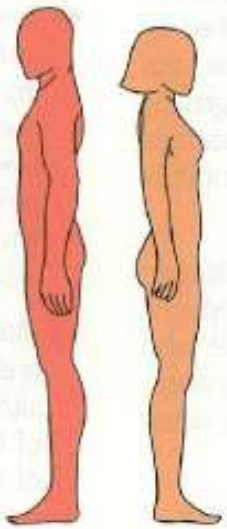
Solid tumors

Breast Cancer

- The most common malignancy in women
- Second to lung cancer in mortality rates
- One in eight women are expected to develop the disease over the course of their lifetime

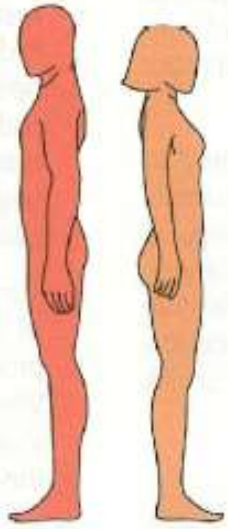
Estimated new cases*

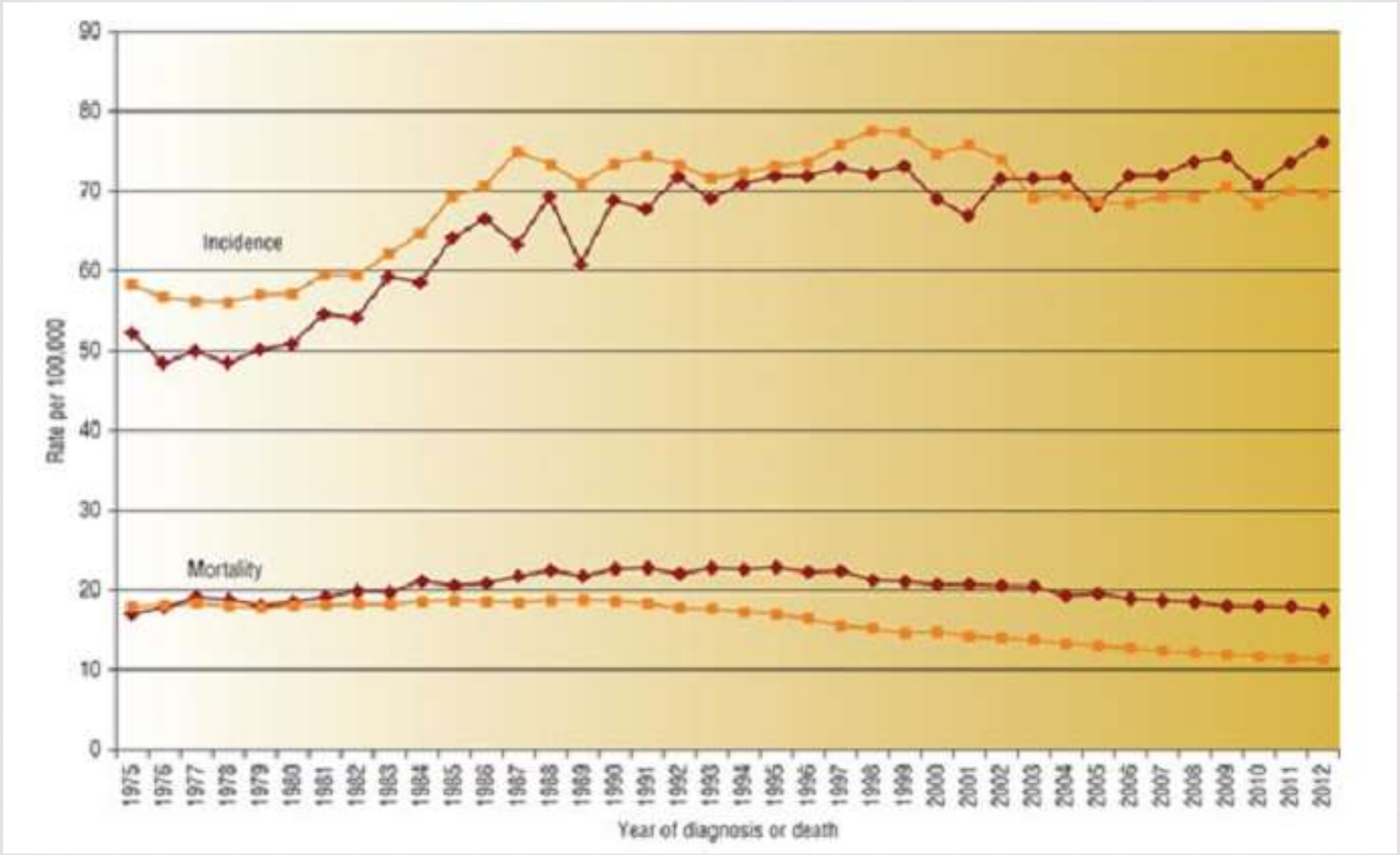
Males			Females		
Prostate	217,730	28%	Breast	207,090	28%
Lung & bronchus	116,750	15%	Lung & bronchus	105,770	14%
Colon & rectum	72,090	9%	Colon & rectum	70,480	10%
Urinary bladder	52,760	7%	Uterine corpus	43,470	6%
Melanoma of the skin	38,870	5%	Thyroid	33,930	5%
Non-Hodgkin lymphoma	35,380	4%	Non-Hodgkin lymphoma	30,160	4%
Kidney & renal pelvis	35,370	4%	Melanoma of the skin	29,260	4%
Oral cavity & pharynx	25,420	3%	Kidney & renal pelvis	22,870	3%
Leukemia	24,690	3%	Ovary	21,880	3%
Pancreas	21,370	3%	Pancreas	21,770	3%
All sites	**789,620**	**100%**	**All sites**	**739,940**	**100%**



