancer can be explained by a harmless condition as well.
  - What are the clues ?
    - Persistent, Progressive, Disabling
    - Symptoms & Signs changes according to the site of origin.
      E.g, pneumonia unresponsive to Abx + Presence of Risk factor "Smoking" → Suspect malignancy
  - Constitutional symptoms:
    - Fatigue, Fever, Sweating, Weight loss.
  - Think about the pathology and site:
    - The Mass is able to invade locally and spread distantly → To bone, brain, lung, liver etc..
      - **Mass:** "E.g. lump"
        - Pressure on vital organs Thyroid, Obstruction of lumens colon.
      - **Invasion:**
        - Blood vessels → bleeding
        - Nerves → pain

Symptoms change with time usually small tumors don't produce symptoms but as they enlarge more problems. E.g. Colon cancer → perforation or obstruction → Acute abdomen.

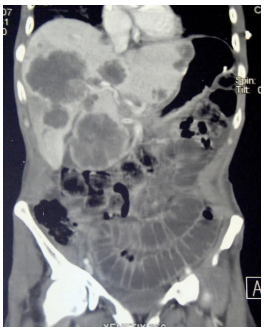
Left lump
further tests CT scan + Biopsy.



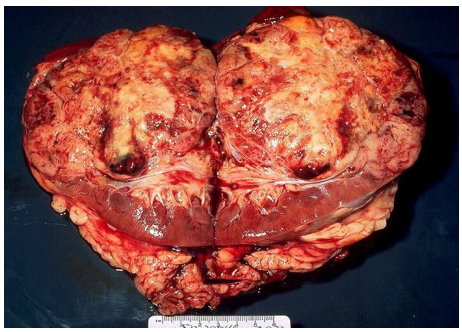
Left Hilar Lymph node
probably malignancy

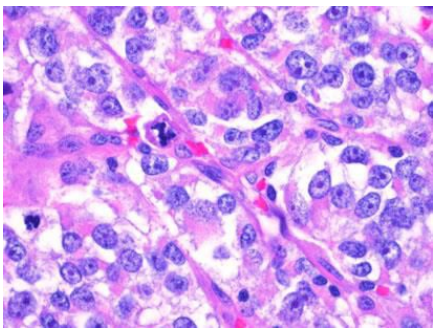


Breast lesion on
Mammogram



Multiple metastasis in
the liver on CT scan





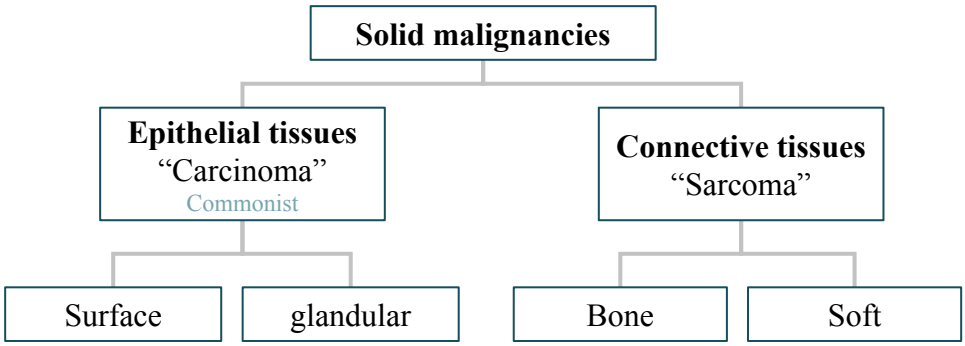
Gross and Microscopic pictures of RCC

2- How to diagnose cancer?

Cancer diagnosis is **NOT** a Clinical or Radiological or Serological diagnosis. Due to the overlap with other diseases especially infection.
It is a Pathological, and A tissue diagnosis.
Except Hepatocellular carcinoma (HCC): Radiology + Hx of cirrhosis + ↑tumor markers are enough to diagnose.

- **Categories of malignant disorders**

- **Liquid malignancies** in Blood
  1. Myeloproliferative disorders = Myeloid Leukemia
  2. lymphoproliferative disorders = Lymphoid leukemia +lymphoma.
- **Solid malignancies:** Colon, Breast, etc..



3- What the essential work up for staging?

Biopsy for tissue diagnosis + Imaging to see the extension of the disease

T= tumor size
N= Node number
M= Metastases yes/no

Clinical TNM By symptoms.
Radiological TNM to see extension.
Pathological TNM By Biopsy.

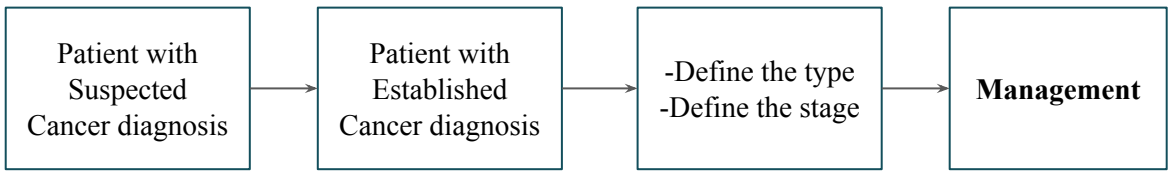
RADIOLOGY:
- X-RAY
- MRI
- CT
- US

SURGICAL STAGING

4- How to treat cancer? Depends on stage + type of cancer so each patient is different.

