433 Teams

# MEDICINE

## 4 | COMMON SOLID TUMORS

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# Objectives:

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|---|
| 1. pathological classification and staging of solid tumors |
| 2. Common solid tumors world wide and in Saudi Arabia |
| 3. 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, and prevention. |

## Classification Of Solid Tumors:

- ✓ Cancers are classified by the**type of cell**that the tumor cells presumed to be theorigin of the tumor. These types include:
- ✓ **Carcinoma**: Cancers derived from**epithelial**cells. This group includes many of the most common cancers**, breast, prostate, lung, pancreas, and colon.**
- ✓ **Sarcoma:** Cancers arising fromconnective tissue(i.e.**bone, cartilage, fat, nerve**), each of which develop from cells originating in**mesenchymal**cells outside the bone marrow.
- ✓ **Germ cell tumor:** Cancers derived from**pluripotent** cells, most often presenting in the **testicle**or**the ovary** (**seminoma**and**dysgerminoma,** respectively).
- ✓ **Blastoma:** Cancers derived from immature "precursor" cells or embryonic tissue. These are also most common in children. blastoma as a suffix, with the Latin or Greek word for**the organ**or tissue of origin as the root.**hepatoblastoma,**
- ✓ 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.**

## EPIDEMILOGY OF COMMON SOLID TUMORS:

**In the KSA., The three most common cancers:**

- ✓ **Men: 1st colorectal, 2nd Lymphoma, 3rd leukemia.**
- ✓ **Women: 1st Breast, 2nd Thyroid, 3rd colorectal.**

**In the U.S., The three most common cancers:**

- ✓ **Men:1stProstate, 2nd lung, 3rd colorectal.**
- ✓ **Women: 1stBreast,2nd colorectal,3rd lung.**

# BREAST CANCER:

## • EPIDEMILOGY:

- 2nd most common cancer.
- 1st most common cancer in females.
- 2nd leading cause of death.
- **Wide age range 20 - +70y.**
- **Over 75% of women who are diagnosed with breast cancer are age 50 or older.**
- **Men can get breast cancer, although this is very rare. For every man who is diagnosed, over 100 women are found to have breast cancer.**
- **Most women—about 80%—who get breast cancer do not have a sister or mother who has breast cancer.**
- **Excluding skin cancer, breast cancer is the most common cancer in women.**
- **1990s the breast cancer death rate declined by the largest amount in over 65 years.**
- **Heart disease is the leading killer of women.**
- **Approx 97% of women diagnosed with breast ca at an early stage survive 5 yrs or more.**
- **There is no single cause of breast cancer. Research has shown that several different factors increase the risk of breast cancer.**

**Hereditary Breast Cancer:**

germ-line mutations: About 25% of familial cancers (or around 3% of all breast cancers) can be attributed to two highly penetrant autosomal-dominant genes: **BRCA1 and BRCA2**

