Lecture 64

Editing file

Medicine Team

Reviewed By
Noura Alturki
Jehad Alorainy

Introduction To Cancer Diagnosis & Treatment

Objectives:

- ★ Definition of cancer.
- ★ Etiology of cancer.
- ★ Staging of malignant diseases.
- ★ Principles of pathological classification of malignant diseases.
- ★ General symptoms and signs of malignancy.
- ★ Principles of cancer management (curative Vs palliative concept).
- ★ Principles of immuno- oncology.

Color index:

Original text Females slides Males slides
Doctor's notes Textbook Important Golden notes Extra

Introduction To Cancer Diagnosis & Treatment

◀ History

- The origin of the word ‘‘cancer’’ is credited to the Hippocratic physicians, who used the terms karkinos and karkinoma.
- Claims that cancer is only a ‘modern, man-made disease’ are false and misleading.
- This is not only scientifically incorrect, but misleading.
- Cancer has always been with us, from ancient civilizations to today.

◀ Defining Cancer

Cancer

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

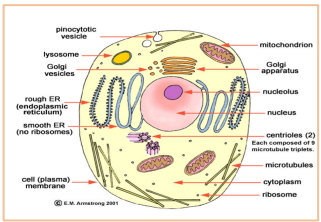
1. Invade surrounding tissues (benign tumors like lipoma and fibroma cannot invade. Locally malignant tumors like Osteoclastoma can invade locally but cannot send distant metastasis. The ture malignant tumors can both invade locally and send metastasis.)
2. Send distant metastases.
3. Lose their functions.

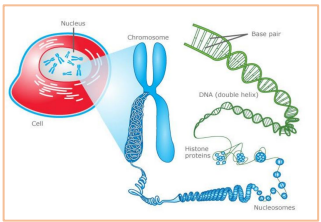
Primary tumors:

- Represent **de novo** tumors in their initial site e.g. Breast cancer inside the breast tissue.

Metastatic tumors:

- Originate from the **distant** growth of the primary tumors to lymph nodes or other organs like liver, lung, bone, brain, etc..





◀ Basic structure of human body

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 carry the genes which are made of DNA → DNA controls cell functions → Cell division

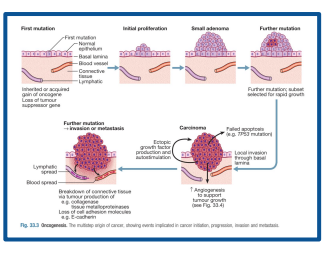
◀ Development of Malignant Disease

01 Stem cell

02 Activation of pro=oncogene

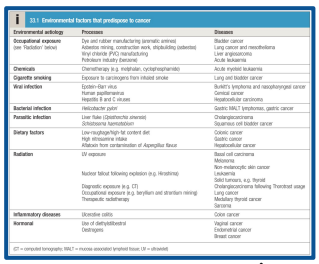
03 Genetic mutation

04 Cell Arrest & clonal expansion



Introduction To Cancer Diagnosis & Treatment

◀ Causes of Cancer



❖ Alter in immunity in cases of autoimmune or immunodeficiency diseases (e.g. AIDS) will alter the process of capturing cancer cells and killing it which can predispose to cancer.

1 DNA Mutations

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

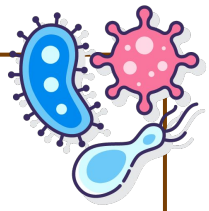
What causes DNA to be mutated?

- Radiation and other environmental factors (Tobacco, Alcohol, Radon, Asbestos, etc).
- Random somatic mutations.
- Inherited germline mutations (Not every pt carrying germline mutation will develop cancer)

