UCSF INTERNAL MEDICINE
RECERTIFICATION REVIEW:
MEDICAL ONCOLOGY

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Medical Oncology 2016 – 6% of exam
Each subtopic – <2% of exam

• Lung cancer - clinical presentation and diagnosis
• Breast cancer
• Neoplasms of the head and neck
• GI or hepatic cancer
• Gynecologic cancer
• Genitourinary cancer
• CNS tumors
• Skin cancer
• Hematologic malignancies
• Soft tissue tumors
• Assorted endocrine tumors and endocrine manifestations of tumors
• Oncologic complications of HIV infection
• Cancer of unknown primary
• Cancer prevention
• Cancer screening
• Oncologic emergencies
• Complications of cancer antituft treatment
• Cancer survivorship
• Other oncology
• (End of life/palliative care in the elderly, listed under geriatric syndromes)

Review

• Epidemiology
• Breast cancer
• Colorectal cancer
• Lung cancer
• Prostate cancer
• Oncologic emergencies, chemotherapy-associated complications, and supportive care issues
• Other topics

EPIDEMIOLOGY
Ten Leading Cancer Types for Estimated New Cancer Cases and Deaths, by Sex, United States, 2016

Annual Age-adjusted Cancer Incidence Rates among Males and Females for Selected Cancers, United States, 1975–2012

Annual Age-adjusted Cancer Death Rates among Males for Selected Cancers, United States, 1930–2012

Annual Age-adjusted Cancer Death Rates among Females for Selected Cancers, United States, 1930–2012
BREAST CANCER

Screening: Breast

- USPSTF (2016)
  - Biennial screening mammogram for women 50-74 y/o
  - Insufficient evidence to assess benefits and harms of screening mammogram in women 75+ (I)
  - Decision to start before 50 should be an individual one and take patient context into account (C)
  - Recommends against BSE (D)

- ACS (2015)
  - Annual mammogram age 45-54; every 2 years 55+
  - Recommends against CBE
  - BSE is an option for women starting in 20s

ONCOLOGY question #1

A 70 year old healthy woman has a screening mammogram showing focal irregular and clustered branching microcalcifications. These have increased from a mammogram done two years prior. On examination, there is no palpable abnormality. You recommend:

A. Follow-up mammogram in 6 months
B. Repeat breast examination in 3 months
C. Ultrasound examination
D. Needle localized or stereotactic core biopsy
E. Fine needle aspiration

ONCOLOGY question #2

A biopsy shows low grade ductal carcinoma in situ with positive margins. You refer the patient to a surgeon who recommends mastectomy with node sampling. The patient returns to you and asks if there is any way to save her breast without placing herself at higher risk. She had one family member with postmenopausal breast cancer, and has been taking HRT for 10 years. What is the best treatment now?

A. Simple mastectomy
B. Local excision with clear margins with subsequent radiation therapy
C. No further surgery
D. Tamoxifen
E. Modified radical mastectomy with sentinel node sampling
Ductal Carcinoma in Situ

- Presence and proliferation of malignant breast ductal epithelial cells without evidence of invasion
- Presenting features
  - Calcifications on mammogram
  - In association with an invasive tumor
  - Less commonly a palpable mass
  - Increasing incidence with age
  - Mortality at 10 years < 2%

DCIS management

- Wide local excision with clear margins
  - No need for mastectomy except if extensive involvement
- Radiation for majority of lesions
  - Reasonable to omit in select, low-risk cases
- Mastectomy only necessary for extensive involvement
- Hormonal therapy with tamoxifen – only agent approved for DCIS in United States
  - In estrogen receptor positive disease
  - Reduces ipsilateral and contralateral in situ and invasive disease, no mortality benefit
  - Only in patients with lumpectomy
  - Need to balance benefit against side effects and risk
- No role for HER2 targeted therapy in DCIS

ONCOLOGY question #3

Which of the following risk factors is incorrectly paired with its effect on a woman's risk of getting breast cancer?

A. childbearing: decreases risk  
B. early menarche: decreases risk  
C. hormone replacement therapy with estrogen/progesterone combination: increases risk  
D. exposure to higher dose oral contraceptives: increases risk  
E. obesity: increases risk

ONCOLOGY question #4

A 35 year old woman comes to establish primary care. She is very concerned about her risk of breast and ovarian cancer as she has two friends who were recently diagnosed. She has never had any breast biopsies, she has no family history of ovarian cancer, but she has two maternal relatives (grandmother and her mother’s cousin) who developed breast cancer at age 70 and 75. A paternal uncle had lung cancer at age 65. Two older sisters are alive and well. On examination she has dense breasts with diffuse nodular changes, but no focal mass. What would you recommend at this time?

A. Refer to genetic counseling for BRCA1 and 2 testing  
B. Refer for discussion of preventive therapy with tamoxifen  
C. Refer for a screening mammogram and ultrasound  
D. Reassure patient that no specific screening is required now, but that you would recommend a screening mammogram sometime after the age of 40.
Risk factors for the development of breast cancer

- Age
- Family history:
  - Two fold increase in risk with a single first degree relative with breast cancer
  - If that relative was postmenopausal, does not predict increased risk of cancer at a young age
- Familial cancer syndromes
  - Premenopausal, bilateral breast cancer, male breast cancer, ovarian cancer, or multiple affected family members
  - More common in ethnically homogeneous populations

Risk factors for the development of breast cancer

- Prior history of invasive or noninvasive breast cancer (RR 5)
- Prior breast biopsies with atypical hyperplasia (RR 2-4)
  - Multiple prior biopsies with benign histology increase risk slightly
- Dense parenchyma on mammography (RR 1.7-4)

Risk factors for the development of breast cancer

- Endogenous hormonal factors
  - Early menarche (<12, RR 1.3)
  - Late menopause (>55, RR 1.5)
  - Nulliparity or age > 30 at first pregnancy (RR 1.9)
  - Short term or no breast feeding
  - High level (nondiagnostic) radiation at young age (RR 3)

- Regular/daily alcohol intake
  - >2 drinks/day (RR 1.7 or higher)

- Post-menopausal exogenous estrogen and progesterone
- High fat, low fiber diet
- Obesity (high estrogen levels in fat)

Causes of hereditary susceptibility to breast cancer

Sporadic

Hereditary

BRCA1 (~70%)

BRCA2 (~20%)

Other single HNPCC genes (~8%) (~2%)
Incidence/prevention

• Overall rate of BRCA mutations
  • In the general population, 1 in 800
  • In the Ashkenazi Jewish population, 1 in 40 carry one of three specific mutations: two in BRCA1 and one in BRCA2
• Other populations, Icelanders, French Canadians, Scandinavian Cohorts, all have their own specific mutations.
• Interventions
  • Prophylactic mastectomy (>90%)
  • Prophylactic oophorectomy (~60%)
  • New screening techniques, e.g. MRI
  • Chemoprevention (not proven)

ONCOLOGY question #5

A 44 year old premenopausal woman in your practice palpates a marble-sized lump in the outer aspect of her left breast while showering. Mammography confirms a 2 cm spiculated lesion corresponding to the palpable area. Needle biopsy reveals an infiltrating ductal carcinoma. She comes to you to discuss her surgical options. You inform her that:

A. Breast conserving surgery (lumpectomy) is absolutely contraindicated because of the large size of the tumor
B. If sentinel lymph node biopsy reveals a positive sentinel node, modified radical mastectomy will be necessary
C. Axillary lymph node dissection is typically performed with a lumpectomy, but not with a modified radical mastectomy
D. Her chances of long-term survival will be similar whether she chooses breast conserving surgery plus radiation or modified radical mastectomy
E. A significant portion of her pectoralis muscle will have to be stripped if she opts for a modified radical mastectomy

ONCOLOGY question #6

The patient above ultimately opts for a breast-conserving approach with axillary lymph node dissection. Surgical pathology findings show a 1.9 cm infiltrating ductal carcinoma, ER/PR positive, Ki67 of 30%, and Her2/neu negative by FISH. 0 out of 29 lymph nodes are positive for carcinoma. She asks you the implications of these pathologic findings. Which of the following would be an incorrect thing to tell her?

A. Expression of hormone receptors is indicative of better prognosis.
B. She has stage I (T1N0) disease.
C. The lack of Her2/neu is an unfavorable prognostic feature, as she cannot receive Herceptin (trastuzumab).
D. She is an appropriate candidate for hormonal therapy.
E. The benefits she will receive from chemotherapy is less than that for a woman with node-positive disease.

ONCOLOGY question #7

The patient recovers uneventfully from her operation. Because of early stage disease, she opts not to receive adjuvant chemotherapy. However, her oncologist has recommended that she receive radiation followed by 5 years of tamoxifen. She is very concerned about short and long term risks. Which one of the following is NOT increased with use of tamoxifen?

