

# **Principles of Surgical Oncology**

### **Objectives:**

- Types of tumors.
- Applied surgical pathology of tumors.
- Pathological basis of tumor staging.
- Tumor staging.
- Principles of biopsy and cytology.
- Principles of surgery of tumors.
- Overview of tumor markers.

### **Resources:**

- Doctor's slides
- Doctor's notes
- Surgical recall
- Davidson

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> COLOR INDEX: Notes , <mark>Important</mark> , Extra , Davidson's <u>Editing file</u> <u>Feedback</u>







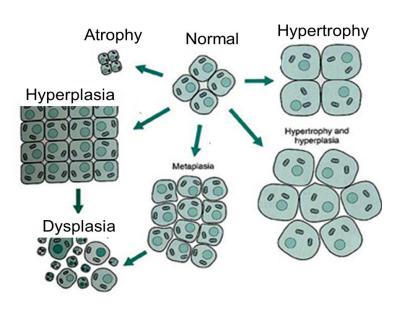
### **Overview:**

A neoplasm or new growth consists of a mass of transformed cells that does not respond in a normal way to growth regulatory systems. These transformed cells serve no use-full function and proliferate in an atypical and uncontrolled way to form a benign or malignant neoplasm. In normal tissues, cell replication is under tight regulatory control. However, when a cancer arises, this is generally due to genomic abnormalities that either increase cell replication or inhibit cell death. The mechanisms by which this abnormal growth activity is induced (carcinogenesis) are complex and can be influenced in many ways: for example, inherited genetic makeup, residential environment, exposure to ionizing radiation or carcinogens, viral infection, diet, lifestyle and hormonal imbalances. These cellular insults give rise to alterations in the genomic DNA (mutations) and it is these mutations which lead to cancer. Mutations can lead to disruption of the cell replication cycle at any point and lead to either activation or , over-expression of oncogenes, or the inactivation of tumour which is dependent on: suppressor genes, or a combination of the two.

## Pathological cell changes:

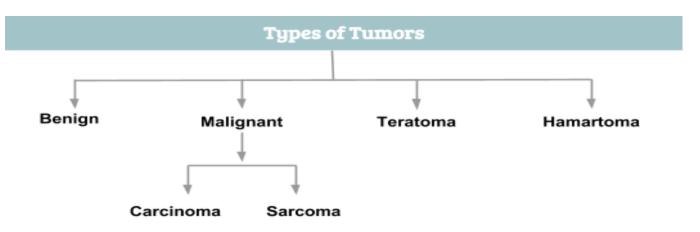
The transmission of cells to different shapes:

- Hypertrophy = increase in cells size .
- Atrophy = decrease in cells size.
- Hyperplasia = increase in cells number .
- Metaplasia =is the reversible transformation of a type of tissue to another tissue that can tolerate irritants
- Dysplasia = is considered a pre-cancer mix between cells (atrophy and hyperplasia).
- Atrophy, hypertrophy and hyperplasia are all normal cells, and have a structure of a normal cell, but when metaplasia reaches dysplasia (premalignant) it can reach to a point where it could change into malignancy.



- Malignant cells behave differently from normal cells, and its function also starts to act differently, and in some tumors can secrete substances that it's not supposed to. For example,
   Bronchogenic small cell carcinoma secretes ACTH, causing ectopic cushing's syndrome.
- Dysplastic cells are not malignant by itself, but it's an indication that there is something that changes the cell's nature, for example: ova of the Schistosoma causes chronic irritation to the transitional cell of the bladder which causes metaplasia and dysplasia and transform the transitional cells to squamous cell epithelium (because it's designed for wear and tear) and eventually causes squamous cell carcinoma. **Squamous cell carcinoma of the bladder is seen in endemic regions of schistosomiasis**.