## • AETIOLOGY: (RISK FACTORS)

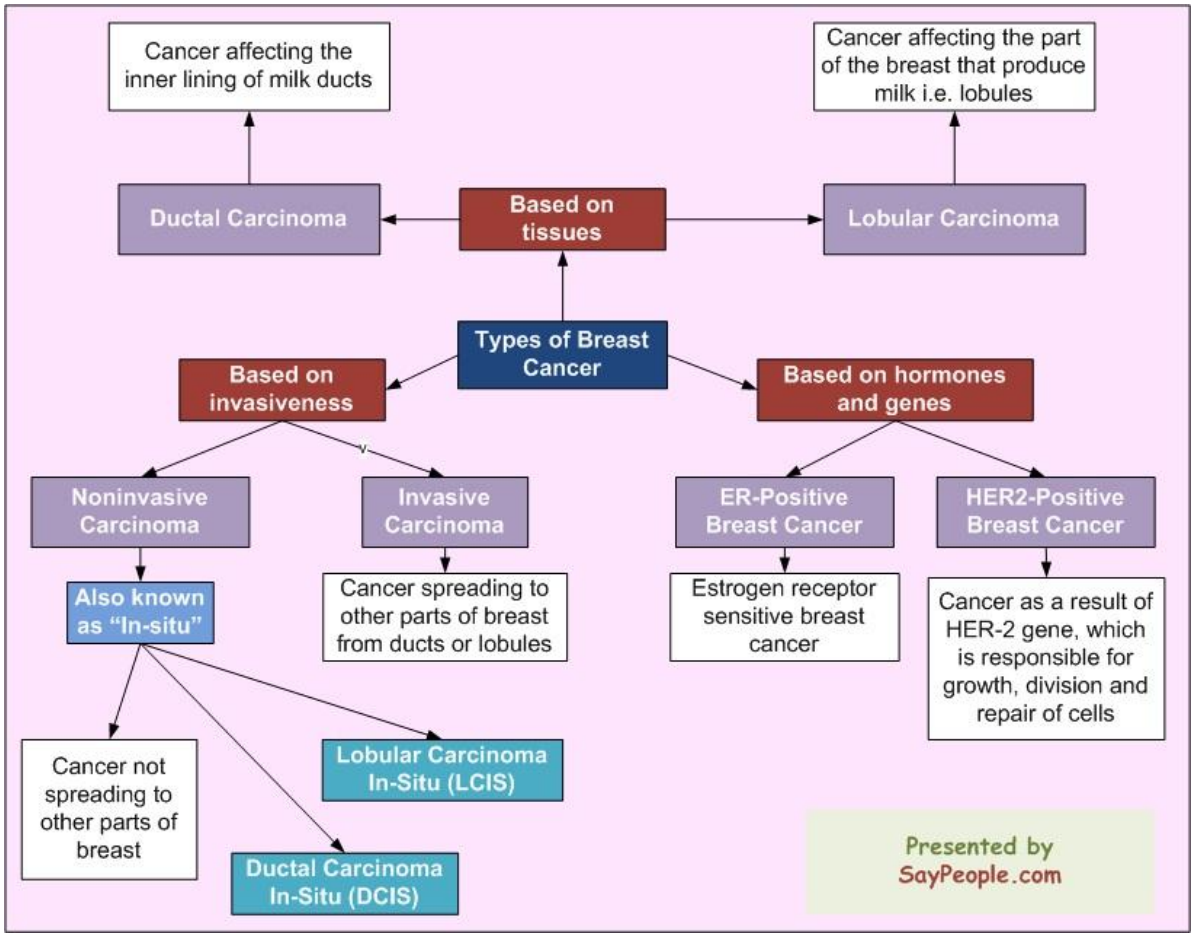
- ✓ History of breast cancer
- ✓ Family history of breast cancer, especially in first-degree relatives
- ✓ Benign breast diseases / atypical hyperplasia
- ✓ Early menarche, late menopause. (Breast cancer can occur in pre, peri and postmenopausal females.)
- ✓ Late first pregnancy/no pregnancy. (Breast cancer can occur during pregnancy ,during lactation.)
- ✓ Exogenous estrogens

old or postmenopausal women come with iron deficiency anemia you have to roll out colon cancer.why post menopausal ? because in premenopausal the main cause is heavy period .

## PATHOLOGY:

- Breast cancer is rare in women under 35. Instead, think of **fibroadenoma** if a young woman presents with a round, movable mass which changes in size over the course of the menstrual cycle. Other breast masses which may occur at any age include cysts (benign if not bloody after aspiration and does not recur) and fibrocystic changes (bilateral breast pain caused by cyclic hormonal stimulation).
- The premalignant in situ breast cancers are **ductal carcinoma in situ (DCIS)** and **lobular carcinoma in situ** (**LCIS**). These entities are usually distinguished histologically.