Estimated deaths

Males			Females		
Lung & bronchus	86,220	29%	Lung & bronchus	71,080	26%
Prostate	32,050	11%	Breast	39,840	15%
Colon & rectum	26,580	9%	Colon & rectum	24,790	9%
Pancreas	18,770	6%	Pancreas	18,030	7%
Liver & intrahepatic bile duct	12,720	4%	Ovary	13,850	5%
Leukemia	12,660	4%	Non-Hodgkin lymphoma	9,500	4%
Esophagus	11,650	4%	Leukemia	9,180	3%
Non-Hodgkin lymphoma	10,710	4%	Uterine corpus	7,950	3%
Urinary bladder	10,410	3%	Liver & intrahepatic bile duct	6,190	2%
Kidney & renal pelvis	8,210	3%	Brain & other nervous system	5,720	2%
All sites	**299,200**	**100%**	**All sites**	**270,290**	**100%**




Incidence
Mortality
Rate per 100,000
0
10
20
30
40
50
60
70
80
90
1975
1976
1977
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1979
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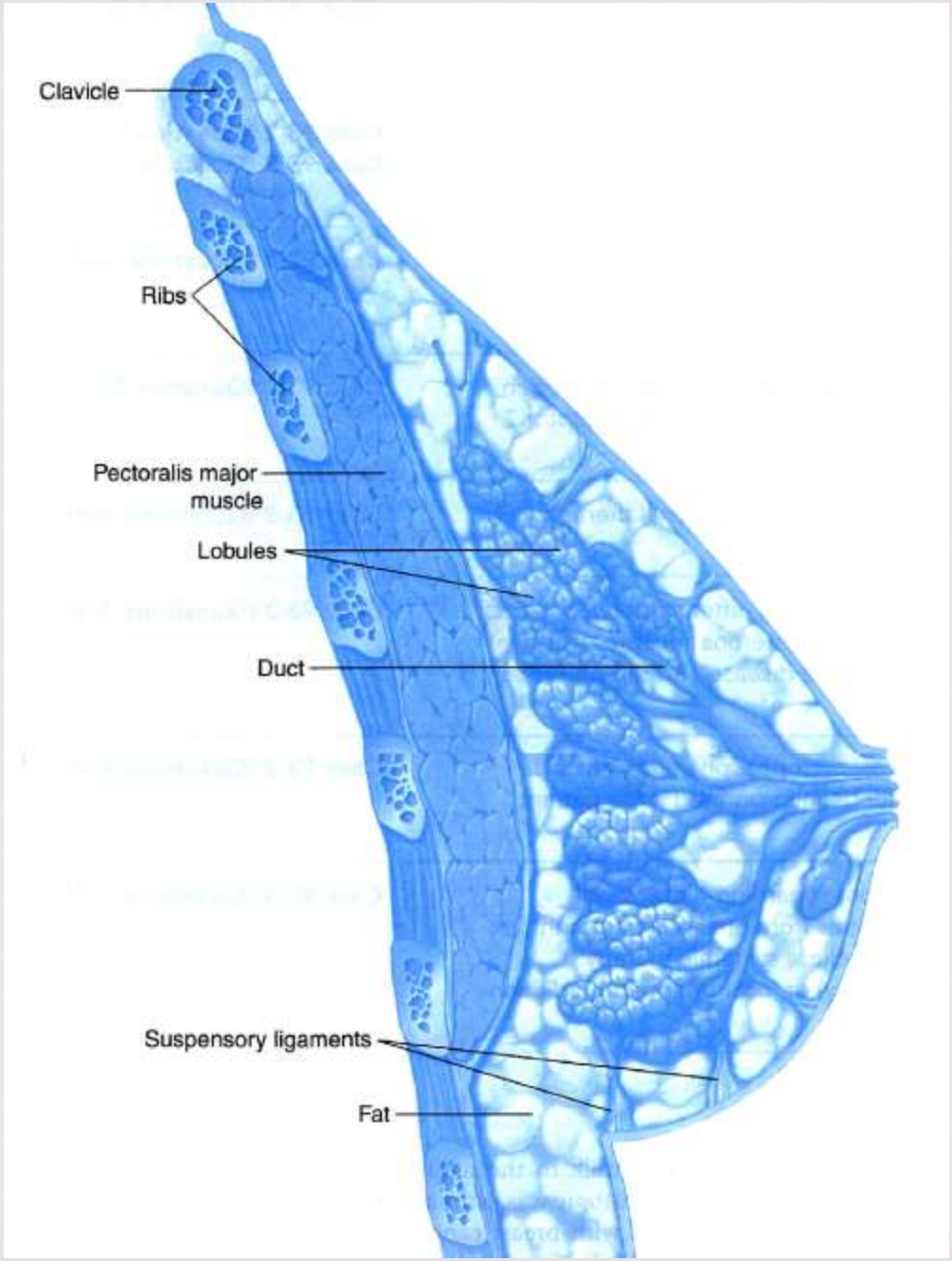
2012
Year of diagnosis or death