# **Types of Tumors**

Benign	Malignant
Benign tumours rarely threaten life but may cause a variety of cosmetic or functional abnormalities.	<ul> <li>Carcinoma: Epithelial origin. Carcinoma is more aggressive than sarcoma.</li> <li>Sarcoma: Mesothelial origin.</li> </ul>
Teratoma	Hamartoma
<ul> <li>Could be benign or malignant.</li> <li>Teratoma is made up of several different types of tissue that are <u>not normally</u> found at that site.</li> <li>Best Example, Dermoid cyst of ovaries and testes, and the testes could have benign teratoma (dermoid cyst) or malignant teratoma.</li> <li>The two main types of tumors in the testes are either teratoma (usually in a younger age around 20s) or seminoma (usually in older people around 40s).</li> </ul>	<ul> <li>Hamartoma is just like teratoma but the difference is that it is composed of tissue that are <u>normally</u> found at that site but are disorganized.</li> <li>Best example, angiomyolipoma of the kidney.</li> <li>&gt; angio : blood vessel , myo : muscle , lipoma : fat.</li> </ul>
<ul> <li>Dermoid cyst of the ovaries shows hair, muscle, bone, tooth.</li> </ul>	<ul> <li>Angiomyolipoma (hematoma) of the kidney. under the ultrasound shows an impression of fat.</li> </ul>

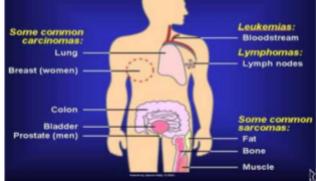


## **Cancer Nomenclature:**

Cancer prefixes point to location:		
Prefix	Meaning	
Adeno	Gland	
Chondro	Cartilage	
Erythro	Red blood cells	
Hemangio	Blood vessels	
Hepato	Liver	
Lipo	Fat	
Lympho	Lymphocyte	
Melano	Pigment cell	
Myelo	Bone marrow	
Муо	Muscle	
Osteo	Bone	

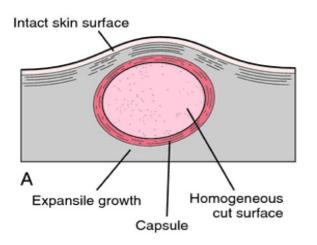
Types	of Malignancies:
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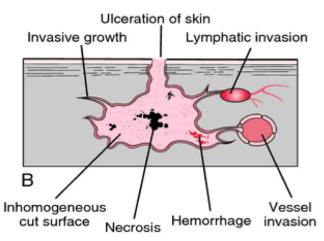
Prefix adeno-	gland h	
chondro-	cartilage	
erythro-	red blood cell	
hemanglo-	blood vessels	1 /
hepato-	liver	
lipo-	fat	
lympho-	lymphocyte	4
melano-	pigment cell	
myelo-	bone marrow	
myo-	muscle	
osteo-	bone	
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feature	Benign	Malignant
Capsule	Encapsulated	<ul> <li>Non encapsulated:</li> <li>Sometimes we can see a capsule in a malignant tumor but it is called a False Capsule (a fibrous tissue that indicates the bodies defence against the tumor).</li> </ul>
Invasion	No invasion	<ul> <li>Usually invades:</li> <li>Invasion: is a Continuity of the primary tumor.</li> <li>Invades adjacent tissues and organs by direct infiltration e.g. bladder cancer invading the uterus or rectum.</li> </ul>
Metastasis	No metastasis	<ul> <li>Metastasis:</li> <li>Metastasis: is a tumor cell that has discontinued from the primary tumor (even if it was near the primary tumor), e.g. presence of bladder tumor cell in lymph node or liver.</li> </ul>