2 Genetic Predisposition

- Retinoblastoma, p53 (tumor suppressor gene), APC, CDKN2A, BRCA1, BRCA2

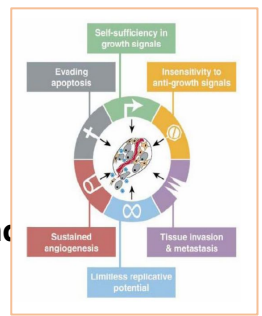
3 Infectious agents



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

◀ Hallmarks of Cancer

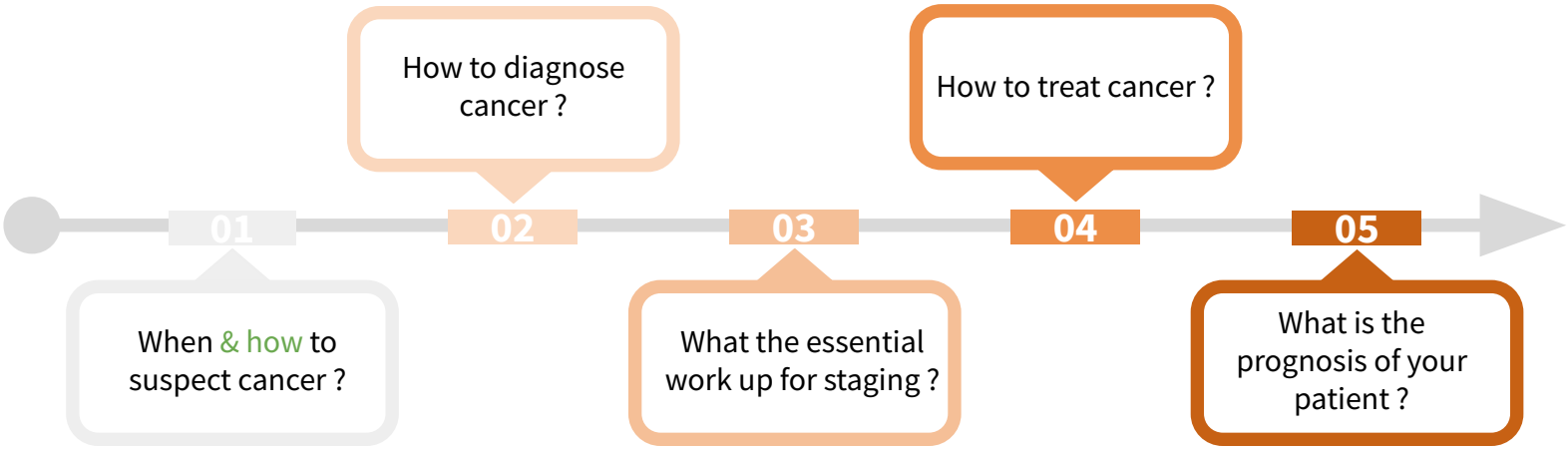
1. **Self-sufficiency in growth signals.**
2. **Insensitivity to growth inhibitory signals .**
3. **Absence of apoptosis.**
4. **Limitless proliferative capacity.**
5. **Sustained angiogenesis**
6. **Tissue invasion and metastasis.**



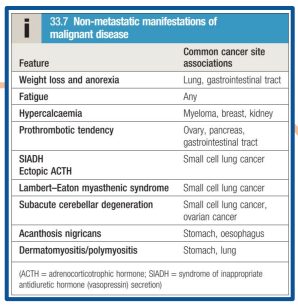
In order of occurrence, the most common cancers in **males** are prostate, lung, and colon. The cancer with the highest mortality in **males** is lung, followed by prostate and colon.
In order of occurrence, the most common cancers in **females** are breast, lung, and colon. The cancer with the highest mortality in **females** is lung, followed by breast and colon.

Introduction To Cancer Diagnosis & Treatment

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



◄ Q1: When to suspect cancer?



i 33.7 Non-metastatic manifestations of malignant disease

Feature	Common cancer site associations
Weight loss and anorexia	Lung, gastrointestinal tract
Fatigue	Any
Hypercalcaemia	Myeloma, breast, kidney
Prothrombotic tendency	Ovary, pancreas, gastrointestinal tract
SIADH Ectopic ACTH	Small cell lung cancer
Lambert–Eaton myasthenic syndrome	Small cell lung cancer
Subacute cerebellar degeneration	Small cell lung cancer, ovarian cancer
Acanthosis nigricans	Stomach, oesophagus
Dermatomyositis/polymyositis	Stomach, lung