| | DCIS | LCIS |
|---|---|---|
| Arise from | Ductal elements | Lobular elements |
| Found | On screening mammogram | Incidentally during biopsy |
| Risk of carcinoma | In the same breast | Either breast |
| Treatment | Lumpectomy<br>If negative margins can't be achieved so mastectomy | Treatment is variable<br>1. Close observation<br>2. selective estrogen receptor modulators<br>3. prophylactic bilateral mastectomy<br><br>-removal of the lesion does not reduce the risk of progression to invasive cancer |




## • CLINICAL PRESENTATION:

- Breast cancer is found in**asymptomatic women on screening mammography**or **by the palpation of a mass by the patient**or a **physician**. When breast cancer presents as a palpable mass, it is hard to the touch. It may also be associated with retraction of the nipple because ligaments in the breast will withdraw and pull the nipple inward.
- Breast cancer is usually**painless**.(can be painful).

**Warning signs and symptoms:**

- ✓ **mass/lump that is painless, hard, and has irregular edges is more likely to be cancerous, but some rare cancers are tender, soft, and rounded.**
- ✓ **Thickening or swelling that persist.**
- ✓ **Nipple pain or retraction or Nipple discharge.**
- ✓ **Breast skin irritation or dimpling.**
- ✓ **Change in the size or shape of the breast.**

**youSuspect Breast Cancer!!!**

- ✓ **Do not just reassure the patient**
- ✓ **Do not give hormonal therapy.**
- ✓ **Do not give antibiotics.**

## • Diagnostic Tests:

Biopsy is the best initial test. The different methods of biopsy are:

• **Fineneedleaspiration(FNA):**FNAisusuallythe**bestinitialbiopsy**.

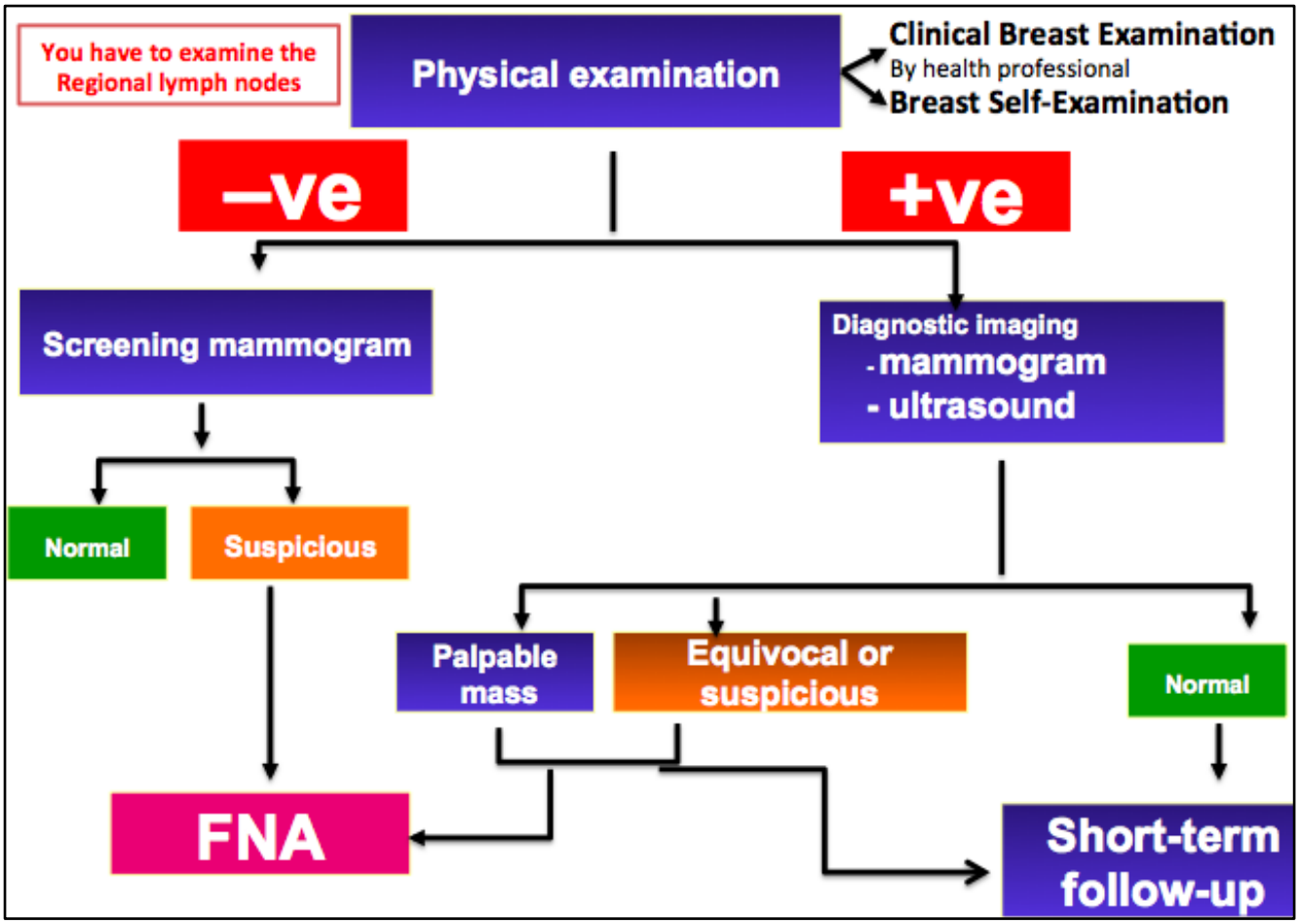
• **Coreneedlebiopsy:**Thisisalargersampleofthebreast.Itismore deforming, but you **can test for estrogen receptors (ER), progesterone receptors (PR), and HER 2/neu**. Difficulties include greater deformity with the procedure and the possibility that the needle will miss the lesion.