A. Ovarian cancer
B. Endometrial cancer
C. Thromboembolic disease
D. Hot flashes
E. Cataracts
Breast cancer

- 1 in 9 women will develop breast cancer sometime in her lifetime
- Increased incidence until 1990, now stable
- Mortality has decreased about 1.8% per year since 1990 and continues to decrease
- Breast cancer is still the leading cause of death for women between the ages of 35 and 54 and the leading cause of cancer death in women over the age of 65

Surgical principles in breast cancer

- A large randomized trial (NSABP B-06) demonstrated no difference in survival between total mastectomy vs. lumpectomy
- Because local recurrence rates are higher following breast-conserving surgery, post-op radiation is routinely given in this setting
- Post-mastectomy radiation, on the other hand, remains controversial
- Two forms of breast reconstruction following mastectomy: TRAM (transverse rectus abdominal flap) or prosthetic implant
- Sentinel axillary node biopsy in clinically node-negative patients to diminish complications of axillary LND, including:
  - Lymphedema (occurs in up to 20% of patients)
  - Loss of cutaneous sensation
  - Decreased shoulder mobility
  - Axillary LND may be omitted in select pts with T1/T2 ER/PR+ pts with < 3 positive sentinel nodes

Contraindications to breast-conserving treatment

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<th>ABSOLUTE</th>
<th>Reason</th>
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<tr>
<td>First/second trimester of pregnancy</td>
<td>Need for postop XRT – dangerous for fetus</td>
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<tr>
<td>Multiple tumors in separate quadrants</td>
<td>Risk of leaving tumor behind, cosmetically impractical</td>
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<tr>
<td>Diffuse microcalcifications on mammography</td>
<td></td>
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<tr>
<td>RELATIVE</td>
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<tr>
<td>Large tumor/breast ratio</td>
<td>Cosmetically impractical</td>
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<tr>
<td>Tumor behind the nipple</td>
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<tr>
<td>Large breast size</td>
<td>Risk of fat necrosis, poor cosmetic outcome from XRT</td>
</tr>
<tr>
<td>Hx of collagen vascular disease</td>
<td>Poor healing with XRT</td>
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Prognostic parameters for breast cancer

(from Bland et al, 1995; Keyomarsi et al, 2002)

- Lymph node status **
- Tumor size
- Histologic/nuclear grade
- Lymphatic/vascular invasion
- Pathologic stage (TNM)
- Estrogen receptor status (ER/PR) [receptor-positive status more favorable]
- DNA content (ploidy, S-phase)
- Her2/neu status [overamplification is negative prognostic factor]
- Cyclin E status [low levels correlate with improved outcomes]
- Oncotype Dx (gene expression profiling)
Adjuvant chemotherapy for breast cancer
- Reduces risk of recurrence and risk of death across all subtypes, including:
  - Premenopausal and postmenopausal women (pre > post)
  - Node-positive and node-negative tumors
  - Hormone-receptor positive and negative tumors
  - Data equivocal for women > 70 y.o.
- Increasingly being used in neoadjuvant setting, especially for bulkier and node-positive tumors
- Commonly used chemotherapy agents: anthracyclines, cyclophosphamide, 5-FU, and taxanes
  - Duration is 4-6 months
  - Role for trastuzumab (Herceptin) in Her2-positive patients

Adjuvant hormonal therapy for breast cancer
- **Hormonal therapy**
  - **Pre-menopausal women**
    - Selective estrogen receptor blockade: anti-estrogenic effects on breast tissue, decreases growth stimulus for breast cancer cells
    - **Tamoxifen**
      - Can be used in all women with ER (+) tumors regardless of age, nodal status, or tumor size
      - Should be continued for 10 years instead of 5
    - Ovarian suppression + exemestane preferred in premenopausal women with high-risk features
  - **Post-menopausal women**
    - Aromatase inhibitors (block peripheral conversion of androgen into estrogen) x 5 years is preferred
      - Anastrazole (Arimidex), letrozole
    - Women that start tamoxifen should switch or complete additional 5 years of AI

Adjuvant hormonal therapy for breast cancer: tamoxifen
- **SIDE EFFECTS**
  - Hot flashes
  - Atrophic vaginitis
  - Endometrial cancer (2.2 per 1,000 women-year)
  - Thromboembolic disease (blood clots) → DVT, pulmonary embolus, stroke
  - Cataract formation
  - Retinopathy
  - In premenopausal women: irregular menses; pregnancy category D; decreased bone mineral density

Recommended screening during tamoxifen use:
- Annual pelvic exam (if uterus still present)
- Annual ophthalmologic evaluation

Follow-up monitoring and surveillance
- History and physical examination every 4-6 months x 5 years, then every 12 months
- Repeat mammography 6 months post-radiation, then annually thereafter
- No proven surveillance CT, CXR, blood work
- For women who maintain fertility, pregnancy appears to be safe
- For women who enter menopause, careful attention must be paid to bone mineral density as this may change rapidly
COLORECTAL CANCER

Screening: Colorectal

- 2016 USPSTF
  - Recommends screening using FOB, sigmoidoscopy, CT colonography, or colonoscopy beginning at age 50 years and continuing until age 75 (A)
  - Recommends against screening age 76-85. There may be considerations that support colorectal cancer screening in an individual patient (C)
  - Recommends against screening age >85 (D)
  - Evidence insufficient to assess CT colonography and fecal DNA testing (I)
- ACS
  - Starting age 50, one of the following: flex sig q5y, colo q10y, barium enema q5y, CT colonography q5y, FOB or FIT q1y

ONCOLOGY question #8
A 64 year-old African-American woman presents for screening colonoscopy. Colonoscopy shows a 3 cm ulcerated polyp at 40 cm; polypectomy reveals adenocarcinoma. Preop staging does not reveal any suggestion of metastases. A left hemicolectomy is performed without complications. Pathologic evaluation shows a moderately differentiated adenocarcinoma extending through the wall of the colon, with 2 of 18 lymph nodes involved. The patient is in your office after recovering from her surgery and is requesting advice regarding further therapy. What do you tell her?

A. She has stage III disease and will not benefit from chemotherapy.
B. She has stage II disease and will benefit from 12 months of chemotherapy.
C. She has stage IV disease and is essentially incurable.
D. She has stage III disease and will benefit from 6 months of chemotherapy.
E. She has stage III disease and should therefore receive both chemotherapy and radiation.

ONCOLOGY question #9
Three years later she is found to have two lesions in the left lobe of her liver. The rest of her staging work-up is completely normal. She is healthy, with an excellent performance status. She would like to be aggressive in treating her disease. What do you recommend?

A. Combination chemotherapy alone
B. Liver resection +/- chemotherapy
C. Hepatic radiation
D. Observation
E. Liver transplant
Cancer arises in polyps via multi-step carcinogenesis.

- High risk populations: screening (20-25 y.o. for known HNPCC, 40 for positive FHx), or 10 years prior to youngest age in immediate family.
- Risk factors:
  - High fat, low fiber diet
  - Inherited cancer syndrome (e.g. FAP, HNPCC)
  - Inflammatory bowel disease (e.g. ulcerative colitis)

Treatment of localized colon cancer

- En bloc surgical resection is mainstay of treatment – based on anatomical considerations
  - Lymph node drainage pattern
  - Vascular pedicle
  - Generally a hemi- or partial colectomy, with lymph node dissection, is the surgical procedure of choice.

- Role of adjuvant chemotherapy +/- XRT depends on tumor location and stage.

Johns Hopkins Gastroenterology and Hepatology Resource Center website: (http://hopkins-gi.jhmi.edu).

Staging system for colon cancer

- T1, T2, T3, T4:
  - T1: cancer limited to the mucosa or submucosa
  - T2: cancer invades through the muscularis propria
  - T3: cancer invades through the serosa, with regional lymph node metastases
  - T4: cancer invades adjacent structures

- N0 = no nodes; N1 = 1-3 (+) LNs; N2 = >4 (+) LNs

- M0 = no metastases; M1 = yes metastases

Adjuvant therapy for colon cancer: general principles

- 5-FU-based chemotherapy improves disease-free and overall survival rates for patients with node-positive (stage III) colon cancer:
  - Current gold standard is 5-FU, leucovorin, and oxaliplatin (FOLFOX) x 6 months.

- Much more controversial for patients with node-negative (stage II) disease:
  - Clinical features at presentation (bowel obstruction, perforation, invasion of adjacent organs) may influence decision.
  - Molecular predictors?

- No role for stage I.
Treatment: metastatic disease

- For patients with isolated liver metastases: resection of metastases can be curative in 20-30%
- Due to ‘closed’ portal venous circulation
- For unresectable disease, chemotherapy improves survival

Drugs available for metastatic colorectal cancer

- 1996:
  - 5-FU. That’s pretty much it.

