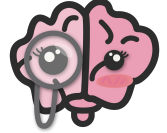


Lecture 65

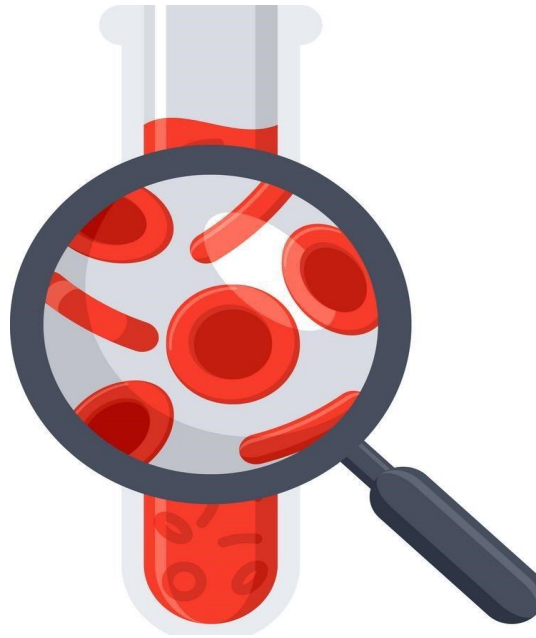
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Reviewed By



Noura Alturki
Jehad Alorainy



Common Solid Tumors

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

Color index:

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

Classification of solid tumors

	Carcinoma	Sarcome	Germ cell tumor	Blastoma
Origin	Epithelial cells	Connective tissue	Pluripotent cells	Immature precursor Embryonic tissue
i.e.	Breast, prostate, lung, pancreas and colon	<ul style="list-style-type: none"> Bone: osteosarcoma cartilage: chondrosarcoma fat: Liposarcoma nerve 	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.

Cancer statistics in KSA

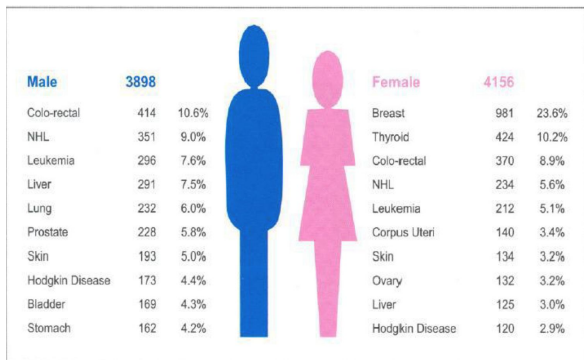
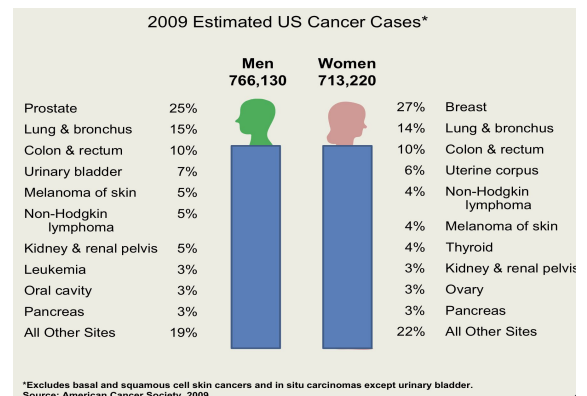


Figure 2.3 Ten Most Common Cancers among Saudis by Sex, 2006

Cancer statistics in US



*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. Source: American Cancer Society, 2009.

