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### **Objectives :**

- ★ Pathological classification and staging of solid tumors
- ★ Common solid tumors worldwide and in saudi arabia
- ★ Study of two common solid tumors: breast cancer and colo-rectal cancer regarding:
  - Risk factors
  - clinical presentation
  - early detection
  - diagnostic tools
  - broad lines of management
  - prevention

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# **Common Solid Tumors**

### Classification of solid tumors

	Carcinoma	Sarcome	Germ cell tumor	Blastoma
Origin	<b>Epithelial cells</b> (do the function)	<b>Connective tissue</b>	Pluripotent cells	Immature precursor Embryonic tissue
i.e.	Breast, prostate, lung, pancreas and colon the following notes are mentioned in the last lecture. 1-surface tumor: SCC+ transitional cell carcinoma 2-glandular: adenocercinoma	<ul> <li>Bone: osteosarcoma</li> <li>cartilage: chondrosarcoma</li> <li>fat: Liposarcoma</li> <li>nerve</li> </ul>	Testicular (seminoma), ovary (dysgerminoma)	Hepatoblastoma
Notes	Most common cancers	each of which develop from cells originating in mesenchymal cells outside the bone marrow.		Most common in children

• Some types of cancer are named for the size and shape of the cells under a microscope, such as; giant cell carcinoma, spindle cell carcinoma, and small cell carcinoma.





1- 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.

2- 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.

Colorectal

3.

# **Common Solid Tumors**

### General principles of solid tumor treatments

#### "According to stage":



1-prognosis = help in Tx plan = allow physician to put expectations (some fatal cancer has poor prognosis like 5 year survival rate, other has better prognosis) -according to prognosis : cause of death in cancer = 1st: lung 2nd: breast
2-Breast cancer can be painful if associated with inflammation - It can be both painful and painless

3--Breast cancer can occur in pre – peri – post menpouse, the message that breast cancer can affect any age group, pregnancy related, during lactation etc.

### Risk factors

estrogen is GF of lactating gland = proliferation = more proliferation more mutation occur (such as P53 mutation; tumor suppressor gene)



- 4: pregnancy is a protective factor as it suppresses estrogen and increase progesterone
- 5: Exposure to estrogen stimulates cell proliferation which will increase the chance of mutations. however, using contraceptive pills doesn't increase the risk as it contains very little amount of estrogen
- 6-low radiation is more dangerous in cancer than high does, why? bc high radiation will cause death immediately, low dose causes mutation = cancer.

### Clinical features



### Diagnosis

#### Suspecting Breast Cancer Is one of the most important steps in diagnosing Early Breast cancer:



### Diagnosis (cont.)

#### → What To do If you Suspect Breast Cancer?



Common MCQ question: we examine the normal breast first, if patient has no signs and normal examination but she is complaining of something in her breast, What should you do? Do <u>Mammogram</u>

1: because hormones can decrease breast cancer but cannot cure it, so it will mask the symptoms and signs for a while and the tumor will grow and spread. 2: or anti-inflammatory, it will decrease the breast complaint but never cure it

3: position: laying down, **start with the normal breast,** examine quadrant by quadrant (clockwise) then examine the center & always remember to **examine the axilla + subrascapular area is part of breast exam** 

# 05

#### Perform Bilateral mammogram, breast US +/- Fine needle aspiration

Triple assessment of any symptomatic breast mass:



#### **Diagnostic tests**

- **Fine needle aspiration (FNA)**: The best initial biopsy. can differentiate between benign and malignant
- **Core needle biopsy**: Where cancer is considered likely, <u>large-bore core needle biopsy should follow</u> <u>FNA</u>, to provide histological confirmation and to assess for factors predictive of prognosis and response to treatment. These features include:
  - Receptor status: ER, PR, HER2/neu
  - grade of tumour
  - *Ki-67 proliferation index*, by which the proportion of cells staining positive for Ki-67 protein (a marker of cellular proliferation) is measured
  - **molecular profiling**, using an assay such as the Oncotype DX, which compares a number of molecular markers to assess risk of recurrence and benefit of chemotherapy.
- **Open biopsy**: The "most accurate diagnostic test" and allows for immediate resection