• **Openbiopsy:**The"**mostaccuratediagnostictest,"**openbiopsy allows for frozen section to be done while the patient is in the operating room followed by immediate resection of cancer.

**Mammography:**Is used to detect and diagnose breast cancer by**screening**women who **have breast symptoms** (problems such as a lump, pain or nipple discharge) and women who are asymptomatic (no breast complaints).**starting at the age of 50. (In KSA over the age of 40.)**

**HER2/NEU:**

**(Human epidermal growth factor receptor 2 or c-erb B2 or neu)** is a glycoprotein overexpressed in 20% to 30% of breast carcinomas. Many studies have shown that overexpression of HER2/neu is associated with a **poor prognosis.** In addition, ongoing studies have shown that HER2/neu- overexpressing tumors respond very well to hormonal or anthracycline chemotherapy regimens e.g. **Trastuzumab (Herceptin).** Therefore evaluation of HER2/neu is important when reporting breast cancer in order to help decide the chemotherapy plan.




- **PROGNOSIS:** To improve patients Prognosis

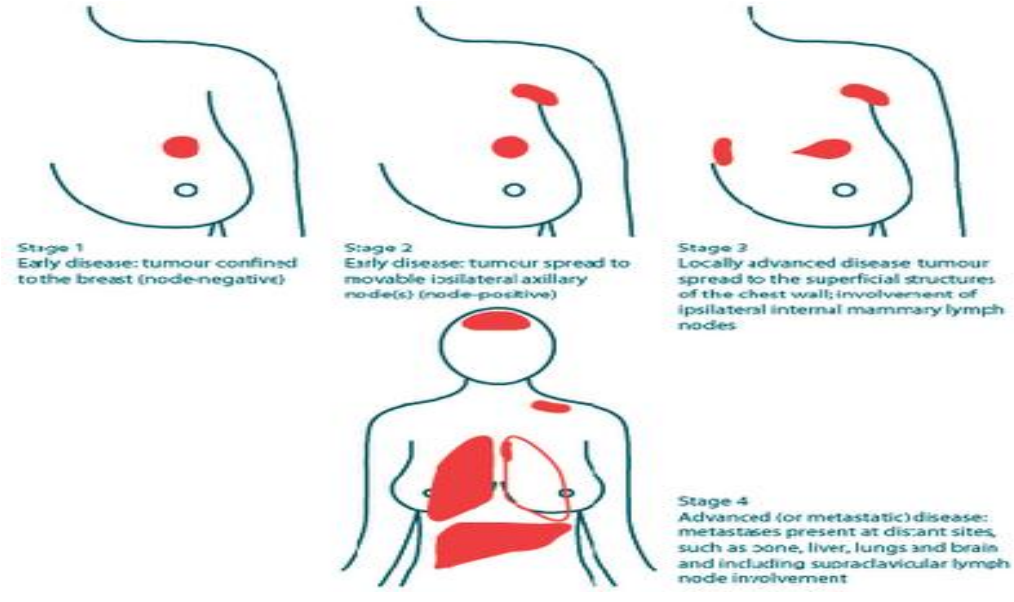
  1-EARLY DIAGOSIS 2-EARLY &PROPER INTERVENTION

- **BREST CANCER STAGING:**

  Early localized:in the breast

  Local advanced:breast + axillary lymph nodes

  Metastases :BB(brain-bones)-LL(lung –liver)




Stage I = 90%

Survival Stage IV = <10% survival

- **MANGEMENT:**

✓ **LOCAL THERAPY: SURGERY&RADIOTHERAPY**

Lumpectomy with radiation is equal in efficacy to modified radical mastectomy but much less deforming. The addition of radiation to lumpectomy is not a small issue. **Radiation** at **the site of the cancer is indispensible in preventing recurrences at the breast**.

✓ **SYSTEMIC THERAPY:CHEOTHERAPY &HORMONAL THERAPY&BIOLOGICAL THERAPY:**

**Estrogen Receptor or Progesterone Receptor >tamoxifen.**

**HER2/NEU ovweexpressing>transuzumab**

**A- HORMONAL THERAPY:**

All Estrogen Receptor or Progesterone Receptor positive patients should receive tamoxifen, raloxifene,(blocks the actions of estrogen) or one of the aromatase inhibitors (inhibit estrogen effect)(anastrazole, letrozole, exemestane). Aromatase inhibitors seem to have a slight superiority in efficacy. If both are available, aromatase inhibitors are better.

***Use tamoxifen when multiple first-degree relatives have breast cancer. It lowers the risk of breast cancer.**

***Those who are positive should receive anti-Her 2/neu antibodies known as trastuzumab. Decreases the risk of recurrent disease.**

## COLON CANCER:


- **EPIDEMILOGY:**
- **1st most common cancer in males.**
- **2nd leading cause of death.**

### #AETIOLOGY: (RISK FACTORS):

- **Age**—everyone over the age of 50 years is at increased risk
- **Adenomatous polyps :**
  a. These are premalignant lesions, but most do not develop into cancer.
  b. Villous adenomas have higher malignant potential than tubular adenomas.
  c.The larger the size, and the greater the number of polyps, the higher the riskof cancer.
- **Personal history of prior CRC (Colorectal Cancer) or adenomatous polyps**
- **Inflammatory bowel disease (IBD):**
  a. Both ulcerative colitis (UC) and Crohn's disease pose an increased risk for colorectal cancer, but UC poses a greater risk than Crohn's disease.
  b. Incidence of **CRC** is 5 % to 10% at 20 years and 12% to 20% at 30 years with

UC.