- 2016:
  - 5-FU
  - Capecitabine (oral 5-FU)
  - Irinotecan
  - Oxaliplatin
  - Bevacizumab (anti-VEGF antibody)
  - Cetuximab, panitumumab (anti-EGFR antibody)
  - Regorafenib
  - TAS-102

MEDIAN SURVIVAL ~ 1 year
MEDIAN SURVIVAL over 2 years

ONCOLOGY question #10

A 34 year old woman comes to see you after a new diagnosis of colon cancer. Her diagnostic colonoscopy did not show any synchronous polyps. You discover that she has a strong family history of colon cancer, including a father who was diagnosed at age 40. Testing of her tumor specimen shows absence of the mismatch repair protein MLH1. Which of the following would not be an appropriate recommendation for her and her family members?

A. Her siblings should undergo screening colonoscopies beginning at age 20.
B. She should receive annual gynecologic screening, including transvaginal ultrasound and endometrial biopsy.
C. She should undergo chest CT scans every 6 months as surveillance for non-small cell lung cancer.
D. She should consider prophylactic TAH/BSO after she has completed childbearing.
E. Her siblings should consider germline testing for MLH1 mutations.

Hereditary colorectal cancer syndromes

- Comprise ~ 20% of all CRC cases
- Most common:
  - HNPCC (Lynch syndrome)
  - FAP (familial adenomatous polyposis)
- Less common:
  - Peutz-Jeghers
  - Cowden syndrome
  - MYH-associated polyposis
  - Juvenile polyposis
HNPCC (Lynch syndrome)
- Autosomal dominant condition caused by germ line mutation in mismatch repair genes (MSH2, MLH1, MSH6, PMS2 most common)
- Accounts for 3 to 5% of all colorectal cancer cases
- Prevalence estimate in general population somewhere between 1:350 to 1:1700
- Average age of onset = 44 years (vs. 64 years in sporadic CRC)
- > 80% penetrance
- More synchronous and metachronous CRC
- More likely right-sided
- Extracolonic manifestations – malignancies seen at higher rates in the following organs:
  - Endometrial
  - Gastric and small intestine
  - Biliary tract

Amsterdam criteria for the clinical diagnosis of HNPCC
- Three or more family members with colorectal cancer or other HNPCC-related cancer (endometrial, small bowel, ureter, renal pelvis)
- Two or more generations affected
- One affected relative must be a first-degree relative of two other affected relatives
- One or more affected before age 50 years
- Exclusion of familial adenomatous polyposis

Bethesda criteria to identify HNPCC families (less stringent than Amsterdam)
- At least one of the following must be present:
  - One member diagnosed with colorectal cancer before age 50 years
  - Presence of synchronous or metachronous colorectal or other HNPCC-associated tumors in an individual, regardless of age
  - Colorectal cancer with microsatellite instability (MSI-high) pathologic features diagnosed in an individual < 60 y.o.
    - Tumor-infiltrating lymphocytes
    - Overt’s like lymphocytic reaction
    - Mucinous/signet-ring differentiation
    - Medullary growth pattern
  - Colorectal cancer or other HNPCC-associated tumor diagnosed in at least 1 first-degree relative younger than 50 y.o., or in 2 first- or second-degree relatives at any age

LUNG CANCER
Screening: Lung

• National Lung Screening Trial (NEJM 2011)
  - Age 55-74, 30+PY
  - Randomized to CXR vs low dose CT (LDCT) annually x 3
  - Closed early by DSMB due to
    - 20% fewer lung cancer deaths
    - 7% less all-cause mortality

Screening: Lung

• 2013 USPSTF
  - Age 55-80, 30+PY, current smoker or quit within 15 years
  - Annual LDCT (until 15 years out or if unwilling/unable to undergo curative surgery)

• ACS
  - Age 55-74, 30+PY, current smoker or quit within 15 years, in good health- “might be a candidate”

ONCOLOGY question #11

A 56 year old woman who never smoked presents with a cough tinged with blood and mild shortness of breath. A CXR reveals multiple bilateral pulmonary nodules and mediastinal adenopathy. A CT scan confirms these findings in addition to a right adrenal lesion. A bronchoscopy with washings reveals neoplastic cells. What is the most likely diagnosis?

A. Squamous cell carcinoma
B. Small cell lung cancer
C. Adenosquamous carcinoma
D. Adenocarcinoma
E. Large cell lung cancer

ONCOLOGY question #12

She is otherwise well without co-existing co-morbidities. Her best treatment option consists of:

A. Surgical resection
B. Best supportive care
C. Mediastinal radiation
D. Systemic chemotherapy with a platinum-based combination
Lung cancer

- Leading cause of cancer deaths worldwide (1.1 to 1.3 million yearly deaths worldwide)
- Surpasses total # of deaths due to breast, colon, and prostate cancers – combined!
- Primary risk factor: cigarette smoking
  - 85% of patients with lung cancer are smokers
  - Responsible for 70% adenocarcinoma, 90% NSCL, 95% SCLC
  - Adenocarcinoma is responsible for more than half of lung cancers in non-smokers
- Other risks
  - Asbestos exposure (markedly enhanced if you also smoke)
  - Other industrial exposures

Types of lung cancer

2 major types:
- Non-small cell lung cancer (80-85%)
  - Adenocarcinoma (50%)
  - Squamous cell carcinoma (30%)
  - Large cell carcinoma (10%)
  - Bronchoalveolar carcinoma (3-5%)
  - Other (3-5%)
- Small cell lung cancer (15-20%)

NSCLC: stage at diagnosis

Standard therapeutic approaches for NSCLC

- **Stage I/II:**
  - Surgery: complete anatomical resection.
  - Adjuvant chemotherapy may be considered (not radiation).

- **Stage III:**
  - Surgery becomes increasingly unlikely (mediastinal LN involvement, contralateral or supraclavicular LNs, tumor invasion into mediastinum, chest wall, trachea, or great vessels).
  - Potentially trimodality, especially IIIA.
  - IIIIB: Concurrent chemoradiation > surgery or sequential

- **Stage IV:**
  - Systemic treatment: chemotherapy, immunotherapy, or targeted therapy
Management of advanced NSCLC

- Systemic therapy is the main modality. Surgery plays little or no role; radiation can be used for palliation.
- Chemotherapy
  - Should be reserved for patients with good performance status
  - Generally consists of platinum with one of a variety of other agents
  - Consideration of bevacizumab (anti VEGF)
- Targeted therapy
  - EGFR mutation → erlotinib
  - ALK rearrangement → crizotinib
  - ROS 1 rearrangement → crizotinib
- Immunotherapy
  - Nivolumab and pembrolizumab approved in second line setting
  - This is in flux; likely approval in front line setting within next 6 months

The most important variable in assessing whether patient is likely to benefit from chemotherapy: performance status

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<td>2002</td>
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<td>Japanese EGFR mutant NSCLC</td>
<td>30+</td>
<td>Gefitinib</td>
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ONCOLOGY question #13

A 68 year man with an 80 pack year smoking history presents with weakness and fatigue for the past 6 months. He has also noted an increase in his chronic cough with blood tinged sputum and a 10 lb weight loss. Laboratory studies reveal a sodium of 122 meq/L with otherwise normal electrolytes. Chest x-ray and CT reveal a large upper lobe mass with mediastinal adenopathy. A biopsy of the mass via the bronchoscope reveals cancer. What is the most likely diagnosis?

A. Adenocarcinoma
B. Adenosquamous carcinoma
C. Large cell carcinoma
D. Small cell carcinoma
E. Squamous cell carcinoma
ONCOLOGY question #14

The patient’s neurologic exam is as follows:

- A+O x 3
- Speech clear and articulate
- Cranial nerves symmetrically intact
- Notable hyporeflexia, esp. in the LEs, with significant bilateral proximal muscle weakness

What do you think might be a likely cause for his neurologic symptoms?

A. Diffuse bilateral cerebral metastases
B. An elevated serum calcium level
C. An autoantibody directed against antigens of the neuromuscular junction
D. A solitary brainstem metastasis
E. An excess production of ACTH producing a Cushing’s-like syndrome

ONCOLOGY question #15

The patient demonstrates a near-complete response to chemoradiation and tolerates treatment reasonably well. However, three months later, you get an urgent phone call from his wife, who states that her husband’s face has become red and swollen, and that he has been having increasing difficulty breathing. You are concerned about the possibility of a locally recurrent tumor and its potential local mass effects. Which of the following could be a cause of your patient’s symptoms?

A. Tumor invasion of lower brachial plexus (C8, T1) by an apical tumor.
B. Recurrent laryngeal nerve entrapment from an invasive mediastinal tumor.
C. Phrenic nerve entrapment from an invasive mediastinal tumor.
D. Involvement of stellate ganglion by an apical tumor.
E. Decreased venous return from the head and neck from an invasive mediastinal tumor.