Men

1. Colorectal
2. Lymphoma
3. Leukemia

Women

1. Breast
2. Thyroid
3. Colorectal

KSA

Men

1. Prostate
2. Lung
3. Colorectal

Women

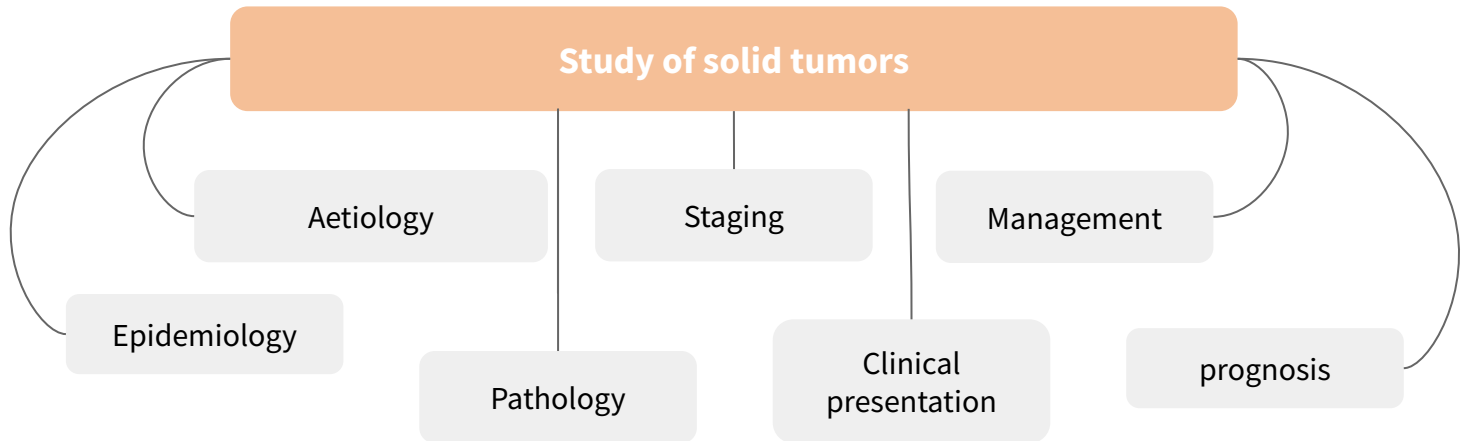
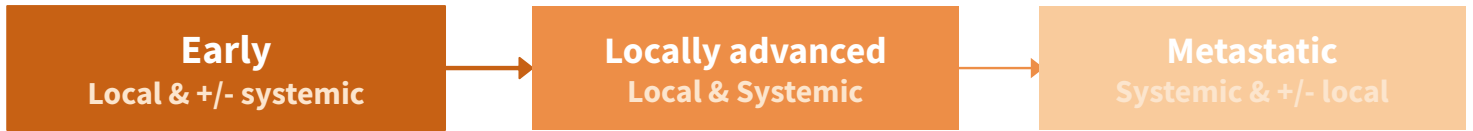
1. Breast
2. Colorectal
3. Lung

U.S

Common solid tumors

General principles of solid tumor treatments

“According to stage”:



A Simple Equation :

LATE PRESENTATION + ADVANCED STAGE
→ POOR OUTCOME

EARLY PRESENTATION + EARLY STAGE
→ GOOD OUTCOME

Breast Cancer



Breast cancer facts



1st most common cancer in **non-smoker** females.



- 2nd most common cancer
- 2nd leading cause of death in **both males and females**.

◀ Risk factors

1

History of breast cancer

2

Family history of breast cancer, especially in first-degree relatives

3

Benign breast diseases / atypical hyperplasia¹

4

Early menarche²

5

late menopause³

6

Late first pregnancy

7

No pregnancy⁴

8

Exogenous estrogens⁵ (e.g. HRT)

9

Radiation HD (hodgkin's disease)

10

genetics:

- 5% of patients with breast cancer have a genetic predisposition.
- The best known are the familial *BRCA* mutant carriers (*BRCA1* & *BRCA2* mutations → Associated with early onset) → very high risk of breast & ovarian cancers
- cancer and – for *BRCA2* mutants – prostate cancer.