Types & staging

- The two most common histologic types of breast cancer are ductal and lobular carcinoma.


Clavicle
Ribs
Pectoralis major muscle
Lobules
Duct
Suspensory ligaments
Fat

Screening

- Breast self-examination
  - Age ≥20 y: optional
- Clinical breast examination
  - Evidence does not support
- Mammography
  - Gold standard
  - Age 40-44 y: opportunity annually
  - Age 45-54 y: annually
  - Age ≥55 y: biennially or
  - opportunity annually (as long as in good health and at least 10 years life expectancy)

MRI

- MRI is recommended in high-risk individuals
  - known BRCA gene mutation
  - untested for the BRCA gene mutation but have a first-degree relative with a BRCA mutation
  - a lifetime risk of experiencing breast cancer of approximately 20% to 25% or more based on risk estimation models
  - strong family history of breast cancer
- Annual mammography and breast MRIs should be initiated starting at the age of 30 years

Known Risk Factors
Gender: female > male
Personal history of breast cancer
Family history of breast cancer (first-degree relatives)
Benign breast "cancer" (i.e., atypical hyperplasia)
Early menarche (<12 years of age), late menopause (>55 years of age)
Late first pregnancy (≥30 years) or no pregnancy
Advancing age
Long-term use of hormone-replacement therapy (estrogen)
Previous chest wall irradiation
Possible Risk Factors
Alcohol
Obesity
High-fat diet

Risk factors

- Gender: Female> male
- Advancing age
- Personal history of breast cancer
- Family history of breast cancer (first-degree relatives)
- Benign breast "cancer" (i.e., atypical hyperplasia)
- Early menarche or late menopause
- Late first pregnancy (>30 years) or no pregnancy
- Long-term use of hormone-replacement therapy
- Previous chest wall irradiation

Genetic factors

- BRCA1 &BRCA2 gens
- BRCAl mutation has a 60% risk of developing breast cancer and a 40% risk of ovarian cancer.
- BRCA2 mutation carriers have 40% risk of breast cancer and lower risk for ovarian cancer (20%).

Clinical Presentation

- Identification of a painless lump
- Nipple discharge or retraction
- Less than 10% with metastatic symptoms:
  - Back pain: bone metastases
  - Headaches/nausea/vomiting: brain metastases
  - Dyspnea: lung metastases
  - Abdominal pain: liver metastases

Diagnosis

- Mammography
- Ultrasonography
- Biopsy
- Full radiologic testing
  - CT scan of the chest, abdomen, and pelvis, and bone scan to assess for metastatic disease.