- **Family history**
  a. **Multiple first-degree relatives** with **CRC**
  b. Any **first-degree relative diagnosed with CRC or adenoma under age 60**
- **Dietary factors—high-fat, low-fiber** diets associated with a higher risk of **CRC**
- **Major polyposis syndromes:**
  - **Familial adenomatous polyposis:**
    - ✓ Autosomal dominant disease is characterized by **hundreds of adenomatous polyps in the colon.** The colon is always involved, and the duodenum is involved in 90% of cases.
    - ✓ **The risk of CRC is 100% by the third or fourth decade of life (in 100% of familial adenomatous polyposis cases).**
    - ✓ Prophylactic colectomy is usually recommended.
  - **Gardner's syndrome:**
    - ✓ **Polyps plus osteomas**, **dental abnormalities**, benign soft tissue tumors, desmoid tumors, sebaceous cysts.
    - ✓ **Risk of CRC is 100% by approximately age 40.**
  - **Turcot's syndrome:**
    - ✓ Autosomal recessive.
    - ✓ Polyps plus cerebellar medulloblastoma or glioblastomamultiforme
  - **Peutz–Jeghers:**
    - ✓ **Single or multiple hamartomas** that may be scattered through entire GI tract: in small bowel (78%), colon (60%), stomach (30%)
    - ✓ Pigmented spots around lips, oral mucosa, face, genitalia, and palmar surfaces
    - ✓ Unlike adenomas, hamartomas have very low malignant potential.
    - ✓ Slightly increased incidence in various carcinomas (e.g., stomach, ovary,breast, cervix, testicle, lung)