Small cell lung cancer staging

• Staging: 2 major categories:
  
  - Limited Stage: Defined as disease confined to one hemithorax. Or disease confined to a single radiation field (30-40%)
  - Extensive stage: Defined as disease outside of a single hemithorax (or radiation port) (60-70%)

  Staging evaluation should include brain imaging

Small cell lung cancer

Standard approach:

• Limited:
  - Chemotherapy x 4-6 cycles
  - Concurrent RT
  - Surgery for responders
  - Prophylactic cranial irradiation
  - 2 yr survival: 20-25%

• Extensive:
  - Chemotherapy
  - Median survival: 9 mo, 2 yr survival: 5%
Paraneoplastic syndromes associated with SCLC

- May be the initial presenting symptom
- Most common paraneoplastic syndromes include
  - Hyponatremia (SIADH)
  - Hypertrophic osteoarthropathy
  - Ectopic ACTH secretion
  - Eaton-Lambert
    - Production of auto-antibodies directed against the presynaptic voltage gated Ca channels of the neuromuscular junction.
    - Classical findings: proximal muscle weakness resulting in decreased ability to perform basic motor tasks; autonomic dysfunction (thus the patient’s dry mouth); and hyporeflexia.
  - Subacute cerebellar degeneration
- Respond to effective treatment of underlying malignancy

Syndromes associated with lung cancer (both SCLC and NSCLC)

1) Pancoast’s syndrome - shoulder pain and ulnar neuropathy due to invasion of lower brachial plexus (C8, T1) by an apical tumor
2) Hoarseness due to recurrent laryngeal nerve entrapment from invasive mediastinal tumors
3) Diaphragmatic paralysis due to phrenic nerve entrapment from invasive mediastinal tumors
4) Horner’s syndrome - invasion of stellate ganglion by an apical tumor
5) Superior vena cava syndrome - compression of the SVC by invasive mediastinal tumors

Screening: Prostate

US Preventive Services Task Force

- 2012
  - The USPSTF recommends against PSA-based screening for prostate cancer (D)
Prostate cancer screening

- Lack of consensus among different medical organizations
  - American Cancer Society: recommend discussing pros/cons of PSA +/- DRE to men over 50
  - Begin screening younger (45) if a positive family history (at age <65) or if African American
  - Frequency to depend on PSA
  - American Urological Association: Updated 2013 guidelines
    - No PSA <40 years old
    - No PSA 40-54 years old if average risk
    - Ages 55-69 should undergo shared decision making
    - Routine interval 2+ years might be considered
    - No PSA 70+ or with life expectancy <10 years
  - If either test is abnormal, diagnosis is made through transrectal ultrasound (TRUS) and prostate biopsy

ONCOLOGY question #16
A 68 year old man is diagnosed with localized prostate cancer, Gleason grade 4+3. The patient wants to consider the possibility of a radical prostatectomy. What should his urologist tell him to expect with this operation?

A. Because of the high likelihood of cure, postoperative monitoring of PSA levels will not be necessary after two years
B. Surgery produces lower cure rates for localized prostate cancer compared to either brachytherapy or external beam radiation.
C. Nerve-sparing surgical approaches can often help preserve erectile function postoperatively, especially in younger men
D. The preferred operation for early stage prostate cancer is performed transurethrally (through the penile urethra)
E. Permanent urinary incontinence is almost inevitable following this operation

ONCOLOGY question #17
Following radical prostatectomy, the patient’s PSA is undetectable. Two years later his PSA begins to rise, from 2.7 to 8.9 to 20.1 ug/L over a 6-month period. You decide to initiate therapy with combined androgen blockade (LHRH agonist + anti-androgen rx). Which of the following is not a side effect of androgen deprivation therapy?

A. Anemia
B. Loss of libido
C. Alopecia
D. Osteoporosis
E. Hot flashes

ONCOLOGY question #18
The patient’s PSA declines to undetectable range on combined-androgen blockade, but then starts rising again after a year. He remains relatively asymptomatic. Your next step is to:

A. Start chemotherapy
B. Increase the dose of the LHRH agonist
C. Stop the anti-androgen agent
D. Offer strontium-89 therapy for presumed skeletal metastases
E. Continue on therapy, as this is likely a ‘flare’ phenomenon
**Risk factors for prostate cancer**

- **Age** - Autopsy series: 30% in 30s / 60% in 60s.
- **Family History** - 10%+ of cases are hereditary.
- **Race**
  - African Americans: Higher than caucasians.
  - Asian and Hispanic: Lower risk than caucasians.
- **Geography?**
- **Diet?**
- **Hormones** - Higher testosterone levels increase risk.

**Gleason score**

- Assessment of histological appearance
- Graded on a scale of 1-5
- Expressed as the sum of two scores: most common and second common
  - i.e. 3+4=7
- Low risk: ≤ 6
- Intermediate risk: 7
- High risk: 8-10
- Predictor of outcome

**Clinical states in prostate cancer**

- No Cancer
- Localized Disease
- Rising Risk
- Hormone Naïve Metastasis
- Hormone Refractory Metastasis
- Death From Non-Prostate Causes
- Death From Disease

- ~ 190,000 New Cases / Year
- ~ 60,000 New Cases / Year
- ~ 27,000 deaths / year

**Treatment options for localized prostate cancer**

- **Radical prostatectomy**
  - Urinary incontinence (60-65% with varying degrees)
  - Impotence (56-65% inability to have erection sufficient for intercourse; statistically better odds with nerve-sparing approach)
  - Fecal incontinence
  - Urinary stricture
- **Radiation therapy**
  - Proctitis, cystitis, enteritis
  - Compared to surgery, better rates of urinary and sexual function, but more problems with bowel function (e.g. rectal urgency)
- **Active surveillance**
  - Increasing utilization for low/low-intermediate risk cancer
  - Androgen deprivation therapy (palliative intent only)
Hormonal therapy

**CLINICAL CONTEXTS**
- Primary therapy for metastatic disease
  - Rising PSA without evidence of disease (no evidence of survival benefit)
- Visible disease
- Adjuvant/neoadjuvant therapy for high risk disease
  - Node positive, large size, high PSA and/or Gleason score

**DEFINITIONS**
- Castration-sensitive: Responsive to therapies that decrease testosterone levels or block the cellular action of testosterone
- Castration-resistant: Rising PSA/disease progression despite serum testosterone < 50 ng/dL, but often still responsive to further hormonal therapies

---

**Side effects of androgen deprivation therapy**

<table>
<thead>
<tr>
<th>Physical</th>
<th>Metabolic/physiologic</th>
<th>Emotional/cognitive</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gynecomastia</td>
<td>Loss of bone (osteoporosis)</td>
<td>Depression</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Weight gain</td>
<td>Lipid changes</td>
<td>Emotional lability</td>
<td>Hot flashes</td>
</tr>
<tr>
<td>Loss of muscle mass, strength</td>
<td>Diabetes</td>
<td>Spatial memory</td>
<td>Loss of libido</td>
</tr>
<tr>
<td>Decreased size penes, testes</td>
<td>Cardiovascular disease</td>
<td>Other cognitive changes</td>
<td>Erectile dysfunction</td>
</tr>
<tr>
<td>Hair changes</td>
<td>Anemia</td>
<td></td>
<td>Lack of initiative</td>
</tr>
</tbody>
</table>

---

**Androgen deprivation therapy and impact on cardiovascular disease risk factors**

- Development of insulin resistance → follow for potential diabetes
- Changes in body composition: increased fat mass, decreased lean body mass → recommend resistance exercises
- Alterations in lipid metabolism (elevated LDL, triglycerides, HDL) → follow lipid panels
- Increased arterial stiffness, hypertension → follow BPs
- Majority of studies demonstrate increased risk of cardiovascular disease, particularly in those with pre-existing CVD

---

**Secondary hormonal maneuvers**

- Trial of **antiandrogen withdrawal** is most common first step after failure of combined androgen blockade.
  - Response proportion to antiandrogen withdrawal is ~15%, with median duration of 3 to 5 months
- After this: for men with still relatively indolent disease, can try:
  - a second anti-androgen agent - enzalutamide
  - adrenal anti-androgen e.g. abiraterone, ketoconazole, estrogen
ONCOLOGY question #19

A patient with a h/o prostate cancer, s/p XRT with PSA recurrence and now on combined-androgen blockade, presents to the E.R. with pain to palpation at T9-10. Strength testing shows generalized moderate weakness of the lower extremities and numbness at the T9 dermatome. DTRs are diminished. An emergent MRI is obtained which shows a 3 cm epidural mass compressing the spinal cord at T9 with associated vertebral bony destruction. After giving him a dose of decadron, what is the most effective intervention?

A. Radiation therapy
B. Emergent neurosurgical decompression with postop XRT
C. Chemotherapy
D. Referral to hospice
E. Withdrawal of the anti-androgen agent
Recognition of spinal cord compression: an oncologic emergency

- Lung, breast, prostate, and kidney most common
- Permanent loss of neurologic function can occur if the pressure of the tumor on the cord is not relieved quickly
- 90% of patients present with back pain as primary symptom
- Constipation and urinary retention are early indicators of autonomic nerve damage
- Start steroids to reduce swelling
- Recent randomized phase III study showed superior outcomes in patients treated with neurosurgical decompression + XRT vs. XRT alone

ONCOLOGY question #20

A 39 year old man with widely metastatic small cell lung cancer is started on chemotherapy with cisplatin and etoposide. Which of the following laboratory/clinical abnormalities would you not expect to see associated with tumor lysis syndrome?