Types and Staging

- The two most common histologic types of breast cancer are ductal and lobular carcinoma.
- Invasive and noninvasive (in situ) disease
  - Invasive ductal carcinoma in ~75% of cases
  - Invasive lobular carcinoma in ~ 5%-10%
- Inflammatory breast cancer
- Staging of breast cancer is determined using the TNM classification.

- Stage I : small tumors (<2 cm) with no lymph node involvement
- Stage II: small tumors with lymph node involvement or larger tumors (> 2 cm and <5 cm) with no lymph node involvement.
- Stage III: large tumors (>5 cm) with lymph node involvement
- Stage IV: disease has metastasized to other distant organs

Prognostic Factors

- Tumor size
- Lymph node status
- Pathologic testing: ER and PR and HER2 status

Treatment modalities

- Surgery
- Radiation therapy
- Hormonal therapy
- Chemotherapy
- Biologic therapy
- Neoadjuvant therapy
- Adjuvant therapy

Surgery & radiation therapy

- Surgery is the definitive treatment in early-stage breast cancer
  - Radical mastectomy
  - Modified radical mastectomy
  - Conservative surgery plus radiation therapy
- Radiation in addition to a modified radical mastectomy:
  - Tumor greater than 5 cm
  - Greater than four positive lymph nodes
  - Positive tissue margins after surgery

Systemic therapy

- To diminish the chance of recurrence, systemic adjuvant chemotherapy, hormonal therapy, or biologic therapy is given.

TABLE 93-3
Overview of the Selection of Adjuvant Treatment

	Adjuvant Hormonal Therapy		Adjuvant Chemotherapy†
Lymph node negative disease	ER/PR (+)	ER/PR (–)	
<0.5 cm	Yes	No	No
0.6 – 1 cm*	Yes	No	Consider
>1 cm	Yes	No	Yes
Lymph node positive disease	ER/PR (+)	ER/PR (–)	
	Yes	No	Yes

- Anthracycline-containing regimens
  - Doxorubicin or epirubicin + cyclophosphamide +/- fluorouracil
- Taxane-containing regimens
  - Lymph node-positive disease
  - Doxorubicin + cyclophosphamide then paclitaxel
- Trastuzumab
  - In HER2-positive

Doxorubicin

- Inhibition of topoisomerase II and double strand DNA breaks
- Myelosuppression, nausea/vomiting, and alopecia
- Cardiomyopathy due to the formation of oxygen free radicals and doxorubicin metal complexes

Cyclophosphamide

- Alkylating agent that works by forming cross-links in DNA, thus inhibiting DNA synthesis
- Nausea/vomiting, myelosuppression, and alopecia
- Risk of secondary leukemias

Paclitaxel

- Binding to the ,B-tubulin subunit of microtubules preventing disassembly and ultimately causing inhibition of mitosis.
- Nausea/vomiting, myelosuppression, neuropathy, and hypersensitivity reactions due to the cremaphor solvent in paclitaxel
- Premedication with dexamethasone and H_1 and H_2 blockers to prevent hypersensitiviry

Trastuzumab

- A monoclonal antibody targeted against the extracellular HER2 protein.
- Cardiac toxicity

Hormonal therapy

- Offered to patients with ER/PR positive disease
- SERMs (tamoxifen)
- Luteinizing hormone-releasing hormone (LH-RH) agonists
- Aromatase inhibitors
- Menopausal status of the patient is used to guide selection of therapy

Tamoxifen

- Blocking estrogen from binding to the estrogen receptor
- Can be used in both premenopausal and postmenopausal women
- Is given 20 mg orally daily for 5 years
- Should be initiated after chemotherapy because it can antagonize the antitumor activity of chemotherapy if given concurrently
- Hot flashes and vaginal discharge
- Thrombosis, pulmonary embolisms, and strokes

Aromatase inhibitors

- Inhibit the production of estrogen by preventing the conversion of androstenedione and testosterone to estrone and estradiol.
- For postmenopausal patients
- Less toxicity than tamoxifen
- AIs are given for 5 years

Metastatic breast cancer

- Treatment is offered to improve quality of life and alleviate symptoms from treatment or disease.
- The mean survival time is approximately 2 to 4 years
- Common sites of metastases include liver, lung, brain, bone, and lymph nodes.
- The choice of therapy is based on the site of disease and other factors that help guide therapy such as ER/PR status