Types of oncology problems:

1. Patient with Suspected Cancer diagnosis
   - Answer the following questions:
     A. Does the patient have cancer? Is it confirmed with Biopsy + Imaging
     B. What type of cancer?
     C. What stage of cancer?
2. Patient with Established Cancer diagnosis



4- How to treat cancer? Cont.

Management Multidisciplinary Team:

- Surgery Surgeons
- Radiation Radiology oncologist
- Medical oncologist

Other Disciplines:

- Radiology, Pathology, Lab -Combined clinics -(Tumor board* Improve the outcome and ↑survival).

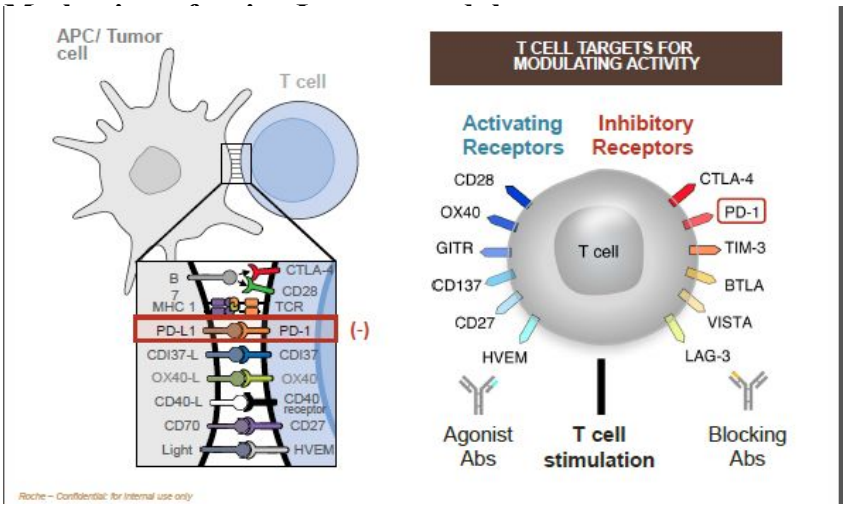
*Team of expert physicians who review and discuss complex cancer patients.

Determine the treatment objective?

- Curative:
  - Treatment:
    - Aggressive, Expensive, recent, updated, complex.
  - Toxicity:
    - Long term , irreversible. E.g. HF, secondary cancer; Lymphoma radiotherapy can cause breast cancer.
- Palliative: Control Symptoms, Improve quality of life, Delay disease progression & complications, Prolong survival.
  - Treatment:
    - Simplest , Avoid hospitalization , Availability, Least toxic.
  - Toxicity:
    - Short term, Acute, Quality of life.

Different Treatment Modalities:

- **Local therapy:** Surgery, Radiotherapy.
- **Systemic therapy:** Chemotherapy, Hormones, Biologicals, Immunotherapy.



4- How to treat cancer? Cont.

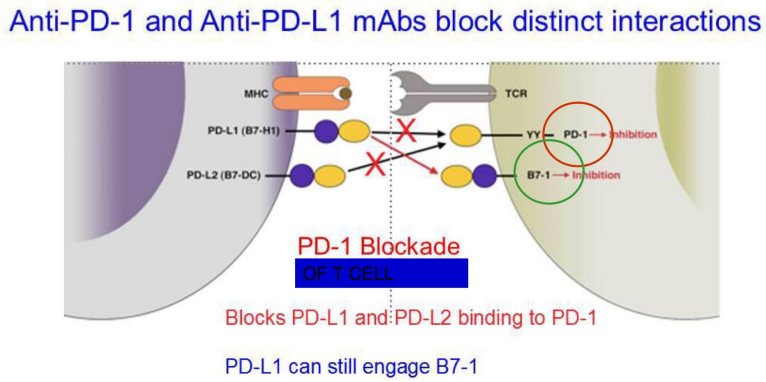
- Mechanism of action Immunomodulators: Cancer can escape the immune system and the body will not be able to recognize it and destroy it.

PROGRAMMED DEATH-1 IMMUNE CHECKPOINT (PD-1):

PD-1 (cell receptor) is overexpressed on tumor infiltrating T cells and these are functionally exhausted cells
Ligands: PDL-1 and PDL-2 (tumor cell /APC)
Higher tumoral PDL-1 expression correlates with decreased overall survival.

Rational: Blocking the PD-1 or PDL-1 pathway would restore/promote the function of chronically exhausted tumor-specific T cells and decrease tumor-induced immune suppression.

The problem with the immunotherapy is that it can affect the whole Immune System and it can cause anything that end with "titis" → Hepatitis, Pancreatitis etc...