A. Hyperuricemia  
B. Hypocalcemia  
C. Oliguric renal failure  
D. Hyperphosphotemia  
E. Hypokalemia

ONCOLOGIC EMERGENCIES (or at least semi-urgent situations)

- Tumor lysis syndrome
  - Rapid release of intracellular contents into bloodstream at life-threatening concentrations
  - High-grade lymphomas, leukemias, less commonly solid tumors
- Malignant hypercalcemia
  - Multiple myeloma, squamous cell NSCLC
  - Most common etiologies: humorally mediated (PTH-related peptide) and osteolytic (bone metastases)

ONCOLOGIC EMERGENCIES (or at least semi-urgent situations)

- Superior vena cava (SVC) syndrome
  - Primary lung, lymphoma, and metastatic to lung (breast, testicular)
  - Rx includes radiotherapy, chemotherapy; also anticoagulation, thrombolysis, stenting
- Venous thromboembolic events
- Febrile neutropenia
Febrile neutropenia

- ANC < 1500 (multiply the WBC by the (% neutrophils + % bands)
- ANC < 500 - severe neutropenia
- Fever > 38.3 degrees C or > 38 degrees for > 1 hour
- For milder neutropenia without localizing signs of infection, oral outpatient therapy in a compliant patient may be reasonable (cipro/augmentin; levofloxacin)
- For higher risk, randomized trials have shown single agent ceftazidine is as effective as multi-agent regimens, and is less costly.
- Persistent fevers
  - Add vancomycin if a port/indwelling vascular access is in place
  - Broaden gram negative coverage for mucosal breakdown
  - Add fungal coverage

Indications for myeloid growth factor support

- **G-CSF** (filgrastim, Neupogen)
  - Secondary prophylaxis in patients with prior episode of febrile neutropenia or treatment delay secondary to prolonged neutropenia
  - Patients with febrile neutropenia at high risk of clinical deterioration (pneumonia, sepsis, fungal infx.)
  - Primary prophylaxis in chemotherapy regimens highly likely to produce febrile neutropenia (ASCO guidelines: risk > 20% with regimen)
  - High risk populations (elderly pts, significant co-morbid conditions)
- **Pegfilgrastim** (Neulasta)
  - Given once with every three week cycle of chemotherapy
  - Cost equivalent to 8-10 doses of G-CSF

ONCOLOGY question #21

A patient with metastatic testicular cancer initiates chemotherapy consisting of the combination of bleomycin, etoposide, and cisplatin. 6 weeks into treatment he comes to your office with a dry cough, dyspnea, and fevers. What is the most likely cause of his symptoms?

A. Pneumocystis carinii pneumonia
B. Development of pulmonary metastases
C. Chemotherapy-induced pneumonitis
D. Secondary lung cancer
E. Chemotherapy-induced cardiac toxicity

Recognizing unique chemotherapy-associated complications

<table>
<thead>
<tr>
<th>CYTOTOXIC AGENTS</th>
<th>Cardiotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthracyclines</td>
<td></td>
</tr>
<tr>
<td>Platinum compounds, taxanes, vinorelbine</td>
<td>Peripheral sensory neuropathy</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Nephrotoxicity, ototoxicity</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Infusion-related anaphylaxis, pneumonitis</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Edema</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Interstitial pneumonitis</td>
</tr>
</tbody>
</table>
You should also be familiar with common toxicities associated with some of the newer targeted agents!

<table>
<thead>
<tr>
<th>Targeted agent</th>
<th>Target</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab, sunitinib, pazopanib</td>
<td>VEGF</td>
<td>Hypertension, bowel perforation, arterial thromboembolic events</td>
</tr>
<tr>
<td>Trastuzumab, lapatinib</td>
<td>HER2</td>
<td>Cardiac toxicity</td>
</tr>
<tr>
<td>Gefitinib, erlotinib</td>
<td>EGFR</td>
<td>Rash</td>
</tr>
<tr>
<td>Everolimus</td>
<td>mTOR</td>
<td>Pneumonitis</td>
</tr>
<tr>
<td>Nivolumab, pembrolizumab</td>
<td>PD-1/PD-L1</td>
<td>Immune-related AEs (colitis, pneumonitis, adrenal insufficiency, parathyroid)</td>
</tr>
<tr>
<td>Vemurafenib, dabrafenib</td>
<td>BRAF</td>
<td>Skin – SCCa, keratoacanthoma</td>
</tr>
</tbody>
</table>

**ONCOLOGY question #22**

A 50 year old gentleman is preparing to start cisplatin-based chemotherapy for metastatic bladder cancer. Which of the following regimens is most appropriate to help control his emesis?

A. Metoclopramide + dronabinol  
B. Prochlorperazine + dexamethasone  
C. Ondansetron  
D. Ondansetron, dexamethasone, + aprepitant  
E. Olanzepine + aprepitant

**ONCOLOGY question #23**

A 64 year old man with metastatic pancreatic cancer has refractory epigastric pain radiating to the back. He is using oxycodone 5-10 mg every 3-4 hours. Which of the following steps would be the least appropriate to help with his analgesia?

A. Referral to pain clinic for consideration of celiac plexus block (neurolysis)  
B. Addition of fentanyl transdermal patch at (50 ug/hr)  
C. Addition of hydrocodone/APAP (Vicodin) 5/500 as needed in between the oxycodone doses  
D. Addition of oxycodin 10-20 mg twice-daily  
E. Consider addition of muscle relaxant and/or lorazepam

**ONCOLOGY question #24**

A 77 year old woman has chronic anemia (Hb 10.5) following completion of chemotherapy for ovarian cancer 6 months ago. She is asymptomatic and has a history of NIDDM, gout, and HTN. She asks you whether she should start on an erythropoiesis-stimulating agent (ESA). What do you tell her?

A. Yes, because it is indicated in anemia of chronic disease (ACD) and will improve your functional status.  
B. No, because it can precipitate gouty flares.  
C. Yes, because it is indicated in anemia of chronic disease (ACD) and can secondarily help with glycemic control.  
D. No, because she likely has an underlying myelodysplastic syndrome that would make ESAs contraindicated.  
E. No, because it should only be used up to 8 weeks following completion of chemotherapy and can be associated with thromboembolic and cardiovascular events.
Nausea and vomiting in cancer patients
- 3 types: acute, delayed, anticipatory
- Classes of anti-emetic agents
  FOR PROPHYLAXIS AND TREATMENT OF ACUTE/DELAYED NAUSEA
  **High therapeutic index** (for chemorx with moderate to high emetogenic potential, e.g., platinum-based, cyclophosphamide)
  - 5-HT3 antagonists: ondansetron (Zofran), granisetron (Kytril)
  - Corticosteroids (dexamethasone)
  - Neurokinin-1 receptor antagonists: aprepitant (Aprendeptant)
  **Lower therapeutic index** (for chemorx with low emetogenic potential)
  - Dopaminergic antagonists: phenothiazines (prochlorperazine), metoclopramide
  - Cannabinoids
  - Olanzapine (Zyprexa)
  FOR ANTICIPATORY NAUSEA
  - Benzodiazepines may be helpful

Pain management of cancer patients
- ~60% of patients with any stage of disease experience significant pain
- Pharmacologic treatment
  - Nonopioid analgesics
  - Opioids
    - No ceiling effects
    - Limited by side effects (sedation, constipation, etc.)
    - Likely development of physical dependence and tolerance; tapering is essential
  - Recommended strategy: combine long-acting analgesic for RTC pain control, + short-acting for breakthrough pain
  - Adjuncts
    - Antidepressants, anxiolytics, muscle relaxants, anticonvulsants

Pain management of cancer patients
Nonpharmacologic approaches
- local anesthetic blocks +/- steroids
- neurolytic/neuroablative blocks
- spinal analgesics
- radiation for skeletal metastases

Other supportive care issues: erythropoietin in cancer patients
- Concerns re: thromboembolic and cardiovascular risk, esp. when targeting a Hgb > 12 g/dL
- Decreases need for PRBC transfusions, but this may not necessarily translate into improvement in QOL
- Some studies have suggested shorter time to tumor progression and higher risk of death in patients receiving ESAs
- Current recommendations and coverage limit usage to patients actively receiving palliative chemotherapy (and up to 8 weeks after final dose)
  - Only initiate when Hgb < 10 g/dL; target is between 10-11 g/dL
A 31 year old male undergoes orchiectomy for a painful left testicular lump. Serum markers show elevated levels of both AFP and β-HCG. Additional therapy may consist of __________ for a presumptive diagnosis of ___________.