- Endocrine therapy is effective in patients with bone-only disease
- Chemotherapy may be used when there is visceral disease (i.e., liver or lung).
- Radiation therapy can be used to target painful bone metastases, to prevent further tumor growth, and to relieve pain.
- Surgery may be performed on bones with impending fractures, spinal cord compression, or brain metastases for palliation

Prevention of Skeletal Events

- Bisphosphonate therapy to decrease the risk of skeletal-related events
- Halt osteoclastic activity leading to stabilization of bony involvement, prevention of fractures, and reduction in calcium levels
- Pamidronate 90 mg intravenously (IV) for 2 hours or zolendronic acid 4 mg IV for 15 minutes once a month.

Lung cancer

Introduction

- Lung cancers may be referred to as non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC)

- 85% of lung cancers are classified as NSCLC

Non-Small Cell Lung Cancer

- Incidence for NSCLC is second to prostate cancer in men and breast cancer for women
- The leading cause of death relative to all of the other cancers
- Neoplastic tissue arises from bronchial epithelium.
  - Squamous cell carcinoma
  - Adenocarcinoma
  - Large cell carcinomas

Risk factors

- Cigarette smoking
  - Increase the risk by up to 30-fold
- Occupational and environmental exposures radon, asbestos
- Certain metals such as chromium and cadmium
- Radiation
- Air pollution
- History of tuberculosis
- Genetic factors

TABLE 94-1

Common Selected Signs and Symptoms for Lung Cancer

Cough
Hemoptysis
Wheeze
Dyspnea
Pain (e.g., chest wall)
Obstruction of vital structures (e.g., esophagus, superior vena cava)

Symptoms are highly dependent on tumor size, location within the chest cavity, and presence of metastases.

Diagnosis

- Computed tomography (CT) or positron emission tomography (PET)-CT scan
- MRI from head
- Biopsy
- Lymph nodes sampled via mediastinoscopy
- Staging is performed to determine prognosis and to guide treatment decision-making.
- The disease has already metastasized in greater than 50% of patients upon initial presentation.

Clinical Stage	Tumor Characteristics
Stage I	Tumor ≤5 cm in greatest diameter with no nodal involvement
Stage II	Tumor >5 cm, but ≤7 cm in greatest diameter with no nodal involvement Tumor ≤7 cm with adjacent lymph nodes involved Tumor >7 cm or invading local structure (i.e., chest wall) with no nodal involvement
Stage III	Any tumor size with adjacent lymph nodes involved or ipsilateral mediastinal and/or subcarinal lymph nodes Tumor invading mediastinum, heart, great vessels, esophagus, or another tumor nodule in different ipsilateral lobe
Stage IV	Any tumor size, any nodal involvement and metastasis to the contralateral lobe, malignant pleural effusions or distant metastasis

Treatment, early stages

- Surgery is the best treatment modality for patients with stages I , II and early stage III
- Adjuvant treatment enhances patient survival
- For stage II ,IIIA and stage IB with tumor size>4 cm
- four cycles of a platinum-based doublet regimen

Late-Stage NSCLC

- Stage IIIB and IV disease are inoperable.
- These tumors often invade the carina, great vessels, vertebral bodies, more distant lymph nodes, metastases, and associated with malignant pleural effusions
- Chemotherapy and radiation therapy
- Stage III, radiotherapy is often given concurrently with chemotherapy
- Stage IV, local treatment with radiotherapy first, followed by chemotherapy