    - ✓ Intussusception or GI bleeding may occur.
  - **Familial juvenile polyposis coli**
    - ✓ **Rare**; presents in childhood; only small risk of CRC
    - ✓ More than 10 and up to hundreds of juvenile colon polyps
  - **Hereditary nonpolyposis CRC**—without adenomatous polyposis

✓ **Lynch syndrome I** (site-specific CRC)—early onset CRC; absence of antecedent multiple polyposis

✓ **Lynch syndrome II** (cancer family syndrome)—all features of Lynch I plus increased number and early occurrence of other cancers (e.g., female genital tract, skin, stomach, pancreas, brain, breast, biliary tract)

- **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 your risk of colon cancer.
- **Radiation therapy for cancer**

- **Constipation. The longer the waste stays in our body the more time bacteria have to work on these waste product ⇒ it becomes carcinogenic ⇒ which exposes to the mucosa and activates carcinogenic process.**

## #PATHOLOGY:

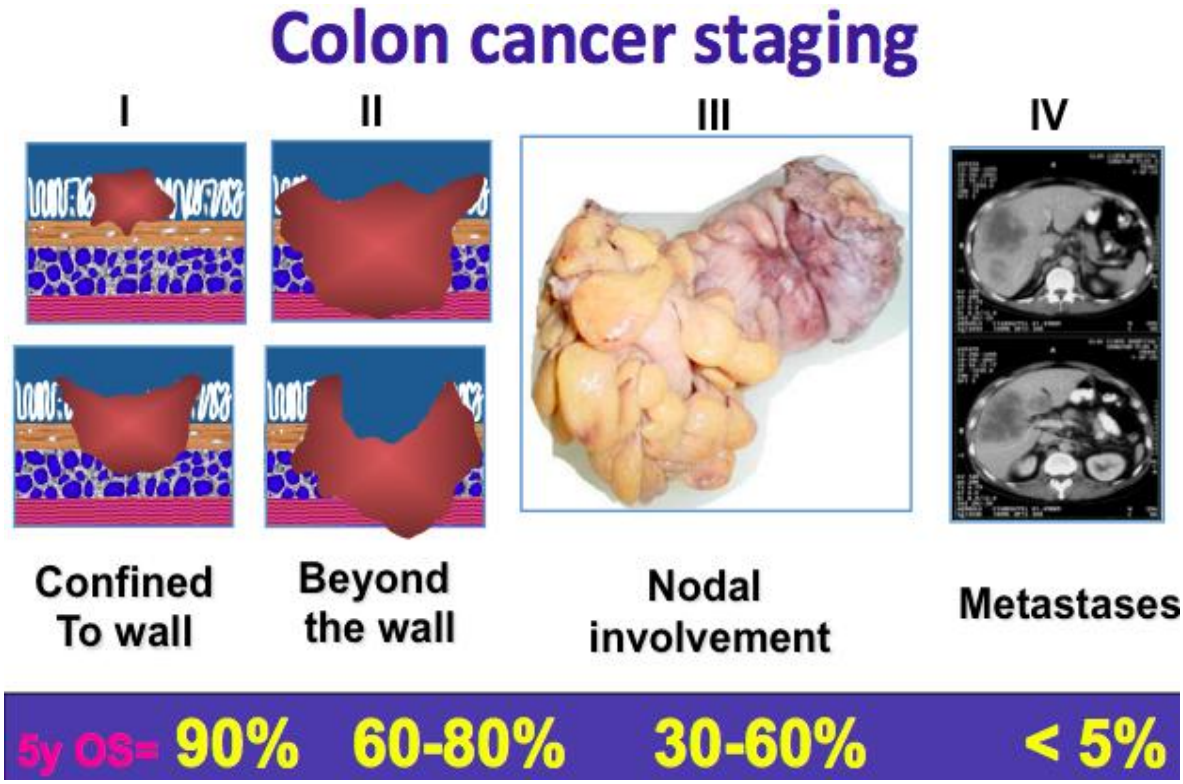
- It starts with a simple cell the mutates and grows into a polyps
- If a polyp is allowed to remain in the colon it can grow into a cancerous tumor that can invade other organs.
- All colorectal tumors arise from adenomas. Majority are endoluminal adenocarcinomas arising from the mucosa. Rarely, carcinoid tumors, lymphomas, and Kaposi's sarcoma may be present but majority are adenocarcinomas.