A. Radiation; seminoma
B. Radiation; non-seminomatous germ cell tumor (NSGCT)
C. Chemotherapy; NSGCT
D. Chemotherapy; seminoma
E. Retroperitoneal lymph node dissection; seminoma

**TESTICULAR CANCER**

**Serum Markers**

- HCG
  - Half-life 24 hours
  - Elevated with seminoma and NSGCT
- AFP
  - Half-life 5-7 days
  - Elevation means to treat as NSGCT, regardless of pathology
- LDH
  - General marker of tumor volume

**TESTICULAR CANCER**

**Risk Factors**

- Cryptorchidism
  - Relative risk: 3-14 fold higher than patients with bilateral descended testicles
  - If unilateral, 5-25% in normally descended testicle
  - 6-14% incidence of testicular cancer in patients with cryptorchidism
  - Orchietomy does not alter risk
- Kleinfelter’s syndrome
- Inguinal hernia?
TESTICULAR CANCER
Treatment: Stage I NSGCT

- Observation: 13-35% Relapse
- Risk Factors: ECC, LVI
- Nerve-sparing possible
- Chemotherapy

Stage I NSGCT
RPLND: 85% with Stage II cured
95% antegrade ejaculation
2-3% Relapse

ONCOLOGY question #26
A 60 year old woman who has been your patient for many years asks you about ovarian cancer screening. Her best friend is under treatment and suggested that she have twice annual CA-125 screening the patient has also read about this on the Internet. She has no family history of breast or ovarian cancers. You recommend:

A. Annual gynecologic examination
B. Annual CA125 levels
C. Annual pelvic ultrasound with CA125
D. A baseline CT scan with CA125
E. Sampling of peritoneal washings

Ovarian cancer:
screening recommendations
- USPSTF 2012: Recommends against screening
- Other approach:
  - Comprehensive family history on all patients
  - None or 1 family member
    - Annual rectovaginal pelvic exam
  - 2 or more family members
    - Genetic counseling
    - Annual rectovaginal pelvic exam, CA125, transvaginal ultrasound
  - Routine screening with CA125 and transvaginal US is not proven to be beneficial

ONCOLOGY question #27
Of the following malignancies of the upper-GI tract, which one has been rising the most in incidence in the United States over the past several decades?

A. Distal gastric cancers among Caucasian males
B. Squamous cell esophageal cancers among African-American males
C. Gastric-oesophageal junction adenocarcinomas among Caucasian males
D. Duodenal adenocarcinomas among Asian-American males
E. Squamous cell esophageal cancers among Caucasian males
Esophageal/gastric cancer: the changing face of esophageal cancer in the United States

- >350% increase in incidence of adenocarcinoma in white males since mid-1970s: now more common than squamous cell
- Most common site: GE junction
- Possible explanations:
  - Increasing incidence of obesity (GERD → Barrett’s esophagus?)
  - Dietary factors
  - Reclassification of gastric cardia cancers as esophageal cancers
  - NO increased risk from H. pylori (Devesa et al., Cancer 1998)

ONCOLOGY question #28

H. pylori infection may be associated with an increased risk of all of the following malignancies except for:

A. Gastric body adenocarcinoma
B. Pancreatic adenocarcinoma
C. Esophageal adenocarcinoma
D. Gastric lymphoma/MALToma

Esophageal/gastric cancer: association between gastric cancer and H. pylori

- H. pylori affects 30-40% of the U.S. population
- Rates even higher in the developing world
- Most affected individuals remain asymptomatic
  - 15% develop gastric/duodenal ulcer disease
  - ≤1% develop gastric cancer
- H. pylori felt to be responsible for 53-60% of all gastric cancers worldwide
  - Reduction in the incidence of gastric cancer parallels the decrease in H. pylori infection
  - Classified as a group I carcinogen by WHO
- Conversely, the presence of H. pylori may be protective against development of esophageal cancer

ONCOLOGY question #29

Which of the following is not a known risk factor for malignant melanoma?

A. Fair skin
B. Family history of melanoma
C. History of topical retinoid use
D. Presence of congenital nevi
E. History of severe sunburns
Malignant melanoma

- Remember your ABCD’s (asymmetry, borders, color, diameter)
- High risk patients:
  - Family history
  - Fair skin
  - Unusual moles or changing mole patterns
  - History of childhood sunburns

ONCOLOGY question #30

Which of the following is not an AIDS-defining malignancy?
A. Anal cancer
B. Cervical cancer
C. Non-Hodgkin’s lymphoma
D. Kaposi sarcoma
E. All of the above are AIDS-defining cancers

Cancers associated with AIDS

<table>
<thead>
<tr>
<th>AIDS-defining</th>
<th>Higher than average risk, but not AIDS-defining*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaposi’s sarcoma</td>
<td>Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>Lung</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>Penis</td>
</tr>
<tr>
<td>Larynx</td>
<td>Oral cavity/lip</td>
</tr>
<tr>
<td>Others: soft tissue sarcomas, testicular seminoma, liver, pancreas, larynx</td>
<td></td>
</tr>
</tbody>
</table>


ONCOLOGY question #31

In which of the following tumor types does definitive treatment typically NOT involve surgical resection?
A. Adenocarcinoma of the rectum
B. Adenocarcinoma of the esophagus
C. Adenocarcinoma of the stomach
D. Squamous cell carcinoma of the anus
E. Carcinoid tumor of the small bowel
Anal cancer

- Associated with HPV infection – patients with pre-existing anal condylomata, dysplasia at increased risk
- Definitive therapy consists of concurrent chemotherapy (mitomycin/5-FU) plus radiation – this has replaced surgery (which requires permanent colostomy) as the standard of care
- Cure rates 60-70%
- Success seen in both HIV (+) and (-) patients, although greater treatment-related toxicities in HIV (+) patients with CD4 count < 200

ONCOLOGY question #32

You are following a 40 year old woman who underwent a liver transplant 4 years ago for primary sclerosing cholangitis. Her current immunosuppressive regimen consists of mycophenolate mofetil (Cellcept) and tacrolimus. Which of the following malignancies is she not at increased risk for?

A. Kaposi sarcoma
B. Non-Hodgkin’s lymphoma
C. Non-melanoma skin cancer
D. Breast cancer
E. Vulvar carcinoma

Common post solid organ transplant malignancies

- Skin/lip
- Lymphoma/PTLD
- Anogenital tract
- Kaposi sarcoma
- Kidney
- Hepatobiliary
- Sarcoma

ONCOLOGY question #33

Which of the following head and neck cancers is associated with Epstein-Barr virus infection?

A. Nasopharyngeal carcinoma
B. Tonsillar carcinoma
C. Tongue carcinoma
D. Hypopharyngeal carcinoma
E. Lip carcinoma
ONCOLOGY question #34

A 64 yof has a recent non-volitional 10-lb weight loss. You perform a CT scan that reveals a 2 cm mass in the pancreatic body. On physical examination, you appreciate erythematous patches and plaques over the trunk and thighs, some areas of which are forming bullae. You suspect that she has a pancreatic that may be secreting:

A. Insulin  
B. Glucagon  
C. Vasoactive intestinal peptide (VIP)  
D. Gastrin  
E. Somatostatin

ONCOLOGY question #35

Imatinib (Gleevec) is a cancer drug used in the treatment of chronic myelogenous leukemia (CML) and gastrointestinal stromal tumors (GIST). This drug is:

A. A monoclonal antibody that blocks epidermal growth factor receptor signaling  
B. A liposomal formulation of a taxane compound  
C. An orally bioavailable small molecule inhibitor of tyrosine kinase activity  
D. An autologous vaccine derived from a patient’s own tumor cells  
E. An antisense molecule directed against a commonly mutated oncogene

Functional islet cell tumors – clinical manifestations

<table>
<thead>
<tr>
<th>Type</th>
<th>Signs/symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulinoma</td>
<td>Hypoglycemia (dizziness, seizures, loss of consciousness, confusion)</td>
</tr>
<tr>
<td>Glucagonoma</td>
<td>Hyperglycemia, necrotizing migratory erythema</td>
</tr>
<tr>
<td>VIPoma</td>
<td>Watery diarrhea, hypokalemia, hypophosphatemia, hyperchlorectricemia</td>
</tr>
<tr>
<td>Gastrinoma</td>
<td>Refractory peptic ulcers (Zollinger-Ellison), diarrhea</td>
</tr>
<tr>
<td>Somatostatinoma</td>
<td>Hyperglycemia, diarrhea, cholelithiasis</td>
</tr>
</tbody>
</table>