◀ Breast health plan



Self Awareness
(monthly self exams (BSE))

- advised for all females >30



Mammogram

- There may be a long period between induction of breast cancer and invasion
- The term '*in situ*' cancer refers to the development of cancerous changes in milk duct epithelial cells that have not yet breached the basement membrane of the ducts
 - This 'pre-cancer' stage of the disease can be picked up on mammography when it is still highly curable, usually by breast-conserving surgery
- **Advised for all in age >50. In high risk females e.g. relative having breast cancer, start screening as early as 40.** In the UK, all women aged **50–70** are offered screening by biplanar digital mammography, often in designated clinics or mobile screening units, **every 3 years**. Patients with abnormal mammograms are recalled for further assessment.

1: but fibroadenoma is not a pre-malignant state

2: early estrogen exposure

3: prolonged period of estrogen exposure, Long-term exposure to the mitotic effects of oestrogens is a predisposing factor to breast cancer development because mutations are more likely to occur at times of DNA replication

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

◀ Clinical features

- most commonly painless, increasing mass that may be associated with nipple discharge, skin tethering, and ulceration
 - in inflammatory cancer edema and erythema
 - Where the cancer may be deeply tethered to pectoralis, when asking the patient to tense the muscle by putting their hands on their iliac crests and pressing inwards the mass loses its mobility.

Warning signs and symptoms

Painless lump or thickening of the skin
(can be painful especially if infected)

Nipple pain or retraction

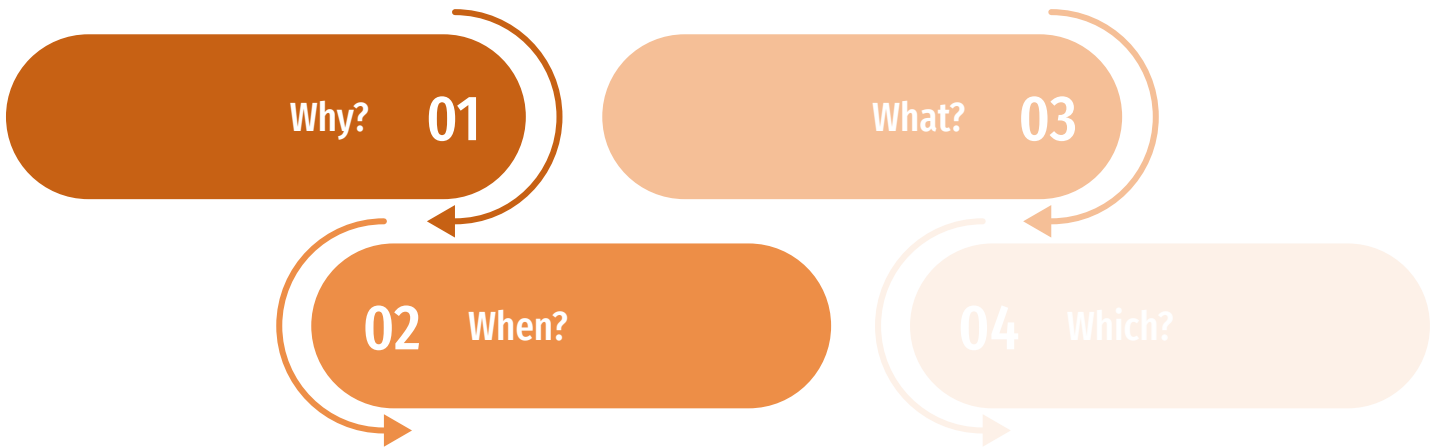
Breast skin irritation or dimpling

Thickening or swelling that persist

Nipple discharge

◀ Diagnosis

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



→ Reasons to *suspect* breast cancer:

◆ Many good reasons to suspect breast cancer. **Remember that Breast cancer is:**



Most common cancer in females & second most common in general



Breast cancer can occur during pregnancy & lactation.