## #CLINICAL PRESENTATION:

- **A change in bowel habits, including diarrhea or constipation or a change in the consistency of your stool**
- **Rectal bleeding (Hematochezia)or blood in your stool**
- **Persistent abdominal discomfort, such as cramps, gas or pain. (CRC is the most common cause of large bowel obstruction in adults. Colonic perforation can lead to peritonitis and is the most life-threatening complication.)**
- **A feeling that your bowel doesn't empty completely**
- **Weakness or fatigue**
- **Unexplained weight loss**
- **Unexplained Fatigue**
- **Unexplained iron deficiency anemia.**

## #STAGING:

Clinical staging done with **CT scan**of chest, abdomen, and pelvis and by physical examination (ascites, hepatomegaly, lymphadenopathy).




## #Screening:

- ✓ **Fecal occult blood testing (FOBT)** has poor sensitivity and specificity. Positive predictive value is only about 20%, but all patients with positive FOBT need a colonoscopy regardless.
- ✓ **Digital rectal examination:** Only about 10% of tumors are palpable by rectalexamination.
- ✓ **Colonoscopy:**
  - **Most sensitive and specific test**; the diagnostic study of choice for patients with a positive FOBT
  - **Diagnostic and therapeutic** (e.g., biopsy, polypectomy)
- ✓ **Flexible sigmoidoscopy:**
  - Can be used to reach the area where approximately 50% to 70% of polyps and cancers occur (with a 60-cm scope)
  - Can be diagnostic in about two-thirds of all CRCs
- ✓ **Barium enema**
  - Evaluates entire colon; complementary to flexible sigmoidoscopy
  - Disadvantage is that any abnormal finding needs to be evaluated by colonoscopy
- ✓ **Carcinoembryonic antigen (CEA)—**not useful for screening; useful for baseline and recurrence surveillance. CEA does have prognostic significance: Patients with preoperative CEA > 5 ng/mL have a worse prognosis.

## #Treatment:

1. **Surgery is only curative treatment of CRC**. Surgical resection of tumor-containing bowel as well as resection of regional lymphatics

2. CEA level should be obtained before surgery .

3. Utility of adjuvant therapy (chemotherapy or radiation therapy) depends on stageof tumor and is beyond scope of this book.

4. **Follow-up is important**, and varies among physicians.

   a. Stool guaiac test

   b. Annual CT scan of abdomen/pelvis and CXR for up to 5 years

   c. Colonoscopy at 1 year and then every 3 years

   d. CEA levels are checked periodically (every 3 to 6 months)

   - A subsequent increase in CEA is a sensitive marker of recurrence.
   - Often, second-look operations are based on high CEA levels postresection.
   - Very high elevations of CEA suggest liver involvement.