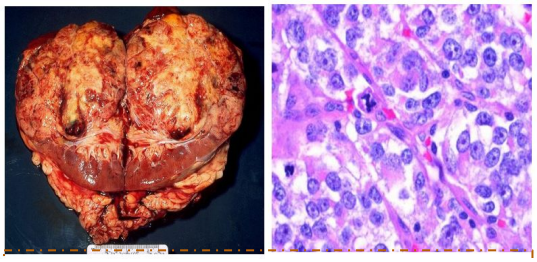
(ACTH = adrenocorticotrophic hormone; SIADH = syndrome of inappropriate antidiuretic hormone (vasopressin) secretion)

Cancer Signs and Symptoms:

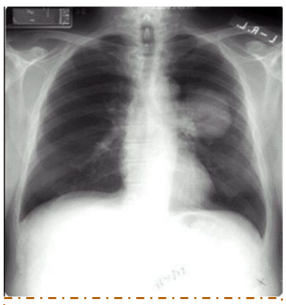
- Cancer gives most people **no** symptoms or signs that **exclusively** indicate the disease.
- Unfortunately, **every complaint or symptom of cancer can be explained by a harmless condition as well** for example:
  - The most common cause of hemoptysis is not lung cancer or TB, it's bronchitis.
  - The most common cause of hematemesis is not stomach cancer or peptic ulcer, it's gastritis.
- **Do not forget the constitutional symptoms:**
  - Fatigue, fever, sweating, weight loss.
  - Sometimes cancer patients present only with constitutional symptoms, especially leukemia and lymphoma patients
- **What are the clues?**
  - **Persistent**, **Progressive**, **Disabling** (prevent the patients from doing daily activity)
  - **Symptoms** & **Signs** changes **according to the site** of origin e.g. stomach cancer causing hematemesis, colon cancer causes bleeding per rectum.
- **Think about the pathology and site:**
  - The Mass is able to **invade locally** and **spread distantly** → To bone, brain, lung, liver
    - **Mass (lump):**
      - **Pressure** on vital organs e.g. cancer in stomach will cause abdominal discomfort
      - **Obstruction** of lumens e.g. cancer in colon will cause constipation or obstruction
    - **Invasion :**
      - Blood vessels → **bleeding** .
      - Nerves → **pain** (if sensory), weakness or paralysis (if motor).

◀ Q2: How to diagnose cancer?

1	• IT IS **NOT** A CLINICAL DIAGNOSIS
2	• IT IS **NOT** A RADIOLOGICAL DIAGNOSIS
3	• IT IS **NOT** SEROLOGICAL DIAGNOSIS
4	• IT IS A **PATHOLOGICAL** DIAGNOSIS
5	• IT IS A **TISSUE** DIAGNOSIS

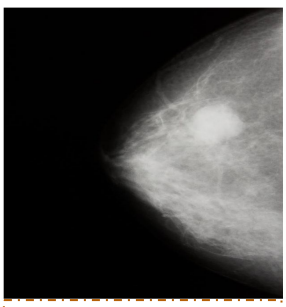


GROSS AND MICROSCOPIC PICTURE OF Renal Cell Carcinoma

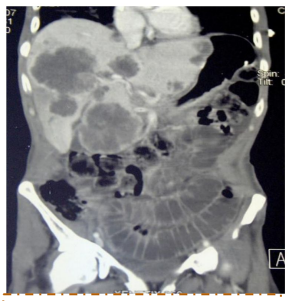


Lung cancer

Lump in the neck (lymphoma)