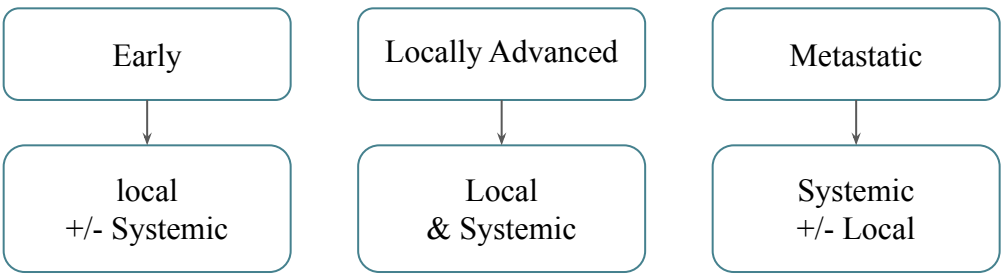
- Categories of malignant disorders

  - **Liquid malignancies:**
    1. Myeloproliferative disorders= leukemia
    2. Lymphoproliferative disorders= lymphoma

    → **Systemic therapy** In exception of some lymphomas

  - **Solid malignancies**

    → **According to stage** and type



5-What is the prognosis of your patient?

What can medicine offer the cancer Patient depends upon

1. The cancer type & extent (stage)
2. The host factors (age , sex , comorbidities)
3. The available tools

- **Tumors that can be cured:**
  - lymphomas, leukemia, early solid tumors +Some locally advanced like colon, lung, breast, RCC, germline, Prostate.
- **Tumors that can have prolonged survival:**
  - Locally advanced and some of the metastatic tumors
- **Tumors that can be palliated:**
  - Metastatic solid tumors

Summary

Cancer Invade surrounding tissues, Send distant metastases, Lose their functions	
Defining Cancer	Primary: De novo tumors in their initial site Metastatic: originate from the distant growth of the primary tumors

causes	Mutation of a normal gene, mutated genes that cause cancer are called oncogenes.
	Predisposition
	• Rb, p53, APC, CDKN2A, BRCA1, BRCA2
	Infectious agents
	• Viral:
	  ○ HPV → cervical cancer
	  ○ Hepatitis → liver cancer
	  ○ EBV → Lymphoma
	• Bacterial:
	  ○ H. pylori → stomach cancer

Development	Starts at the stem cell → Activation of pro=oncogene → Genetic mutation → Cell Arrest & clonal expansion
Hallmarks	• Self-sufficiency in growth signals • Insensitivity to growth inhibitory signals • Absence of apoptosis • Limitless proliferative capacity • Sustained angiogenesis • Tissue invasion and metastasis

Summary cont..

Signs and Symptoms	Persistent, Progressive, Disabling Changes according to the site of origin Constitutional symptoms: Fatigue, Fever, Sweating, Weight loss.
Diagnosis	Pathological, and A tissue diagnosis.

Categories of malignant disorders	• Liquid malignancies
	  ○ Myeloproliferative disorders
	  ○ lymphoproliferative disorders
	Systemic therapy In exception of some lymphomas
	• Solid malignancies
	  ○ Epithelial tissues "Carcinoma"
	  ○ Connective tissues "Sarcoma"
	According to stage
	Early: local, +/- Systemic
	Locally Advanced: Local & Systemic
	Metastatic: Systemic +/- Local

Treatment objective	**Curative:** • **Treatment:** Aggressive, Expensive, recent, updated, complex. • **Toxicity:** Long term , irreversible. E.g. HF, secondary cancer; Lymphoma radiotherapy can cause breast cancer. **Palliative:** Control Symptoms, Improve quality of life, Delay disease progression & complications, Prolong survival. • **Treatment:** Simplest , Avoid hospitalization , Availability, Least toxic. • **Toxicity:** Short term, Acute, Quality of life.
Treatment Modalities	**Local therapy:** Surgery, Radiotherapy. **Systemic therapy:** Chemotherapy, Hormones, Biologicals, Immunotherapy.
Prognosis	**Depends on:** The cancer type & extent (stage) The host factors (age , sex , comorbidities) The available tools

Questions:

1. which one of the is not true regarding the cancer ?

   A. Every neoplasm is considered as a cancer since it is uncontrolled cell growth.
   B. The definitive diagnosis should be on pathological and tissue basis.
   C. Some Infectious agents such as EBV and HPV are known to be cargenous agent.
   D. A metastatic tumor without identifying a primary origin after the basic work up can classified as Unknown primary.

   Correct Answer: A

2. A 45-years old female was diagnosed to have cancer of the cervix. Which ONE of the following viruses is claimed as an etiological factor?

   A. Epstein-Barr virus
   B. Hepatitis C virus
   C. Human immunodeficiency virus
   D. Human papillomavirus

   Correct Answer: D

3. 2. Which ONE of the following is considered a characteristic of malignant tumors?

   A. Ability to form their own blood vessels
   B. Consuming and responding to the host growth factors
   C. High apoptotic activity
   D. Low mitotic activity

   Correct Answer: A