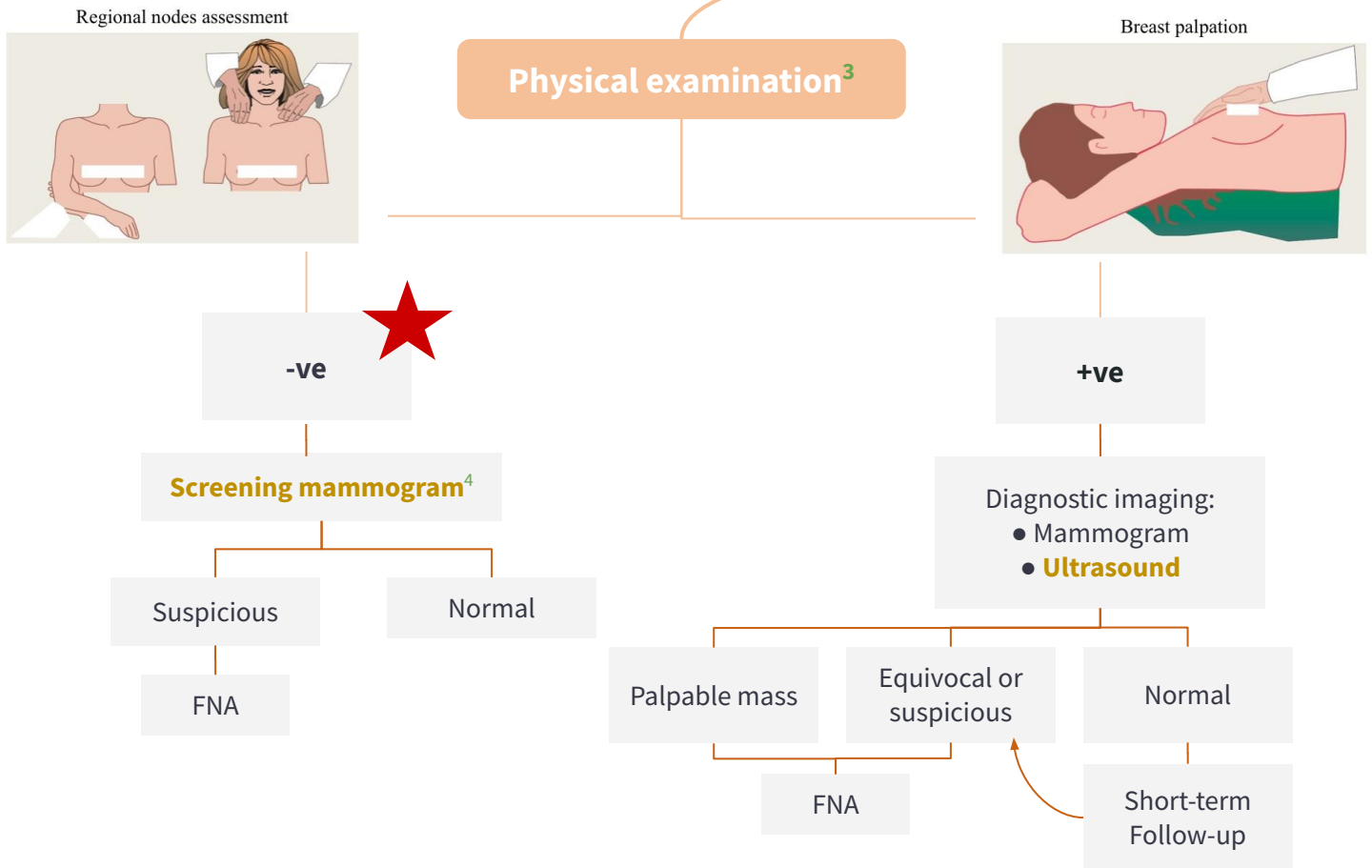
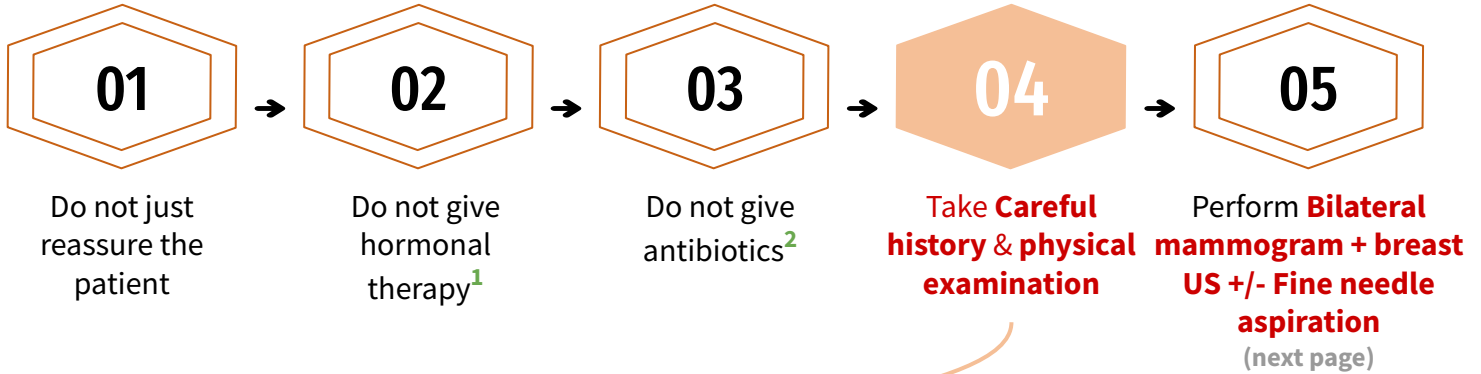
Wide age range 20 to +70y