## Cont. Types of Malignancies:

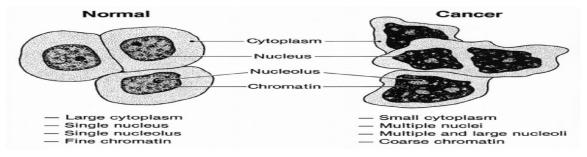
feature	Benign	Malignant
Treatment	<ul> <li>Local excision of benign.</li> <li>(description of the pictures below): A benign papillary lesion in the colon treated by local excision only.</li> </ul>	<ul> <li>Radical excision.</li> <li>Examples of radical excision in colon cancer is right hemicolectomy, which removes colon, mesentery, lymph nodes, and the blood supply.</li> <li>+\- Chemotherapy or Radiotherapy or both.</li> </ul>
Pictures		
	<ul> <li>(1st Pic) Ultrasound showing a benign tumor in the breast.</li> <li>Fibroadenoma of the breast also called breast mouse because it's mobile, and it is the most common benign tumor of the breast.</li> <li>Treatment local excision of the tumor.</li> </ul>	<ul> <li>Malignant tumor of the breast .</li> <li>Treatment: radical excision.</li> </ul>



## **Characteristics of Malignant cell:**

- Uncontrolled growth and loss of contact phenomena<sup>1</sup> are the main characteristics of malignant cells.
- Loss of contact phenomena believes to be the cause of increase bad behavior of the malignant cells.
- **Carcinoma in situ:** is the presence of tumor cells inside the epithelium but did not invade the basement membrane, it is very serious, and it is considered as malignant (not premalignant).

	Normal cell	Malignant cell
Normal versus malignant cells	<ul> <li>large cytoplasm</li> <li>single nuclei</li> <li>single nucleoli</li> <li>fine chromatin</li> </ul>	<ul> <li>Small cytoplasm</li> <li>Multiple nuclei</li> <li>Multiple and large nucleoli</li> <li>Coarse chromatin</li> <li>Malignant cells: Chromatin indicates chromosomes, and under the multiplication phase you see coarse chromatin and also called in pathology (mitotic figure) which appears dark under the microscope.</li> <li>Under the microscope the malignant cells appear in different sizes which is called in pathology (pleomorphism).</li> <li>Why do malignant cells have small cytoplasm? Because the nucleus enlarges before division, and then when the cell splits into two cells, it also splits the cytoplasm with it.</li> </ul>



## Examples of thyroid tumors and their behaviors:

- **Papillary carcinoma of the thyroid:** usually in young people, more in females, and metastasize to the lymph nodes then it metastasize to the bloodstream.
- Follicular : usually in middle aged people, more in males, and metastasize to the bloodstream.
- Anaplastic: usually in elderly, can invade and metastasize to the blood and lymph nodes.

<sup>&</sup>lt;sup>1</sup> loss of contact phenomenon: just like if you have a cut wound in your hand, the skin eventually will stop growing as the two edges 'contact' and cover the wounded part. why? Because of contact phenomenon; malignant cell lose these signals leading to disorganized growth and arrangement.



# **Tumor Grading & Differentiation**

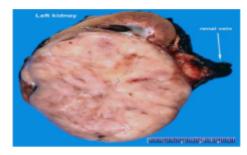
Grading	Differentiation
<b>Describes the histologic characteristics of cancer cells</b> mainly talk about cell layers. e.g. grade I, II, III.	Describes the characteristics of cancer cells in reference to their resemblance to the cell of origin. e.g. well differentiated ,moderately differentiated, poorly differentiated, anaplastic.

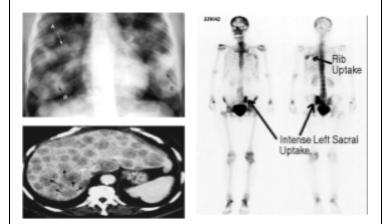
macroscopic features , invasion or metastasis.