### Staging of Breast cancer

Stage 1 (early disease)	Stage ll (early disease)	Stage Ill (locally advanced)	Stage IV (advanced)
Confined to the breast ( <b>Node-negative</b> ) (Tumor <2cm)	Spread to <b>movable</b> <b>ipsilateral axillary</b> <b>nodes (node-positive)</b> (Tumor 2-5cm)	Spread to the superficial structure of the <b>chest wall</b> <b>involvement</b> of ipsilateral internal mammary lymph node, or skin fixation, and/or <b>fixed axillary</b> <b>nodes</b>	<b>Metastasis</b> present at distant sites such as bone, liver, lungs and brain including supraclavicular lymph node involvement
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internal mammary node irradiation is occasionally given in selected higher-risk cases.



### Therapy (cont.)

#### management of Advanced disease

management of patients presenting with metastatic disease depends on the extent and location of disease.

- Widespread visceral disease
  - Patients are advised to have systemic chemotherapy (with or without HER2-directed therapy), followed by endocrine therapy if the cancer is ER-positive. Treatment is unlikely to be curative but may well delay death by long periods, during which quality of life may be good.
- Limited metastatic disease
  - patients who present with one or only a few sites of metastatic disease (oligometastatic disease) Aggressive treatment with ablative focal therapy to those oligometastatic sites (e.g. radiofrequency ablation, stereotactic radiation or surgical metastasectomy)
- Indolent metastatic disease that is not immediately life-threatening
  - If the cancer is ER-positive, primary endocrine therapy may hold the disease at bay for long periods; chemotherapy may be delayed until
  - Breast cancers driven by HER2 or mammalian target of rapamycin (mTOR) may also benefit from cyclin inhibitors or mTOR inhibitors such as everolimus.
- Metastatic disease confined to regional lymph node
  - An aggressive regime of neoadjuvant chemotherapy, surgery to breast and axillary nodes, regional radiotherapy and long-term endocrine or HER2-directed therapy offers a chance of cure.
- Relapsed disease after previous systemic therapy
  - The timing between the previous therapy and relapse is important, as re-introduction of agents may be sensible only if the cancer has not been exposed to a particular group of drugs for a number of years.
  - New agents (i.e. ones to which the cancer has not been exposed) are preferable, and eribulin is a chemotherapy agent that has value in this situation.

### Survival rates by stage of Breast cancer



The earlier the stage is, the better chances for survival. As seen in the graph: **5-year survival rates:** 

- in stage I can be as high as 90% (96%),
- Stage II: 81%
- Stage III: 52%
- Stage IV: 18%

### What is the colon

- The Colon is a long, coiled, tubular digestive tract.
- It basically acts as a waste processor, Takes digested food in the form of Solid waste pushing it out of the rectum and anus.
- The **Colorectal tube** is a prime location for the development and growth of small **polyps** or **tumors**
- colon cancer is common in men + affect any site of colon

### **Risk factors**

#### Older age

- About 90 percent of people diagnosed with colon cancer are older than 50.
- Can occur in any age, but it occurs much less frequently if < 45 years of age.
- Screening (colonoscopy) beginning at age 50.

#### A personal history

- If a patient already had colon cancer or adenomatous polyps (even though it is noncancerous), there is a greater risk of colon cancer in the future.
- History of some other type of Cancer.

#### Inflammatory intestinal conditions

• Ulcerative colitis and Crohn's disease, can increase a patient's risk of colon cancer.

#### Inherited syndromes that increase colon cancer risk.

Familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer (also known as Lynch syndrome).