Breast cancer can occur in pre, peri & post menopausal females

◀ Diagnosis (cont.)

➔ What To do If you Suspect Breast Cancer?

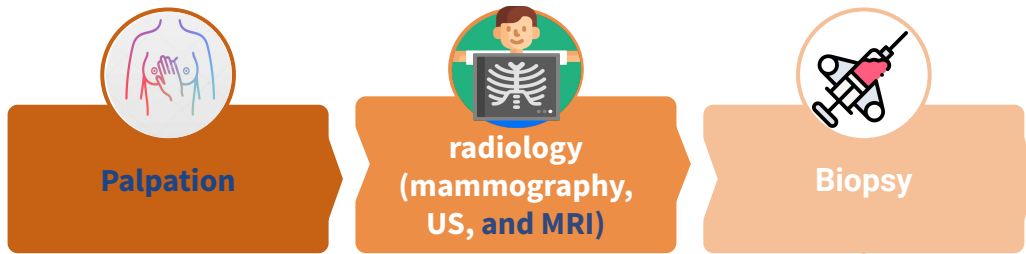


1: because hormones can decrease breast cancer but cannot cure it, so it will mask the symptoms and signs for a while and the tumor will grow and spread.
 2: or anti-inflammatory, it will decrease the breast complaint but never cure it
 3: position: laying down, examine quadrant by quadrant (clockwise) then examine the center & always remember to examine the axilla
 4: or US if patient is young

05

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




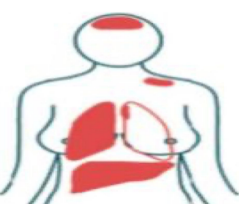
Triple assessment of any symptomatic breast mass:



Diagnostic tests

- **Fine needle aspiration (FNA):** The best initial biopsy. can differentiate between benign and malignant
- **Core needle biopsy:** Where cancer is considered likely, large-bore core needle biopsy should follow FNA, 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 II (early disease)	Stage III (locally advanced)	Stage IV (advanced)
Confined to the breast (Node-negative) (Tumor <2cm)	Spread to movable ipsilateral axillary nodes (node-positive) (Tumor 2-5cm)	Spread to the superficial structure of the chest wall involvement of ipsilateral internal mammary lymph node, or skin fixation , and/or fixed axillary nodes	Metastasis present at distant sites such as bone, liver, lungs and brain including supraclavicular lymph node involvement
			

◀ Therapy

management of early disease

01 Local therapy

→ surgery:

- ◆ surgical options include
 - *wide local excision* and *segmental mastectomy* with breast conservation for masses of **less than 3cm in diameter**
 - *simple mastectomy*, with or without reconstruction, is used **for larger tumours**.
- ◆ The choice is dictated by:
 - The location
 - Extent of the breast mass
 - Patient preference.
- ◆ Clear histological margins around the cancer are important for cure.
- ◆ In the absence of clinical or ultrasound evidence of lymphadenopathy, surgery to the axilla can be minimized if sentinel lymph node-guided sampling excludes local spread. otherwise, dissection to level three is required if there are clinically involved nodes, in order to gain local control and provide prognostic information to guide adjuvant treatment.
 - The greater the amount of axillary surgery, the greater is the risk of postoperative lymphoedema.