Degree of differentiation provides information about cancer aggressiveness and progression			
Well differentiated	Moderately differentiated	Poorly differentiated	Anaplastic
Cancer cell looks and behaves like the normal cells in the tissue (slow growing and less aggressive).	You still can see that it's glandular.	<ol> <li>Indicates that the cancer is rapidly growing with no time for the cells to be differentiated.</li> <li>Most of them are more susceptible to chemotherapy agents b\c they are weak due to the rapid development and growth.</li> </ol>	Cancer cells that divide rapidly and have little or no resemblance to normal cells. 1. If we find an enlarged lymph node but we don't know the origin, we send it to the lab. If it's a well differentiated tumor, the pathologist will be able to identify the cell of origin. 2. However, in poorly differentiated or anaplastic tumors, the pathologist will not be able to identify the cell of origin, he will only be able to confirm the malignancy.
well	Moderate	Poorly	Anapistic



Local invasion	Metastasis
<ul> <li>Within the organ.</li> <li>Adjacent organs.</li> <li>Malignant cells secrete a number of factors that may determine their biological behaviour and promote growth at both primary and metastatic sites. The matrix metalloproteinases (MMPs) are endo-proteinases with enzymatic activity directed against components of the extracellular matrix. Their action facilitates tumour cell invasion and metastasis by degrading extracellular collagens, laminins and proteoglycans.</li> </ul>	<ul> <li>Lymphatic :Regional &amp; distant lymph nodes.</li> <li>Homogeneous: e.g. Liver, lung, bones.</li> <li>Transcoelomic e.g peritoneal &amp; pleural cavity.</li> <li>Implantation e.g. needle tracks, wounds.</li> <li>Most of the tumors metastasis occur in the Liver, lung, bones and the lymph nodes because these areas receive the majority of the blood supply.</li> <li>Transcoelomic metastasis (celom=cavity), Colon cancer can metastasis through the peritoneal cavity. The tumor invades the adventitia and serosa and swims in the peritoneal fluid and lands in the cavity, causing patches of tumor cells in the abdomen that are discontinued from the primary tumor, this is called peritoneal seedlings ( yeige).</li> </ul>





- CXR shows cannon ball appearance which indicates multiple lung metastasis.
- Bone scan shows hot spot which indicates bone metastasis. It appears that way because the area of the tumor has more blood supply which takes more isotope material and appears hot spot in the scan. The scan can't differentiate between a tumor and acute inflammatory response except with good history.



# **STAGING OF MALIGNANT TUMORS**

Staging describes the primary tumor, its relation with the organ of origin, adjacent and distant organs.

• Types of Tumor Staging:

### 1-Classical:

stage I, II =confined to the organ.	stage III= direct invasion with no	stage IV= metastasis
	metastasis	

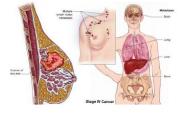
### **2-TNM:**

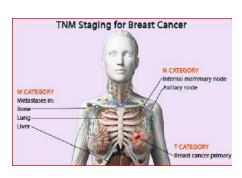
- T1, No, Mo
- **T (description of the primary Tumor) :**T1,2,3,Tis,Ta,Tb
- **N Node :** N0, 1, 2, 3
- **M Metastasis :** M0,1,2,3

## Why Do We Stage Malignant Tumors?

- To decide the treatment.
- Primary is different than secondary treatment.
- To plan the treatment: (Surgery, radiotherapy, chemotherapy)
- To assess the prognosis.
- To define the extent of disease.

TNM Classification (American Joint Commission on Cancer)		Dukes' Classification		
Stages	Т	N	М	Stages
Stage 0	Tis	NO	MO	
Stage I	T1	NO	MO	A
olage i	T2	NO	MO	B1
Stage II	Т3	NO	MO	B2
otaye li	Τ4	NO	MO	B2
Stage III	T1, T2	N1 or N2	MO	C1
orage III	T3, T4	N1 or N2	MO	C2
Stage IV	Any T	Any N	M1	D







# **Clinical presentation of Malignancy**

- Whenever you deal with a malignant tumor, always remember that there is a primary tumor & there may be secondaries.
- Remember that the patients does not always present with the symptoms of the primary tumor, they can present with symptoms of the secondary tumor.