#### Family history of colon cancer and colon polyps.<sup>2</sup>

- Patients are more likely to develop colon cancer if they have a parent, sibling, or child with the disease (specially parent and sibling)
- If more than one family member has colon cancer or rectal cancer, their risk is even greater.

#### ooo Other risk factors

- Low-fiber, high-fat<sup>1</sup> diet (most important) because it leads to Chronic constipation <sup>3</sup>
- A sedentary lifestyle.
- Diabetes  $\rightarrow$  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 risk of colon cancer
- Radiation therapy for cancer

1: when bacteria act on the fat it will produce toxins that affects the epithelial lining of the GI tract which has a carcinogenic effect

- 2: removal of polyps is protective from colon cancer.
- 3: Why constipation increase the risk? increase exposure to waste that is changed by bacteria to carcinogens (Duration increased -> make the risk increase)



# Colon cancer (cont.)

Can invade

other organs

If a polyp is allowed to remain

in the colon it can grow into a

cancerous tumor

# Pathogenesis of colon cancer

starts with a simple cell the **mutates** 

**→** 

### Symptoms

grows into

a polyps



Common MCQ question: **Post-menopausal females** presenting with iron deficiency **anemia** should undergo a **colonoscopy** to rule-out colon cancer.

### screening & early detection

→ Why does this contribute to a better survival?

#### Early detection = Early stage = Better survival

- Patients aged over 35–40 years presenting with new large bowel symptoms should be investigated. **Digital examination of the rectum** is essential and examination of the colon should be performed in all cases.
- **Population-based screening** of people over the age of 50 years by regular faecal occult blood (FOB) testing
- **Colonoscopy: is the 'gold standard'** technique for examination of the colon and rectum and is the investigation of choice for high-risk patients.
- Flexible sigmoidoscopy: alternative option
- CT colonography (imaging): fast and low-risk, and offers equivalent sensitivity to colonoscopy.
  - Disadvantages include reduced sensitivity to detect polyps of less than 6 mm
- Screening for high-risk patients by molecular genetic analysis
- Carcinoembryonic antigen (CEA): Obtain baseline levels in all patients before initiating treatment
- Better public and physician awareness

All of these contribute to More cases are diagnosed at earlier stage of disease.

1: Tumours of the left colon, fresh rectal bleeding is common and obstruction occurs early. Tumours of the right colon present with anaemia from occult bleeding or with altered bowel habit, but obstruction is a late feature.

# Colon cancer (cont.)

## Staging

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Confined to wall	Beyond the wall	Nodal involvement	Metastasis		
5 years Overall survival					
90%	60-80%	30-60%	<5%		

### Management

Depending on the location, options are:

- surgery (mainly)
- Chemotherapy
- radiation (if in the rectum)

### **Protective measures & prevention**

#### Decrease the risk

**Dietary fibre** 

Aspirin and other NSAIDs.

- Vegetable, garlic, and fruits.
- Exercise.
- Milk, calcium consumption

#### Prevention

- low-fat, high-fibre diet for the prevention of sporadic colorectal cancer, along with endoscopic screening, is recommended for at- risk patients with a strong family history and for inherited syndromes.
- Non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin.