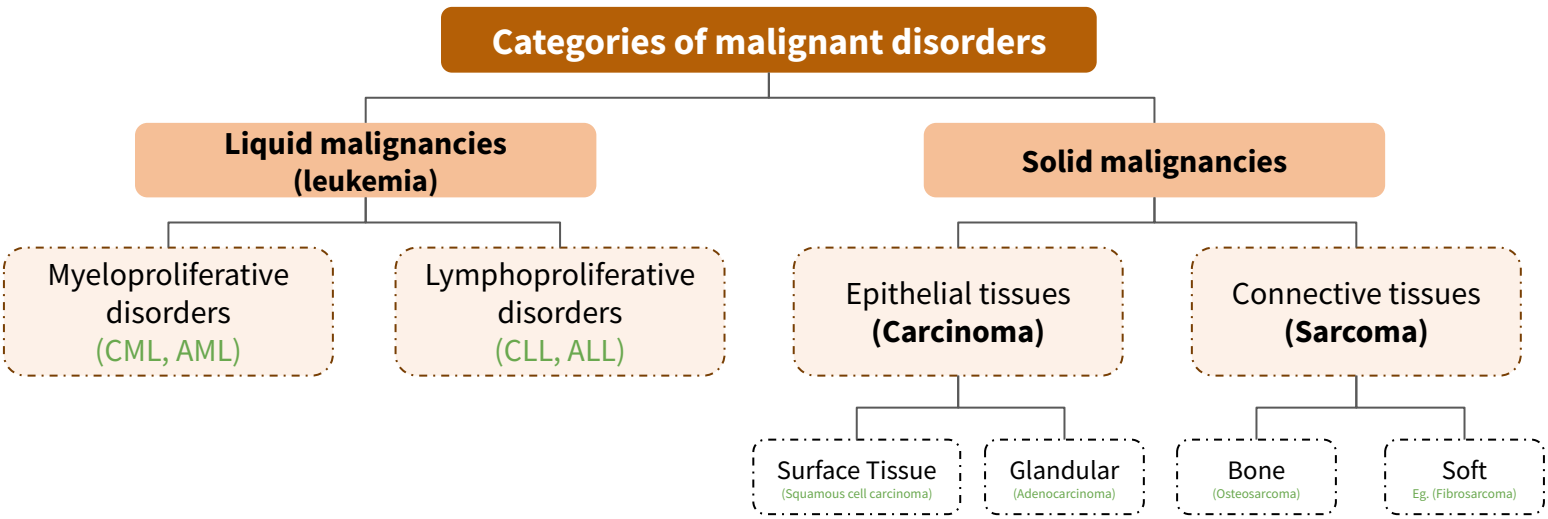


Breast cancer with nodule in the breast



liver metastasis in the left and right lobes

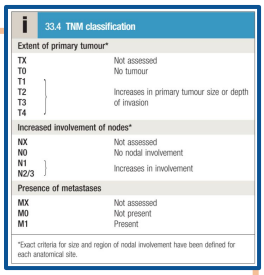
◀ Categories of malignant disorders



An area for your notes or something..

Introduction To Cancer Diagnosis & Treatment

◀ Q3: What the essential work up for staging?



33.4 TNM classification

Extent of primary tumour*	
TX	Not assessed
T0	No tumour
T1, T2, T3, T4	Increases in primary tumour size or depth of invasion
Increased involvement of nodes*	
NX	Not assessed
N0	No nodal involvement
N1, N2/3	Increases in involvement
Presence of metastases	
MX	Not assessed
M0	Not present
M1	Present

*Exact criteria for size and region of nodal involvement have been defined for each anatomical site.

- **TNM** (T= tumor, N= Node, M= Metastases)
  - **Clinical** TNM
  - **Radiological** TNM
  - **Pathological** TNM
- **Radiology:**
  - **XRay**
  - **MRI:** preferred technique for brain and pelvic imaging. It is widely employed for the staging of rectal, cervical and prostate cancers.
  - **CT:** is a key investigation in cancer patients and is particularly useful in imaging the thorax and abdomen.
  - **US:** is useful in characterising lesions within the liver, kidney, pancreas and reproductive organs. Endoscopic ultrasound is helpful in staging upper gastrointestinal and pancreatic cancers.
  - **PET scan:** It can accurately assess the severity and spread of cancer by detecting tumour metabolic activity following injection of small amounts of radioactive tracers such as fluorodeoxyglucose (FDG).
- **Surgical Staging**

◀ Q4: How to treat cancer?

1) Types of oncology problems:

- Patient with Suspected Cancer diagnosis
- Patient with Established Cancer diagnosis (Answer the following questions):
  - Does the patient have cancer?
  - What type of cancer?
  - What stage of cancer?

2) Management Multidisciplinary:

- Surgery, Radiation, Medical ONC.
- Others Disciplines: Radiology, Pathology, Lab, Combined clinics, Tumor board.