Targeted agents in oncology

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoclonal antibodies</td>
<td>Rituximab (anti-CD20)</td>
<td>NHL</td>
</tr>
<tr>
<td></td>
<td>Trastuzumab (anti-Her2/neu)</td>
<td>Breast</td>
</tr>
<tr>
<td></td>
<td>Bevacizumab (anti-VEGFR)</td>
<td>Colon, lung, breast</td>
</tr>
<tr>
<td></td>
<td>Cetuximab (anti-EGFR)</td>
<td>Colon, head and neck</td>
</tr>
<tr>
<td>Small molecule inhibitors</td>
<td>Imatinib (BCR-ABL, KIT)</td>
<td>CML, GIST</td>
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<tr>
<td></td>
<td>Erlotinib (EGFR)</td>
<td>NSCLC, pancreas</td>
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<td></td>
<td>Sorafenib (VEGFR, Raf K)</td>
<td>RCC, HCC</td>
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<tr>
<td></td>
<td>Sunitinib (VEGFR, C-KIT, PDGFR)</td>
<td>RCC, GIST</td>
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</table>
APPENDIX: ‘Nuts and bolts’ information about other malignancies

- Testicular
- Gynecologic
  - Ovarian
  - Cervical
  - Endometrial
- Pancreatic
- Bladder
- Melanoma
- Cancers of unknown primary

TESTICULAR CANCER

**Incidence**

- Peak age 15-44 years
  - Most common solid malignancy in young men
- Cure rate exceeds 90%
  - 300-400 deaths/year
- 0.2% likelihood during lifetime
- Rare in African Americans
- 2% bilateral

**Evaluation**

- Imaging of primary lesion
- Serum tumor markers
  - HCG
  - Alpha-fetoprotein
  - LDH
- Metastatic evaluation
  - Chest
  - Abdomen
  - Pelvis
TESTICULAR CANCER
Treatment: Seminoma

- Seminoma
  - Low Stage
    - Observation: 15-20% Relapse
  - High Stage
    - Radiation: 2% Relapse
    - RPLND or resection if any residual mass > 3 cm

- Chemotherapy Stages IBC

TESTICULAR CANCER
Treatment: Stage I NSGCT

- Stage I NSGCT
  - Observation: 13-35% Relapse
  - RPLND: 65% with Stage II cured
  - Chemotherapy: 2-3% Relapse

- Risk Factors: ECC, LVI
  - Nerve-sparing possible
  - 95% antegrade ejaculation

TESTICULAR CANCER
Risk Groups for Advanced Disease

- NSGCT
  - Good Prognosis
    - HCG < 50,000, AFP < 1000, LDH < 1.5 normal
    - No non-pulmonary metastases
  - Intermediate Prognosis
    - HCG 5000-50,000, AFP 1000-10,000, LDH 1.5-1.5 normal
    - Non-pulmonary metastases
  - Poor Prognosis
    - HCG > 50,000, AFP > 10,000, LDH > 1.5 normal
    - Non-pulmonary metastases
    - Mediastinal primary

- Seminoma – BEST PROGNOSIS
  - Good Prognosis
    - No metastases outside of lung
    - Any markers
  - Intermediate Prognosis
    - Metastases outside of lung
    - Any markers
  - Poor Prognosis
    - None

Chemotherapy for testicular cancer

- Standard chemotherapy consists of 2-4 cycles of PEB (cisplatin, etoposide, bleomycin)
- Major toxicity to be aware of: bleomycin-associated pulmonary fibrosis
- Long term cardiovascular and second-malignancy risk
- Mortality from treatment is < 0.1%
- Salvage therapy works approx 30% of the time
  - 20% – 40% of patients with relapsed GCT can be cured with high dose chemotherapy/stem cell transplant
Ovarian cancer

- Second most common gynecologic malignancy in the US
- Most lethal gynecologic malignancy
- 70% of patients present with advanced disease
- Majority are epithelial in origin
  - Rare germ cells and stromal tumors

Ovarian cancer: risk factors

<table>
<thead>
<tr>
<th>Increase</th>
<th>Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>OCPs</td>
</tr>
<tr>
<td>Family history</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Infertility/low parity</td>
<td>Tubal ligation</td>
</tr>
<tr>
<td>Personal cancer history</td>
<td>Breast-feeding</td>
</tr>
</tbody>
</table>

Ovarian cancer: screening recommendations

- USPSTF 2012: Recommends against
- Other approach:
  - Comprehensive family history on all patients
    - None or 1 family member
      - Annual rectovaginal pelvic exam
    - 2 or more family members
      - Genetic counseling
      - Annual rectovaginal pelvic exam, CA125, transvaginal ultrasound
      - Consider clinical trial participation
  - Routine screening with CA125 and transvaginal US is not proven to be beneficial

Ovarian cancer: surgical rx

- For early stage disease: TAH/BSO plus adequate staging (includes pelvic and aortic lymph node sampling, omentectomy, random peritoneal biopsies)
  - In younger women, reproductive conservation may be appropriate for very early stage disease
  - Approximately 30% will have histologic evidence of metastatic disease

- For advanced stage disease: En bloc resection of uterus, ovaries and pelvic tumor, removal of diaphragmatic and peritoneal implants, +/- bowel resection, splenectomy
  - Significant survival advantage for women optimally cytoreduced
**Ovarian cancer: chemotherapy**

- Chemotherapy given for all but the lowest stage cancer
  - All patients should receive a taxane and a platinum
  - Response rate is high (> 70%)
- Intraperitoneal chemotherapy for optimally debulked ovarian cancer improves survival
- Median survival: 38 months for stage III/IV
- 75% of patients relapse
  - Treatment options include additional surgical cytoreduction, additional chemotherapy

**Cervical cancer: #1 leading cause of cancer mortality in women worldwide (500,000 annually)**

**RISK FACTORS:**

- Early age of intercourse
- Number of sexual partners
- Smoking
- Lower socioeconomic status
- High-risk male partner
- Other sexually transmitted diseases
- Up to 50% of the U.S. population is infected with HPV

**Cervical cancer: etiology**

- Cervical cancer is a sexually transmitted disease.
- HPV DNA is present in virtually all cases of cervical cancer and precursors.
- Some strains of HPV have a predilection to the genital tract and transmission is usually through sexual contact.
  - Little understanding of why small subset of women are affected by HPV.
  - HPV may be latent for many years before inducing cervical neoplasia.
  - More common in young women, who are also more likely to clear infection

**Cervical cancer etiology (2)**

- HPV subtyping to help in management of ASC-US
  - Atypical squamous cells of uncertain significance
  - If associated with high risk subtypes (16, 18, 31, 32, etc), colposcopy and biopsy indicated
  - If HPV negative, can repeat PAP in 12 months
- FDA approval of cervical cancer vaccine (protective against 4 HPV strains)
  - Requires 3 vaccines over 6 month period
  - Intended for females who are not yet sexually active
Cervical cancer: screening window of opportunity

- Single Pap false negative rate is 20%.
- The latency period from dysplasia to cancer of the cervix is variable.
- 50% of women with cervical cancer have never had a Pap smear.
- 25% of cases and 41% of deaths occur in women 65 years of age or older.

Cervical cancer: Pap smear result

- Normal: Repeat annually
- ASCUS/AGUS: Consider colposcopy, treat any evident infection, repeat within 2 months
- LGSIL: Consider colposcopy with directed biopsy, consider HPV testing, consider repeat in 3 months
- HGSIL: Consider colposcopy with directed biopsy
- Invasive Cancer: Refer to Gynecologic Oncologist
- Unsatisfactory: Repeat within 3 months

ASCUS: Atypical squamous cells of undetermined significance
AGUS: Atypical glandular cells of undetermined significance
HGSIL/LGSIL: High grade (CIN II and III) and low grade squamous intraepithelial lesion (CIN)

Cervical cancer: colposcopic biopsy result

- Mild/Moderate Dysplasia: Observation vs. LEEP
- Severe Dysplasia/ CIS: LEEP
- Invasive Cancer: Refer to Gynecologic Oncologist

LEEP: Loop Electrocautery Procedure
Usually done by gynecologist, or trained practitioner

Treating early-stage cervical cancer

- Conization or simple hysterectomy (removal of the uterus) - microinvasive cancer
- Radical hysterectomy - removal of the uterus with its associated connective tissues, the upper vagina, and pelvic lymph nodes. Ovarian preservation is possible.
- Chemoradiation therapy
Treating advanced cervical cancer

- Chemoradiation is the mainstay of treatment
  - 4-5 weeks of external radiation
  - Two or more implants (brachytherapy)
- Concurrent cisplatin-based chemotherapy significantly improves the chances of survival
- Radiation treats the primary tumor and adjacent tissues and lymph nodes
- Chemotherapy acts as a radiation sensitizer and may also control distant disease

Endometrial cancer: major points you need to know

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>35,000</td>
<td>2,900</td>
</tr>
<tr>
<td>2000</td>
<td>36,100</td>
<td>6,500</td>
</tr>
<tr>
<td>2012</td>
<td>~ 60,000</td>
<td>~ 10,000</td>
</tr>
</tbody>
</table>

Endometrial cancer: types and risk factors

**Type I**
- Estrogen Related
- Younger and heavier patients
- Low grade
- Perimenopausal
- Exogenous estrogen

**Type II**
- Aggressive
- Unrelated to estrogen stimulation
- Occurs in older & thinner women
- Potential genetic basis
- Lynch syndrome
- Familial trend

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>&gt;30 LBS</td>
<td>3</td>
</tr>
<tr>
<td>&gt;50 LBS</td>
<td>10</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>2</td>
</tr>
<tr>
<td>Late Menopause</td>
<td>4</td>
</tr>
<tr>
<td>Unopposed Estrogen</td>
<td>9.5</td>
</tr>
<tr>
<td>Atypical Hyperplasia</td>
<td>2.9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.8</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Endometrial cancer: who needs an endometrial biopsy?