Asymptomatic	
Symptoms related to the primary	<ul> <li>lies on the surface of the body:         <ul> <li>may become visible</li> <li>change in shape or pigmentation</li> <li>bleed, or discharge mucus or pus.</li> </ul> </li> <li>Obstruction of hollow viscus or duct:         <ul> <li>in a bronchus → pulmonary collapse</li> <li>In a segment of bowel → intestinal obstruction</li> <li>In bile duct or pancreatic duct → jaundice, or pancreatitis.</li> </ul> </li> <li>A tumour within a closed space:         <ul> <li>may cause pressure symptoms. For example, increased intracranial pressure may complicate intracerebral tumours, and paraplegia may arise from a spinal cord tumour.</li> </ul> </li> <li>Invasion of an organ:         <ul> <li>may compromise its normal functions and cause organ failure. Invasion of tissues such as the pancreas, bone or nerves can cause severe pain. A cancer can also mimic the pain of benign disease: for example, dyspeptic symptoms in stomach cancer.</li> </ul> </li> <li>Secretory tumours: can produce characteristic clinical syndromes.         <ul> <li>Tumour of the adrenal cortex &gt; Cushing's syndrome.</li> <li>Parathyroid tumor &gt; hypercalcaemia.</li> <li>An islet cell tumour of pancreas &gt; hypoglycemia.</li> <li>Secretory products may be inappropriate to the site of a tumour. Such 'ectopic' secretion occurs predominantly in tumours of neuroendocrine origin, and produces a variety of endocrine syndromes.</li> </ul></li></ul>



symptoms related to the secondaries	<ul> <li>For example:         <ul> <li>A patient that presents with hemoptysis could be because of a tumor, either primary like bronchogenic carcinoma or secondary like lung metastasis from Renal cell carcinoma, and the hemoptysis is the first presentation of the patient.</li> <li>Pathological fracture (easy fracture of the bone) could be a first symptom of a cancer that metastasized to the bone causing pathological fracture.</li> <li>60 y/o female had sudden low back pain, after investigations, she was discovered to have breast cancer□.</li> </ul> </li> </ul>
Incidental finding	<ul> <li>For example:         <ul> <li>If a patient presents with an upper abdominal pain, and you did an ultrasound of the abdomen and found a tumor in the kidney which you didn't think of .</li> </ul> </li> </ul>
Weight loss and cachexia	<ul> <li>Weight loss and Cachexia are late manifestations of most malignant tumors except GI which affects the absorption and Lung cancer (bronchogenic carcinoma).</li> <li>In GIT cancers, as the cancers being in upper parts of alimentary tract, as faster in causing weight loss. (esophageal cancer develops weight loss faster than gastric and colon cancer).</li> <li>Bronchogenic carcinoma is also known to cause a fast weight loss.</li> <li>Weight loss is often the key symptom that alerts both patients and their doctor to the possibility of malignant disease. A proportion of patients become so emaciated that they appear to die of starvation. This syndrome is known as cancer cachexia, and is clinically characterized by anorexia, severe weight loss, lethargy, anaemia and oedema.</li> </ul>

## **Investigation of Malignant Tumors:**

Initial investigations to make the diagnosis should proceed in a logical order, starting with simple blood tests (e.g. tumour markers) and progressing through more complex imaging investigations.

Investigate for the primary	Investigate for the secondaries	
<ul> <li>depend on the site</li> <li>depend in the histology</li> <li>define the local extension</li> </ul>	<ul> <li>Look for metastasis.</li> <li>Usually liver, lung and bones.</li> </ul>	
Both will define the <b>diagnosis &amp; stage</b> .		