3) Determine the treatment Objective:

- Either **Curative** or **Palliative** (Surgical procedures are often the quickest and most effective way of palliating symptoms.)

Curative	Palliative
Therapy: • Aggressive, Expensive, recent, updated, complex. **Toxicity:** • Long term, irreversible	**Therapy:** • Simplest , Avoid hospitalization, Availability Least toxic **Toxicity:** • Short term, acute, quality of life

Different Treatment Modalities	
Local therapy: • Surgery & Radiation therapy	**Systemic therapy:** • Chemotherapy • Hormones • Biologicals • Immune therapy

◄ Q4: How to treat cancer? cont.

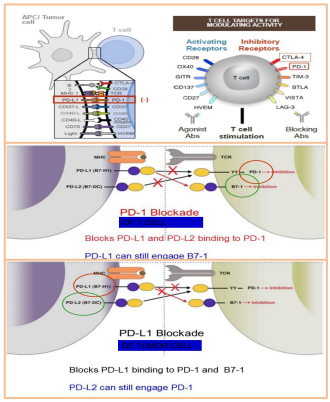
Mechanism of Action of Immunomodulators

The theory is to use the immune system (which is inhibited by the tumor) by removing the inhibition and allowing the cytotoxic T cells kill the cancer cells.

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

Rationale:

- 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



- **Liquid malignancies:**
  - Treated systemically
- **Solid malignancies:**
  - Treated according to stage

General Staging of solid malignancies

Early	Locally Advanced	Metastatic
local +/- Systemic[1]	local & Systemic[2]	Systemic +/- Local[3]

◄ Q5: What is the prognosis of your patient?

❖ **What can medicine offer the cancer patient?**

- ➢ The cancer type & extent (stage)
- ➢ The host factors (age, sex, comorbidities)
- ➢ 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.

1- local treatment mainly, systemic treatment is adjuvant.
2- start systemic to decrease the size then local to remove it.
3- mainly systemic, local for symptoms control.

Summary

Cancer Definition:

- **A term used for diseases in which abnormal cells divide and escape the body control, these cells are able to:**
  - Invade surrounding tissues (benign tumors like lipoma and fibroma cannot invade. Locally malignant tumors like Osteoclastoma can invade locally but cannot send distant metastasis. The ture malignant tumors can both invade locally and send metastasis.).
  - Send distant metastases
  - Lose their functions.
- **Primary tumors:**
  - Represent de novo tumors in their initial site e.g. Breast cancer inside the breast tissue.
- **Metastatic tumors:**
  - Originate from the distant growth of the primary tumors to lymph nodes or other organs like liver, lung, bone, brain, etc..

Causes of Cancer

- **DNA Mutations:**
  - Cancer arises from the mutation of a normal gene.
  - Mutated genes that cause cancer are called oncogenes.
  - Radiation and other environmental factors (Tobacco, Alcohol, Radon, Asbestos, etc).
  - Random somatic mutations.
  - Inherited germline mutations.
- **Genetic Predisposition**
  - Retinoblastoma, p53 (tumor suppressor gene), APC, CDKN2A, BRCA1, BRCA2
- **Infectious agents**
  - **Viral:** HPV – cervical cancer, Hepatitis – liver cancer, EBV - Lymphoma
  - **Bacterial**: H. pylori – stomach cancer

Hallmarks of Cancer:

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

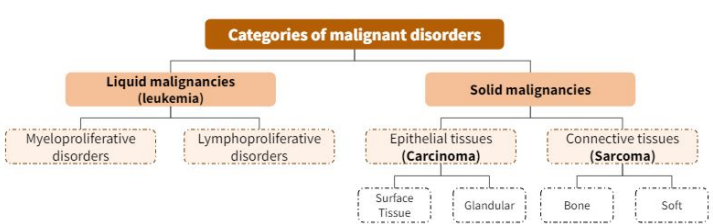
Q1: When to suspect cancer?

- 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.
  - **Do not forget the constitutional symptoms:**
    - Fatigue, fever, sweating, weight loss.
  - **What are the clues?**
    - Persistent, Progressive, Disabling and prevents it's patients from doing daily activity.
    - Symptoms & Signs changes according to the site of origin.
  - **Think about the pathology and site:**
    - The Mass is able to <u>invade locally</u> and <u>spread distantly</u> → To bone, brain, lung, liver .