→ radiotherapy:

- ◆ **All patients who undergo breast-conserving surgery for early breast cancer require postoperative radiotherapy** to the breast to provide security of local control equivalent to that conferred by mastectomy
- ◆ Those undergoing mastectomy who have disease close to resection margins also require radiotherapy to the chest wall and regional nodes.
- ◆ The axillary nodes are spared radiotherapy if the axilla has been dissected (to avoid arm lymphoedema) but supraclavicular nodes are included
- ◆ internal mammary node irradiation is occasionally given in selected higher-risk cases.

◀ Therapy (*cont.*)

management of early disease (*cont.*)

02 Systemic Therapy

→ systemic therapy: (endocrine treatment and chemotherapy)

- ◆ For locally advanced breast cancers, systemic therapy (***neoadjuvant therapy***) is sometimes given to downstage the cancer before locoregional treatment with surgery and radiotherapy.
- ◆ The term '***adjuvant therapy***' applies to systemic treatment that is given after definitive locoregional therapy aim is to destroy microscopic residual disease that may have disseminated elsewhere in the body
- ◆ Those with node-positive breast cancer, large primaries, oestrogen receptor-negative cancers and HER2 cancers are good examples of patients who would usually derive a significant survival advantage from adjuvant systemic therapy.

→ targeted: Hormonal and Biological therapy

◆ HER2-positive disease

- HER2-positive cancers tend to behave aggressively but respond to treatment with HER2 inhibitors such as trastuzumab and pertuzumab
- endocrine therapy is used subsequently if tumours are also ER-positive
- If indicated, radiotherapy is usually given following systemic therapy

◆ Oestrogen receptor-positive disease

- adjuvant endocrine therapy is delivered, often for as long as 10 years after surgery. There are two strategies for endocrine therapy:
 - ***oestrogen receptor blockade*** using tamoxifen or fulvestrant
 - ***oestrogen deprivation*** using aromatase inhibitors such as letrozole
 - ◆ premenopausal women with higher-risk ER-positive disease, there is an advantage for complete ovarian suppression (laparoscopic oophorectomy or luteinizing hormone-releasing hormone (LHRH) agonist therapy) plus aromatase inhibition.
 - ◆ The addition of cyclin inhibitors (e.g. palbociclib, abemaciclib) to an aromatase inhibitor or fulvestrant significantly enhances the response rate

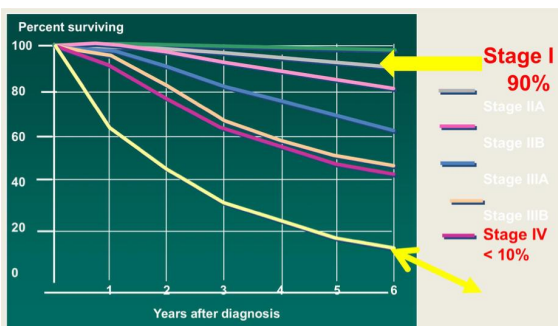
◀ Therapy (cont.)

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

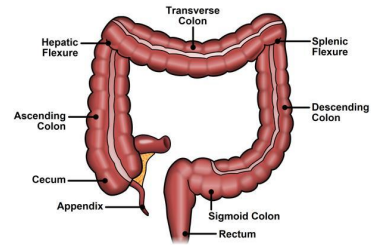


The earlier the stage is, the better chances for survival. As seen in the graph: **5-year survival rates:**

- 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**



◀ 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.