- Postmenopausal bleeding
- Any woman with atypical cells on Pap
- Postmenopausal women with endometrial cells on Pap
- Perimenopausal intermenstrual bleeding
- Abnormal bleeding with history of anovulation
- Thickened endometrial stripe via sonography depending on age
Endometrial cancer: transvaginal ultrasound screening

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>&lt;5mm</th>
<th>6-10mm</th>
<th>11-15mm</th>
<th>&gt;15mm</th>
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</thead>
<tbody>
<tr>
<td>Atrophy</td>
<td>93%</td>
<td>7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>58%</td>
<td>42%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyp</td>
<td>53%</td>
<td>47%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>18%</td>
<td>41%</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td>Grigoriu: Maturitus 23:9-14,1996</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Endometrial cancer: survival by clinical stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>%</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>70.2</td>
<td>76.3</td>
</tr>
<tr>
<td>II</td>
<td>17.8</td>
<td>59.2</td>
</tr>
<tr>
<td>III</td>
<td>8.1</td>
<td>29.4</td>
</tr>
<tr>
<td>IV</td>
<td>3.6</td>
<td>10.3</td>
</tr>
</tbody>
</table>

Modified: FIGO 1991

Endometrial cancer: therapy

- Surgical staging improves survival stage for stage
- Adjuvant therapy
  - Radiation therapy
    - Brachytherapy or external beam
  - Hormonal or chemotherapy
  - No clear survival advantage to any modality
- Advanced disease
  - Chemotherapy and hormonal therapy
  - Modest benefit at best
  - No clear survival advantage

Pancreatic cancer

Typically presents at an advanced stage

- 15 resectable
- 35 locally advanced
- 50 metastatic
Pancreatic cancer: surgical approach

Whipple resection: pancreaticoduodenectomy
Patients who recover well: adjuvant gemcitabine-based chemotherapy; role of postoperative radiation is controversial

Pancreatic cancer: advanced disease

• For advanced (inoperable) pancreatic cancer, chemotherapy is the appropriate treatment
  • Long-time standard = gemcitabine-based regimen; new data suggests a more aggressive combination (FOLFIRINOX = 5-FU, leucovorin, irinotecan, plus oxaliplatin) may represent the new gold standard for good performance-status patients
  • May improve quality of life in some patients (stabilize weight, lessen pain requirements)
  • Median survival for metastatic disease is short (< 1 year)

Bladder cancer

• 67,160 new cases annually in U.S.; 13,750 deaths (Jemal 2007)
• 70-80% present with superficial (Ta, Tis, T1) disease
• Most important prognostic factors:
  • Depth of penetration into bladder wall/lymph node metastases
  • Tumor differentiation

Bladder cancer – earlier stage disease

Treatment of superficial bladder cancer:
• TUR with fulguration +/- adjuvant intravesical BCG or chemotherapy
  • Intravesical therapy most commonly used for patients with recurrent disease and/or multiple tumors
  • Segmental cystectomy (rarely indicated)
  • Radical cystectomy in selected patients with extensive or refractory superficial tumor
  • High risk of recurrence following initial resection (as high as 80%)
Bladder cancer – later stage disease

*Treatment of more advanced disease (muscle-invasive):

- Radical cystectomy
  - Includes bladder, perivesical tissues, prostate, and seminal vesicles in men; uterus, tubes, ovaries, anterior vaginal wall, and urethra in women
  - May or may not be accompanied by pelvic lymph node dissection
  - Neoadjuvant chemotherapy is associated with a modest survival benefit
  - Adjuvant chemotherapy is frequently administered in the absence of good data

- For non-operative candidates: definitive chemoradiation can occasionally provide long-term survival

- Cisplatin-based combination chemotherapy is associated with a survival advantage in metastatic disease

- Atezolizumab (anti-PD-L1 Ab) is recently FDA approved in post-platinum setting

Melanoma – staging and surgical principles

- **T stage** = tumor thickness (<1 mm; 1-2 mm; 2-4 mm; > 4 mm)
  - Surgical excision: how wide margins are necessary?
    - For lesions < 2 mm thick: excision margin of 1 cm is adequate
    - For lesions 2-4 mm thick: 1-2 cm margin
    - For lesions > 4 mm thick: at least a 2 cm margin

- Lymph node dissection
  - Occult nodal involvement in 20-25% of patients with 1-4 mm thick melanomas
  - Not necessary in early-stage patients; controversial whether this is needed in patients with higher T stage
  - Emerging role of sentinel LN biopsy

Melanoma – systemic therapy

- **In the adjuvant setting:**
  - Randomized studies have shown improved relapse-free (and in some instances, overall survival with interferon-a-2b in patients with high T stage or node-positive disease
  - Role of adjuvant therapy in earlier stages is less certain

- **For metastatic disease:**
  - Biologic therapy (including INF, IL-2) = RR 15-20%; significant toxicities (fatigue, depression with INF; capillary leak syndrome with hi-dose IL-2)
  - Chemotherapy = RR 15-30%
  - Vaccines
  - Newer treatment options:
    - Pembrolizumab or nivolumab = monoclonal antibody vs PD-L1, immune check-point
    - Ipilimumab = monoclonal antibody vs CTLA-4, immune check-point
    - BRAF inhibitors – targets BRAF oncogene mutated in a majority of melanomas

Cancers of unknown primary

- **Common sites of presentation:**
  - Liver
  - Lungs
  - Bones
  - Lymph nodes

- **Common histology** (Hainsworth/Greco, NEJM 1993)
  - Adenocarcinoma (60%)
  - Poorly differentiated carcinoma/poorly differentiated malignant neoplasm (35%)
  - Squamous cell carcinoma (5%)
Cancers of unknown primary – how your pathologist can help you

- Request special immunoperoxidase stains
- On rare occasions, tumor-specific chromosomal abnormalities may be identified (i(12) for germ cell tumors)

<table>
<thead>
<tr>
<th>If you suspect...</th>
<th>Immunostain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>ER/PR</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>PSA</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Leukocyte common antigen</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>Cytokeratin (non-specific)</td>
</tr>
<tr>
<td>Neuroendocrine tumor</td>
<td>Chromogranin, synaptophysin</td>
</tr>
</tbody>
</table>

Cancers of unknown primary – diagnostic workup

- Utility of tumor markers
  - AFP, b-HCG (young pt with mediastinal or RP nodes in whom you suspect germ cell tumor)
  - PSA (elderly male with bony lesions)
  - CA125 (female with peritoneal carcinomatosis)
  - CA19-9 (pancreatobiliary primary)
- Appropriate radiologic or endoscopic evaluation depending on specific signs/symptoms
  - Generally a “shotgun approach” is unproductive

Cancers of unknown primary: special cases

- Women with peritoneal carcinomatosis
  - Check CA-125; in general, ex-lap with maximal surgical cytoreduction & appropriate, then in analogous to ovarian CA
- Woman with axillary LN
  - ER/PR staining, mammogram and consider breast MRI; modified radical mastectomy generally recommended
- Patient with other peripheral lymph nodes
  - Upper or mid-cervical LN: generally head and neck primary. Full ENT evaluation; recommend radical neck dissection and/or high-dose XRT.
  - Lower cervical or supraclavicular LN: more likely lung primary. Eval with bronchoscopy; if nothing, treat similar to that of higher cervical involvement.
  - Inguinal LN: anoscopy, colposcopy; inguinal LN dissection +/- XRT

Cancers of unknown primary – final thoughts

- Despite extensive workup, no primary site will be identified in the majority (~ 60%) of patients
- Cancers of unknown primary site account for approximately 3% of all cancer diagnoses! (Pavlidis et al, Eur J Cancer 2005)
- Chemotherapy in these circumstances is thus empiric, usually platinum-based; response rates can be ~ 45%
  - Favorable prognostic features for treatment response: tumor location in lymph nodes, fewer metastatic sites, younger age, poorly differentiated histology (Hainsworth and Greco, 2000)
  - Prognosis overall remains poor, but long-term survival is possible
<table>
<thead>
<tr>
<th>Diseases where adjuvant therapy is considered (in specific contexts)</th>
<th>Diseases where neoadjuvant therapy is considered (in specific contexts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Breast</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Rectal</td>
</tr>
<tr>
<td>Lung</td>
<td>Lung</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Esophageal</td>
</tr>
<tr>
<td>Stomach</td>
<td>Bladder</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Soft tissue sarcoma</td>
</tr>
</tbody>
</table>

**Answer Key**

| 10. C | 20. E | 30. A |