Q2: How to diagnose cancer?

1	• **IT IS NOT A CLINICAL DIAGNOSIS**
2	• **IT IS NOT A RADIOLOGICAL DIAGNOSIS**
3	• **IT IS NOT SEROLOGICAL DIAGNOSIS**
4	• **IT IS A PATHOLOGICAL DIAGNOSIS**
5	• **IT IS A TISSUE DIAGNOSIS**

Categories of malignant disorders



Summary

Q3: What the essential work up for staging?

- **TNM** (T= tumor, N= Node, M= Metastases)
  - Clinical TNM
  - Radiological TNM
  - Pathological TNM
- **Radiology:**
  - XRay, MRI, CT, US, PET scan.
- **Surgical staging.**

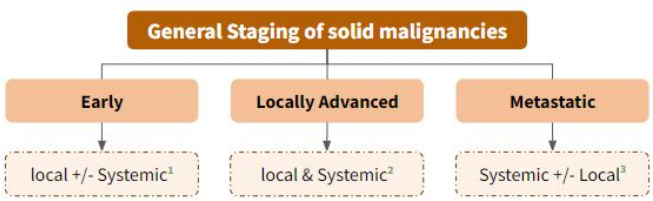
Q4: How to treat cancer?

- **Types of oncology problems:**
  - Patient with Suspected Cancer diagnosis
  - Patient with Established Cancer diagnosis (Answer the following questions):
    - Does the patient have cancer?
    - What type of cancer?
    - What stage of cancer?
- **Management Multidisciplinary:**
  - Surgery, Radiation, Medical.
  - Others Disciplines: Radiology, Pathology, Lab, Combined clinics, Tumor board.
- **Determine the treatment Objective:**
  - Either Curative or Palliative

Curative	Palliative
Therapy: • Aggressive, Expensive, recent, updated, complex. **Toxicity:** • Long term, irreversible	**Therapy:** • Simplest , Avoid hospitalization, Availability Least toxic **Toxicity:** • Short term, acute, quality of life

Different Treatment Modalities	
Local therapy: • Surgery & Radiation therapy	**Systemic therapy:** • Chemotherapy • Hormones • Biologicals • Immune therapy

- **Mechanism of Action of Immunomodulators**
  - 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
- **Liquid malignancies:**
  - Treated systemically
- **Solid malignancies:**
  - Treated according to stage



Q5: What is the prognosis of your patient?

- **What can medicine offer the cancer patient?**
  - The cancer type & extent (stage)
  - The host factors (age, sex, comorbidities)
  - The available tools

1 Tumors that can be cured	2 Tumors that can have prolonged survival	3 Tumors that can be palliated
• lymphomas, leukemia, early solid tumors.	• Locally advanced and some of the metastatic tumors.	• Metastatic solid tumors.

Lecture Quiz

Q1: Cancer is diagnosed:
A- Clinically.
B- Radiologically.
C- Serologically.
D- Tissue & Pathology.

Q2: Which ONE of the following is a characteristic of locally malignant tumors?
A) Invade locally but cannot send distant metastasis
B) Invade locally and can send distant metastasis
C) Cannot invade locally but can send distant metastasis
D) Cannot invade locally and cannot send distant metastasis

Q3: 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

Q4: All of the following are hallmarks of cancer , except:
A- Sustained angiogenesis .
B- Tissue invasion .
C- Insensitivity to growth inhibitory signal .
D- Presence of apoptosis .

Q5: In liquid malignancies , the proper treatment is:
A- Systemic therapy .
B- Local therapy .
C- Local & systemic .
D- Local , +/- systemic .

Answers: Q1:D | Q2:A | Q3:A | Q4:D | Q5:A

THANKS!!

This lecture was done by:

- Nawaf Albhijan
- Faisal AlMusaeed

Note taker:

- Nawaf Albhijan

Females co-leaders:
Raghad AlKhashan
Amirah Aldakhilallah

Males co-leaders:
Mashal AbaAlkhail
Nawaf Albhijan

Send us your feedback:
We are all ears!