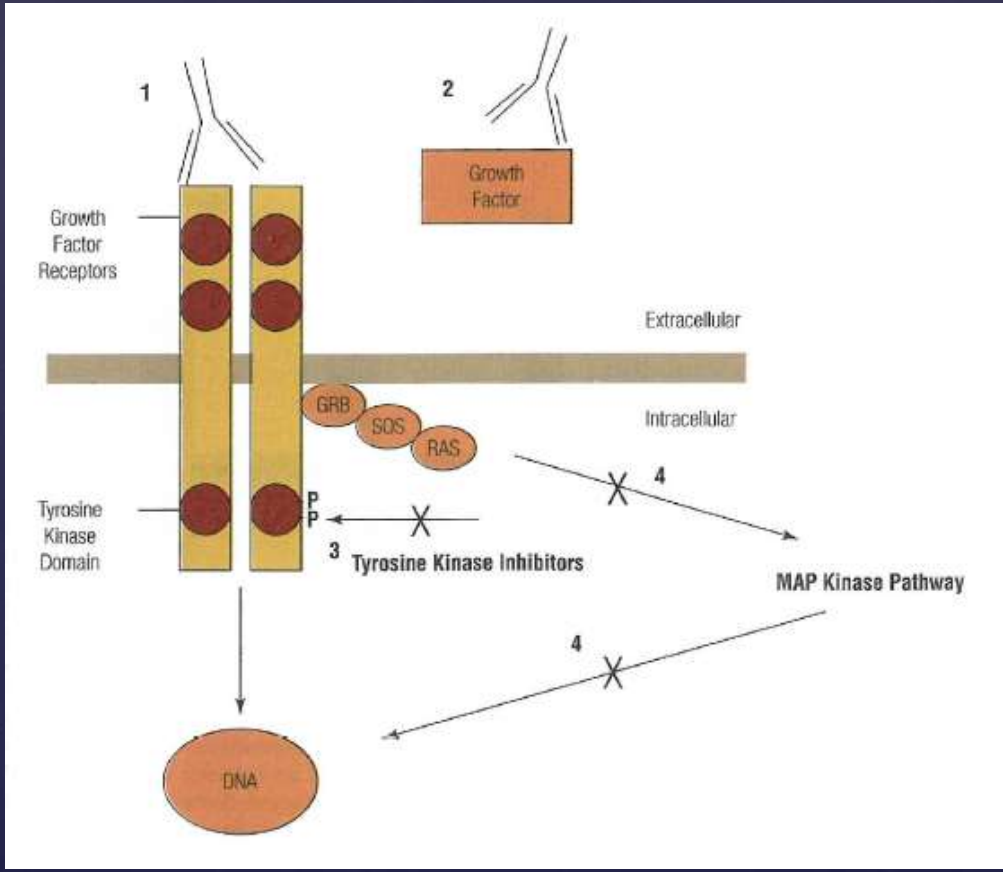
- Platinum-based doublet cytotoxic combination therapy, for 4 to 6 cycles
- Tumors that are positive for EGFR somatic mutations are often more responsive to erlotinib
- Then maintenance therapy
  - Use of one of the agents given in first line
  - Or switch maintenance

Cisplatin & carboplatin

- The cytotoxicity of the platinum derivatives depends on platinum binding to DNA and the formation of intrastrand cross-links or adducts between neighboring guanines
- Cisplatin is predominantly associated with ototoxicity, nephrotoxicity, and neurotoxicity, whereas carboplatin is predominantly associated with myelosuppression

Erlotinib

- Selective EGFR-tyrosine kinase inhibitor
- Diarrhea and rash



Small Cell Lung Cancer

- The disease is much more highly attributable to smoking than NSCLC
- Relative to NSCLC, these tumors generally have a more rapid doubling time, a higher growth fraction, and early development of widespread metastases
- Highly sensitive to chemotherapy and radiotherapy
- Derived from neuroendocrine cells in the bronchus

- SCLCs usually arise centrally and present as a large hilar mass with bulky mediastinal lymphadenopathy that can cause cough and dyspnea
- limited stage disease:
  - disease confined to the ipsilateral hemithorax and encompassed in a tolerable radiation field
- Extensive disease:
  - Disease beyond the ipsilateral hemithorax including malignant pleural, pericardial effusion or hematogenous metastases

Clinical presentation

- Weight loss
- Fatigue, with decreased physical activity
- Hemoptysis
- Superior vena cava syndrome
  - Restrict blood return to the heart, resulting in head and facial swelling
- Paraneoplastic syndromes
  - SIADH & Cushing syndrome

- Metastasis to bone, liver, adrenal glands, and brain.

Treatment modalities

- Surgery has a very limited role
- Radiation is useful in treating patients with limited stage disease, concurrently with chemotherapy
- Prophylactic cranial irradiation is the standard of treatment for patients with limited stage and extensive stage diseases
- Systemic chemotherapy is the treatment of choice because it is effective for tumor cells progressing through the cell cycle and its utility for treating metastases.

Chemotherapy

- Platinum-based combinations with etoposide or, irinotecan for six cycles
- SCLC has a very high rate of recurrence;
- Therefore, second-line therapy is usually implemented(single agent)
- A recurrence that occurs within 6 months of treatment with first-line therapy is considered resistant and other agents are selected.