## How we obtain material for histology:

## Local Effects of Tumours:

Local Effects of Tumours:		
cytology	biopsy	
<ul> <li>Examination of morphology of individual cells under the microscope.</li> <li>Exfoliative : urine (voided urine specimen, for urinary bladder carcinoma), sputum:</li> <li>the epithelial layer multiplies and the superficial cells fall down so try to collect it &amp; benefit from it</li> <li>"without any effort from the doctor "as in sputum or urine sample.</li> <li>Fluid aspiration (ascitic fluid,pleural fluid)</li> <li>Fine needle aspiration (FNA): a very fine (thin) needle that enters a solid tumor taking cells from it, then stain the cells on the slide and look under the microscope for any malignant cells.</li> <li>Pap smear is used for screening of cancer of the cervix and it is also considered to be cytology.</li> </ul>	<ul> <li>Examination of histological tissue characteristics under the microscope.</li> <li>Core biopsy E.g. Tru-cut: core of tissue removed for histological examination Usually done if the lump is apparent and distinct and localized , Commonly done through endoscope.</li> <li>Incisional biopsy : removes a small accessible piece of the lesion for histological examination (open,forceps, needle)</li> <li>Excisional biopsy: Complete removal of a discrete lesion without a wide margin and without it being considered curative of the malignancy. E.g. Remove breast lump for histology.</li> </ul>	
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	surgeon can remove it all at once. Incisional Biopsy:	

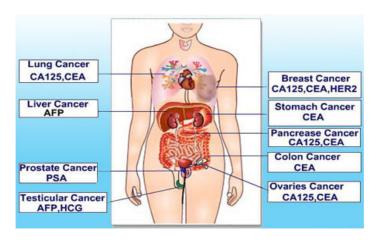
When the surgeon takes a small part only.





- Substances which if present in the blood or tissues **may** indicate malignancy.
- The concept is very important.
- There are many tumor markers.
- Most are non-specific.
- Important in diagnosis: (general findings + tumor markers>> Dx)□ E.g. patient with testicular tumor "clinically" and was found to have a high level of the tumor marker>> the patient has teratoma not seminoma.
- Important for screening :the early detection, incidence of disease. Males over 40 years old do PSA. Mammography for carcinoma of the breast, PAP smears for cervical carcinoma, Others: CEA, α-fetoprotein, HCG.
- Important in follow up: E.g. A Patient with a prostate cancer and a high PSA, and we treated the cancer, the PSA will decrease, during the follow up we noticed an increase in PSA marker, what does that indicate? **Recurrence of the tumor.**

CEA	Colon cancer, lung cancer, breast cancer, stomach cancer, pancreas cancer and ovaries cancer
CA125	Lung cancer, breast cancer, pancreas cancer and ovaries cancer.
AFP	Testicular cancer and liver cancer
PSA	Prostate cancer
HCG	Testicular cancer
HER2	Breast cancer
CA 19-9	pancreas cancer





## Hormones & Cancer

### • Hormones related to tumor growth:

- Usually sex hormones (testosterone, estrogen).
- They may have a relation to tumor growth
- Hormone receptors
- The concept can be used in treatment.
- Good examples are the 'hormone-dependent' cancers of the breast, prostate and endometrium, which require a 'correct' balance of hormonal secretion from the endocrine glands of the host for their continued growth.

E.g. In breast cancer, ask the histologist to find any estrogen receptors. That will affect the treatment plan and prognosis. Also the prostate needs testosterone to live, so if we block the testosterone secretion by drugs, the tumor will stop growing .

Growth of the prostate and the malignant cells are dependent on the testosterone. So we control the malignancy by either removing the primary producing organ of the tumor, which is the testes, or blocking one of these pathways.

When the tissue is taken from a cancerous breast and gets sent into the lab, we may find estrogen receptors which could be treated with anti estrogen (Tamoxifen), thus decreasing the effect of estrogen on the breast. This way we're minimizing growth of the malignant cells.

### • Hormones may be produced by tumors:

- Originally hormone producing organ e.g. adrenals
- Originally non-hormone producing organ e.g. lung (bronchogenic carcinoma)



Recall (EXTRA):