5. **About 90% of recurrences occur within 3 years after surgery.**

## #PREVENTION of Cancer:

| Passive Prevention* | Active prevention |
|---|---|
| **Discover Etiological factors⇒Avoid theses factors** | **Discover pre-malignant lesions ⇒ get rid of them before developing invasive cancer.** |
| **Examples:**<br>✓ **For lung cancer avoid smoking and exposure to asbestos.**<br>✓ **For breast cancer avoid obesity/weight gain as an adult, estrogen/progesterone use and alcohol use.**<br>✓ **General health maintenance a healthy diet and exercise, avoid smoking and drinking.** | **Examples:**<br>✓ **In colon cancer→detect polyps and perform colectomy.**<br>✓ **In breast cancer → ductal carcinoma in-situ (DCIS).**<br>✓ **Eliminate or prevent pre-invasive disease before invasion develops using chemoprevention and surgery.** |

*However, primary prevention is not an easy task because social change is difficult and takes a long time. Also, sometimes it's not good enough in high-risk people.

# MCQs

Note: at the end there is an explanation for each question .

1-A 66-year-old postmenopausal woman presents with a painless breast mass and is found to have a 3- cm infiltrating ductal breast cancer. Sentinel node sampling reveals metastatic cancer in the sentinel node; a formal axillary node dissection shows that 4 of 13 nodes are involved by the malignant process. Both
estrogen and progesterone receptor are expressed in the tumor. There is no evidence of metastatic disease outside the axilla. In addition to lumpectomy and radiation therapy to the breast and axilla, what should her treatment include next?

a. No further treatment at this time
b. Radiation therapy to the internal mammary nodes
c. Platinum-based adjuvant chemotherapy
d. Bilateral oophorectomy
e. Adjuvant hormonal therapy (tamoxifen or aromatase inhibitor).

2/A 37-year-old woman presents for evaluation of a self-discovered breast mass. There is no family history of breast cancer; she is otherwise healthy. Examination reveals a 1.5-cm area of firmness in the right upper outer quadrant. No skin changes are noted. You attempt to aspirate the mass, but no fluid is obtained; a mammogram is ordered and is normal. Which of the following is the most appropriate next step in management?

a. Refer the patient for further evaluation to a surgeon or comprehensive breast radiologist.
b. Reevaluate the patient in 6 months.
c. Give oral contraceptives to decrease ovulation and help shrink the lesion.
d. Recommend tamoxifen to decrease her chance of developing cancer.
e. Reassure the patient.

**Answers: 1-e , 2-a**

**Explanation :**

**The answer is E** .This woman is at high risk of recurrent breast cancer, an ultimately fatal event. Adjuvant therapy has been shown to decrease the chance of recurrence by 40%. This translates into a proven survival advantage for the woman; the advantages of treatment far outweigh the risk of side effects. Therefore, no therapy or only local therapy (eg, radiation therapy) would represent inadequate treatment. Postmenopausal women who are ER or PR positive are generally treated with adjuvant hormonal therapy. Premenopausal women, or women whose tumor does not contain ER or PR, will usually need adjuvant chemotherapy. Both tamoxifen (an estrogen receptor antagonist) and aromatase inhibitors (eg, letrozole, anastrozole) are effective in decreasing the rate of recurrence. Although aromatase inhibitors may be slightly more effective than tamoxifen, they are much more expensive, can produce troublesome side effects, and unlike tamoxifen do not improve bone density. This choice is often based on the preference of the patient and her oncologist.

2- **The answer is A**. A breast mass, even in a young woman, requires definitive evaluation. Although most such masses are benign, breast cancer is still the most common cause of cancer death in this age group. Risk factor assessment cannot provide sufficient reassurance. A negative mammogram never rules out breast cancer. Either excisional biopsy or, in selected hands, fine-needle aspiration with follow-up, will be needed to detect cases of breast cancer before metastases outside the breast have occurred. Reassurance and reevaluation in 6 months may lead to delay in diagnosis of breast cancer.

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