COLORECTAL CANCER

- The malignant growth of tumor that begins from the inner wall of the colon or rectum.
- The third most common cancer in the United States for both men and women
- For both adult men and women, colorectal cancer is the third leading cause of cancer-related deaths

- An abnormal growth of tissue known as a polyp originating from the innermost wall of the colon
- The process of transformation from a benign polyp to malignant disease can take several years.
- Once this transformation occurs, the cancer begins to spread through the wall of the colon or rectum, where it can eventually invade the blood, lymph nodes, or other organs directly.

Risk factors

- Age
  - Greater than 90% of patients diagnosed are older than 50 years of age
- Male sex
- History of previous colonic polyps
- Inflammatory bowel disease
- Diet consisting primarily of red meat, high fat, and low fiber
- Sedentary lifestyle, obesity, excessive alcohol consumption, and long-term smoking

Risk factors

- Inherited genetic mutations
  - Hereditary nonpolyposis colon cancer (HNPCC), also known as Lynch syndrome
  - Familial adenomatous polyposis (FAP)

- Regular consumption of milk or calcium
- Use of aspirin or NSAIDs

Clinical Presentation & Diagnosis

- Symptoms often subtle and can mimic "generalized" symptoms associated with numerous other benign conditions
- A change in bowel habits
  - Prolonged constipation or diarrhea
  - Rectal bleeding
  - Abdominal pain or bloating
- Unintentional weight loss, anemia, and weakness
- Colonoscopy or sigmoidoscopy for diagnosis and biopsy to confirm the presence of cancer

- Computed tomography (CT) scan of the chest, abdomen, and pelvis
- Blood test for a baseline carcinoembryonic antigen (CEA) level

Screening

- Colon and rectal cancers can be prevented by removal of precancerous tissue
- Fecal screening test
- Endoscopy
- CT colonography

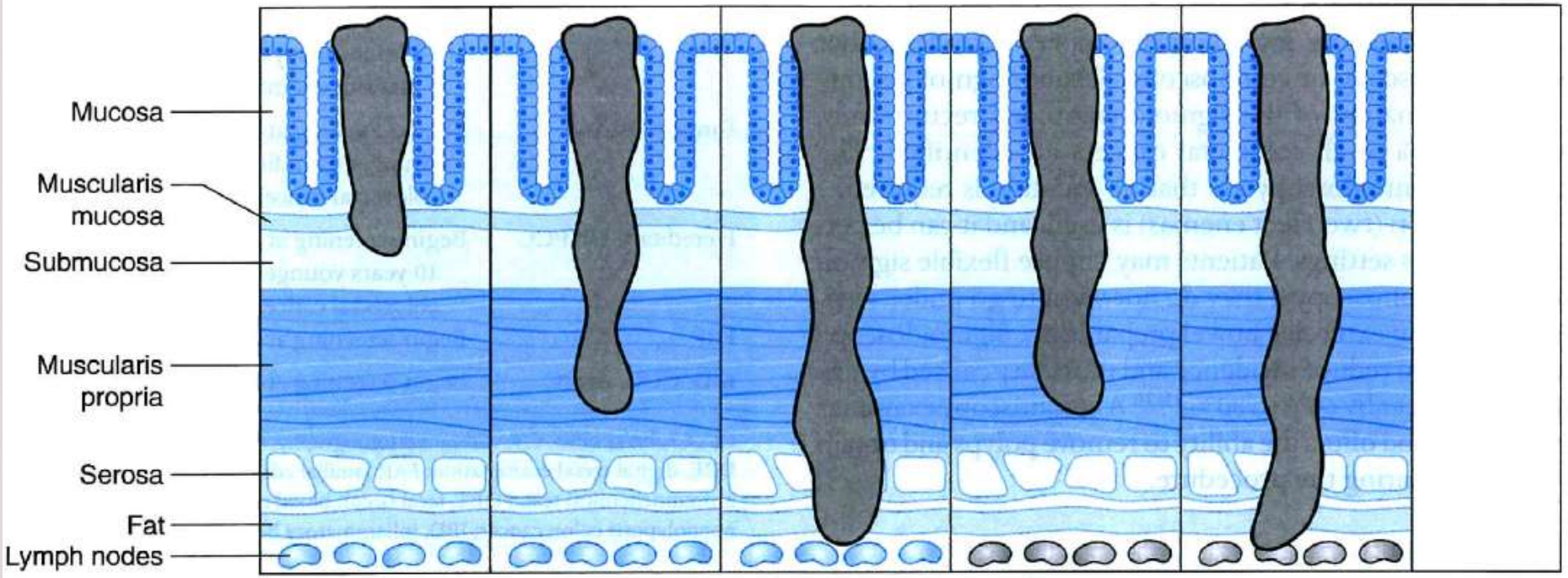
- Any man or woman at average risk of developing colorectal cancer should begin screening at age of 50 years
- Annual FOBT/FIT
- One of the following:
  - Sigmoidoscopy every 5 years
  - CT colonography every 5 years
  - Colonoscopy every 10 years