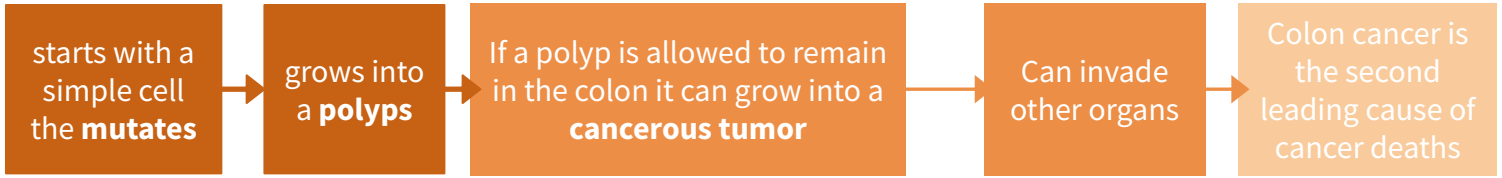
- Patients are more likely to develop colon cancer if they have a parent, sibling, or child with the disease (specially parent and sibling)
- If more than one family member has colon cancer or rectal cancer, their risk is even greater.

Other risk factors

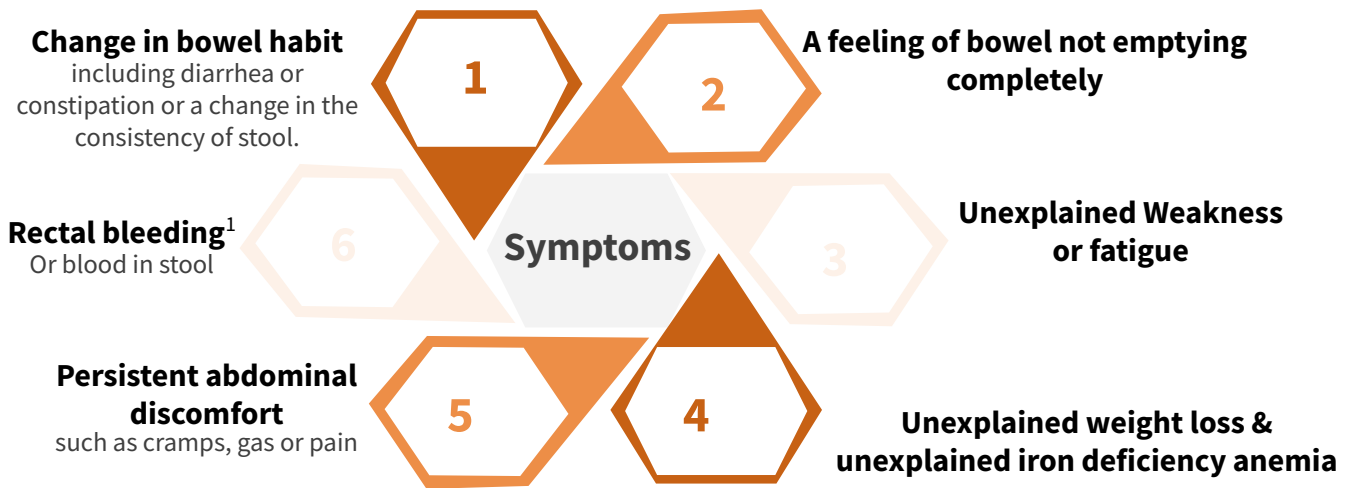
- Low-fiber, high-fat¹ diet (most important) because it leads to **Chronic constipation**
- A sedentary lifestyle.
- Diabetes → Insulin resistance may have an increased risk of colon cancer
- Obesity.
- Smoking: People who smoke cigarettes may have an increased risk of colon cancer.
- Alcohol: Heavy use of alcohol may increase 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

Pathogenesis of colon cancer



Symptoms



→ **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?