Define: Surgical oncology Surgical treatment of tumors XRT Radiation therapy In situ Not invading basement membrane Benign Nonmalignant tumor-does not invade or metastasize Malignant Tumors with anaplasia that invade and metastasize Adjuvant RX Treatment that aids or assists surgical treatment = Chemo or XRT Neoadjuvant RX Chemo, XRT, or both BEFORE surgical resection Brachytherapy XRT applied directly or very close to the target tissue (e.g., implantable radioactive seeds) **Metachronous tumors** Tumors occurring at different times Synchronous tumors Tumors occurring at the same time What tumor marker is associated with colon cancer? CEA What tumor marker is associated with hepatoma? Alpha-Fetoprotein (AFP) What tumor marker is associated with pancreatic carcinoma? CA 19-9 What is paraneoplastic syndrome? Syndrome of dysfunction not directly associated with tumor mass or mets (autoimmune or released substance) What are the most common cancers in women? 1- Breast 2- Luna 3- Colorectal What are the most common cancers in men? 1- Skin cancer 2- Prostrate 3- Lung 4- Colorectal What is the most common cancer causing death in both men and women? Lung



# Summary

Types of tumors	1. Benign       3. Teratoma         2. Malignant       4. Hamartoma         • Carcinoma       • Sarcoma
Benign	<ul> <li>Encapsulated</li> <li>No invasion</li> <li>No metastasis</li> <li>Treatment: Local excision</li> </ul>
Malignant	<ul> <li>Non encapsulated</li> <li>Usually invade</li> <li>Metastasis</li> <li>Characteristics: Uncontrolled growth and loss of contact phenomena.</li> <li>Treatment: Radical excision</li> </ul>
Tumor Grading & Differentiation	<ul> <li>Grading: Describes the histologic characteristics of cancer cells mainly talk about cell layers. e.g. grade I, II, III.</li> <li>Differentiation: Describes the characteristics of cancer cells in reference to their resemblance to the cell of origin. e.g. well differentiated, moderately differentiated, poorly differentiated, and anaplastic.</li> </ul>
Tumor Staging	<ul> <li>Describes the primary tumor, its relation with the organ of origin, adjacent and distant organs.</li> <li>TNM staging system: T – Tumor : T1,2,3, Tis, Ta, Tb N – Node: N0, 1, 2, 3 M – Metastasis: M0,1,2,3</li> </ul>
Cytology vs Biopsy	<ul> <li>Cytology: It gives the morphology of individual cell. Types:</li> <li>Exfoliative (Ex. urine, sputum).</li> <li>Fluid aspiration (Ex. ascitic fluid, pleural fluid).</li> <li>Fine needle aspiration cytology "FNAC" (from a solid tumor)</li> <li>Biopsy: histological (piece of tissue) characteristics.</li> <li>Incisional biopsy (open, needle, forceps)</li> <li>Excisional biopsy</li> </ul>
Tumor Markers	<ul> <li>Lung cancer: CA125, CEA</li> <li>Breast cancer: CA125, CEA, HER2</li> <li>Liver cancer: AFP</li> <li>Stomach cancer: CEA</li> <li>Pancreas: CA125, CEA</li> <li>Colon cancer: CEA</li> <li>Ovaries: CA125, CEA</li> <li>Prostate cancer: PSA</li> <li>Testicular cancer: AFP, HCG</li> </ul>



- Q1- A 55 years old female came to ER complaining of fever and a significant weight loss. A chest X-ray was done and they found cannon balls in her lung . What does it indicate?
- A- TB
- B- Lung abscesses
- C- Tumor metastasis
- D- NSCC

#### Q2- Which one of the following is the stage of T1N1M1 based on TNM classification?

- A- stage ||
- B- stage |V
- C- stage |||
- D- stage 0

#### Q3- Which one of the following is a cytological feature of malignant tumors ?

- A- coarse chromatin
- B- single nucleus
- C- large cytoplasm
- D- fine chromatin

#### Q4- Which of the following is <u>NOT</u> from the clinical characteristics of cachexia ?

- A- severe weight loss
- B- night sweat
- C- anemia
- D- anorexia

#### Q5- A 60 years old patient came to follow up after right hemicolectomy for colon cancer. Which of the following you will order to know if he responded to treatment?

- A- CT
- B- US
- C- Tumor marker
- D- Blood hormones

#### Answers:

1: C 2: B 3: A 4: B 5: C