CEA

- Act as an adhesion molecule that facilitates malignant colon cancer cell interaction with healthy tissue and promotes tumor dissemination
- High specificity (87%) for detecting occult colorectal cancer
- Very low sensitivity (36%)
- CEA level greater than 5 mg/mL before surgery is a poor prognostic indicator
- Is primarily used to monitor for the recurrence of disease after treatment

Staging

Stage	I		II	III		IV
Extent of tumor	T_1 No deeper than submucosa	T_2 Not through muscularis	T_3 Through muscularis	N_1 1–3 lymph node metastases	N_2 ≥4 lymph node metastases	M Distant metastases
Stage at presentation — Colon	23%		31%	26%		20%
Stage at presentation — Rectal	34%		25%	26%		15%



Treatment

- Surgery
  - For patients with stages I, II, and III disease, and selected patients with metastatic stage IV disease.
- Radiation
  - Reserved for patients with rectal cancer.
- Chemotherapy

Chemotherapy for Localized Colorectal Cancer

- 5'-FU combined with leucovorin
- Single-agent capecitabine
- Combination of 5'-FU and oxaliplatin
- Chemotherapy should begin approximately 4 to 6 weeks after surgery and continue for a total of 6 months.

5' -FU

- A fluorinated analog of uracil
- In the presence of folates, fluorodeoxyuridine monophosphate binds tightly to and interferes with the function of thymidylate synthase.
- This enzyme is required for synthesis of thymidine, one of the four essential building blocks of DNA
- The triphosphate metabolite is incorporated into RNA as a false base, and interferes with its function

5' -FU

- The toxicity of 5' -FU will vary depending on its dose, route, and schedule of administration.
- Bolus administration is associated with more severe neutropenia and mucositis
- Continuous infusion administration is associated with more severe palmar-plantar erythrodysesthesia or hand-foot syndrome

Capecitabine

- Orally active pyrimidine analog of uracil and is a prodrug of 5-FU
- It generates higher levels of 5-FU selectively within some tumors
- Chronic twice-daily oral dosing of capecitabine produces sustained 5-FU levels similar to continuous intravenous infusions of 5-FU

Oxaliplatin

- The newest member of the platinum family
- Myelosuppression, primarily neutropenia and thrombocytopenia, and neurotoxicity are dose-limiting toxicities associated with its use
- Can cause acute, reversible neuropathy consisting of either paresthesias or dysesthesias
- Occur in greater than 90% of patients receiving oxaliplatin
- Triggered by direct contact with anything cold

- Hypersensitivity reactions
- The severity of these allergic reactions can range from mild itching or flushing to anaphylaxis.
- Mild cases are often managed through premedication with antihistamines or corticosteroids in addition to prolonging the infusion of oxaliplatin
- Desensitization protocols for severe reactions

Clinical Surveillance for Recurrence

- Patients treated definitively for localized disease should be monitored regularly for at least 5 years
- CEA level obtained every 3 to 6 months for the first 2 years, then semiannually thereafter
- CT scan of chest, abdomen, and pelvis performed at least annually for 3 years
- Colonoscopy should be performed within a year of surgical resection or approximately 1 year from original colonoscopy, and then repeated again in 3 years

Metastatic Colorectal Cancer

- Single-agent therapy
  - Irinotecan, 5'-FU, capecitabine
- Combination chemotherapy
  - IFL, FOLFIRI, FOLFOX
- The use of monoclonal antibodies
  - Bevacizumab, cetuximab, and panitumumab

Irinotecan

- Inhibits topoisomerase I enzyme activity
- The active metabolite of irinotecan, SN-38, is capable of producing acute abdominal cramping and diarrhea
- Atropine
- Loperamide

Bevacizumab

- Antiangiogenesis agents
  - Directed against circulating VEGF
- Hypertension
- Bleeding episodes
- Thrombotic events


خسته نباشید