# Summary

#### Common solid tumors

#### The most common solid tumor in KSA are: Breast cancer in women & Colorectal in men

	Breast cancer	Colon cancer
Risk factor	<ul> <li>Family history</li> <li>Benign breast diseases</li> <li>Early menarche or late menopause</li> <li>Late first pregnancy / no pregnancy</li> <li>Exogenous estrogens</li> <li>Radiation (HD)</li> </ul>	<ul> <li>Older age         <ul> <li>Screening (colonoscopy) beginning at age 50.</li> </ul> </li> <li>Personal history</li> <li>Family history</li> <li>Inherited syndrome</li> <li>Inflammatory intestinal condition</li> <li>Chronic constipation</li> </ul>
Clinical manifestation	<ul> <li>Painless lump</li> <li>Thickening or swelling</li> <li>Breast skin irritation or dimpling</li> <li>Nipple pain or retraction</li> <li>Nipple discharge</li> </ul>	<ul> <li>Change in bowel habits</li> <li>Rectal bleeding</li> <li>Persistent abdominal discomfort</li> <li>Unexplained iron deficiency anemia</li> </ul>
Investigation	<ul> <li>Radiology (mammography, ultrasound)</li> <li>+/- Fine needle aspiration</li> <li>Core biopsy</li> <li>Open biopsy</li> </ul>	<ul> <li>Colonoscopy</li> <li>Post-menopausal females presenting with iron deficiency anemia should undergo a colonoscopy to rule-out colon cancer.</li> <li>Endoscopic biopsy</li> <li>CT chest, abdomen &amp; pelvis</li> </ul>
Management	Local therapy: → Surgery → Radiotherapy Systemic therapy: → Chemotherapy → Hormonal therapy → Biological therapy	Depending on the location, options are: • surgery (mainly) • Chemotherapy • radiation (if in the rectum)
Prevention	Passive prevention:         →       eat a healthy diet         →       Exercise         →       Don't smoke         →       Don't drink         Active prevention:       →         →       Chemoprevention         →       Surgery	

### Lecture Quiz

Q1: What is the best modality for colon cancer diagnosis?

- A. X-ray
- B. colonoscopy
- C. serum carcinoembryonic antigen (CEA)
- D. MRI

Q2: 30 years old pregnant female in her 6 months of pregnancy came to the clinic complaining of right nipple retraction. Breast examination revealed normal breast, no masses and no lymph nodes enlargement, except retraction of right nipple. What is your appropriate next step?

- A. Biopsy from right nipple
- B. Perform ultrasound of breast immediately
- C. Perform mammogram and ultrasound of breast after delivery
- D. Reassure and close follow up

Q3: A 57-year-old woman with adenocarcinoma of the sigmoid colon with liver metastasis is attending for cycle six of her palliative FOLFOX chemotherapy. Which tumour marker can be measured in the blood test to indicate the effect of the chemotherapy?

- A. a-fetoprotein (aFP)
- B. B-human chorionic gonadotrophin (B-hCG)
- C. CA 19-9
- D. CA 125
- E. CEA

A 39-year-old woman has undergone a wide local excision for a 0.5cm ductal carcinoma of her right breast. Sentinel node biopsy, histology and staging scans have confirmed the disease as T1N0M0. Histology has confirmed the cancer as oestrogen and progesterone receptor positive. Which of the following statements is most accurate regarding this female's treatment options?

- A. She should receive radiotherapy
- B. She is not suitable for radiotherapy
- C. She is not suitable for tamoxifen therapy
- D. She requires no further treatment
- E. She should be considered for cetuximab therapy

Q5: A 64-year-old man presents to accident and emergency following a collapse. He describes a blackout, subsequently regaining consciousness when on the floor. He presently feels well and describes no other symptoms. However, he mentions that he has unintentionally lost some weight over the past few months. There is no past medical history. Blood tests reveal a haemoglobin level of 9g/dL with a mean cell volume on 71 fL. The most appropriate next investigation of this patient is:

- A. Flexible sigmoidoscopy
- B. Endoscopy
- C. Colonoscopy
- D. Endoscopy and colonoscopy
- E. Profile of tumour markers

Q6: A 27-year-old African-American woman comes to the clinic because of a painless breast mass. She first noticed it a month ago. She does not report any nipple discharge. She has no significant past medical history. Her mother was diagnosed with breast cancer at age 57. Physical examination shows a round, mobile, 2 cm mass in the upper outer quadrant of her right breast. Which of the following is the most appropriate next step in management?

- A. An ultrasound and mammogram
- B. Genetic testing for BRCA1 and BRCA2
- C. Mammogram only
- D. Patient reassurance
- E. Ultrasound only

# GOOD LUCK !