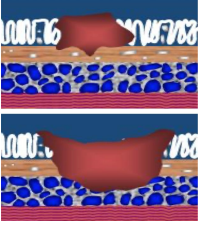
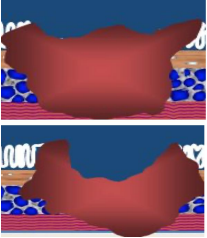

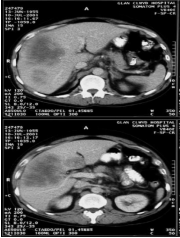
Early detection = Early stage = Better survival

- 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
- 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.

◀ Staging

I	II	III	IV
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

- Vegetable, garlic, and fruits.
- Exercise.
- Milk, calcium consumption
- Dietary fibre
- Aspirin and other NSAIDs.

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.

Can we prevent Breast or Colon cancer?

1 Passive prevention



Discover Etiological factors Avoid these factors

eg. Smoking, Asbestos



Avoid Breast cancer risk factors

- Weight Gain as an adult / obesity → obesity is a risk factor for any type of cancer
- Estrogen & Progestin use, when using oral contraceptive pills, try to avoid the ones containing estrogen
- Alcohol use and smoking.
- To improve patients prognosis:
 - Early diagnosis
 - Early and proper intervention

General health maintenance

- Eat a healthy diet
- Don't smoke
- Don't drink too much
- Exercise/ maintain optimal weight



2 Active prevention

Eliminate or **prevent** pre-invasive disease before invasion develops

- Chemoprevention
- Surgery

Discover Pre malignant lesions Get rid of them before developing invasive cancer

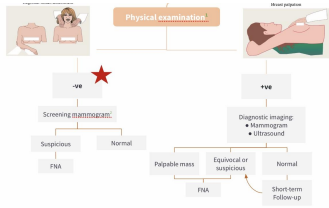
- Colonic polyps & DCIS

Prevention is not an easy task → social change is difficult and takes a long time & it is not good enough for high risk people

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 style="list-style-type: none"> ● Family history ● Benign breast diseases ● Early menarche or late menopause ● Late first pregnancy / no pregnancy ● Exogenous estrogens ● Radiation (HD) 	<ul style="list-style-type: none"> ● Older age <ul style="list-style-type: none"> ○ Screening (colonoscopy) beginning at age 50. ● Personal history ● Family history ● Inherited syndrome ● Inflammatory intestinal condition ● Chronic constipation
Clinical manifestation	<ul style="list-style-type: none"> ● Painless lump ● Thickening or swelling ● Breast skin irritation or dimpling ● Nipple pain or retraction ● Nipple discharge 	<ul style="list-style-type: none"> ● Change in bowel habits ● Rectal bleeding ● Persistent abdominal discomfort ● Unexplained iron deficiency anemia
Investigation	<ul style="list-style-type: none"> <input type="checkbox"/> Radiology (mammography, ultrasound) <input type="checkbox"/> +/- Fine needle aspiration <input type="checkbox"/> Core biopsy <input type="checkbox"/> Open biopsy 	<ul style="list-style-type: none"> <input type="checkbox"/> Colonoscopy <ul style="list-style-type: none"> <input type="checkbox"/> Post-menopausal females presenting with iron deficiency anemia should undergo a colonoscopy to rule-out colon cancer. <input type="checkbox"/> Endoscopic biopsy <input type="checkbox"/> CT chest, abdomen & pelvis
Management	<p>Local therapy:</p> <ul style="list-style-type: none"> → Surgery → Radiotherapy <p>Systemic therapy:</p> <ul style="list-style-type: none"> → Chemotherapy → Hormonal therapy → Biological therapy 	<p>Depending on the location, options are:</p> <ul style="list-style-type: none"> ● surgery (mainly) ● Chemotherapy ● radiation (if in the rectum)
Prevention	<p>Passive prevention:</p> <ul style="list-style-type: none"> → eat a healthy diet → Exercise → Don't smoke → Don't drink <p>Active prevention:</p> <ul style="list-style-type: none"> → 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

THANKS!!

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*Send us your feedback:
We are all ears!*

