Oncology Pearls for the Boards

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"Pearl" - a beautiful thing produced as the result of a long, irritating process which seems pointless at the time it is being endured

Oncology Pearls

- Oncologic emergencies
- Important issues for common cancers
- Screening in different populations
- Oncology issues in primary care

Case #1

60 y.o. man with 80 pack-yr smoking hx c/o 1 week history of facial swelling and shortness of breath.
Physical examination: distended neck veins, prominent chest wall venous distention, facial edema.
Chest CT: bulky right hilar/mediastinal lymphadenopathy

Case #1

A. Proceed with mediastinoscopy or bronchoscopy to obtain tissue diagnosis
B. Initiate heparin and radiation with plan to biopsy when swelling improves
C. Initiate steroids and heparin with plan for biopsy when swelling improves
D. Initiate heparin and emergent stent placement then biopsy once swelling improves
E. Explain to patient this is metastatic cancer and he should consider hospice
### Oncology pearl

- Describe the signs and symptoms of and optimal treatment for superior vena cava syndrome.


### SVC Syndrome

**Superior vena cava:**
- Carries blood from head, torso, and arms (~1/3 blood supply) to heart
- Can be externally compressed (more common) or thrombosed
  - Compression usually due to mediastinal mass
  - Most common malignancies – lung cancer (both NSCLC and small cell) and lymphoma

### Signs and symptoms

- Physical examination
  - Jugular venous distension
  - Venous distension of superficial veins on chest
  - Facial edema and plethora
- Symptoms
  - Shortness of breath
  - Cough
  - Hoarseness

### Management of SVC

- Tissue diagnosis critical for Rx decisions
  - Prognosis depends on underlying disease
- Treatment plan depends on tumor histology
  - Chemo-insensitive cancers (e.g. NSCLS) treated with upfront XRT
  - Chemo-sensitive tumors (e.g. small cell, lymphoma) treated with upfront chemo
  - Stent placement not usually done 1st line in cancers that may respond to chemo/RT
  => Rarely fatal

### Case #2:

64 y.o. male with metastatic prostate cancer to bone with metastases to ribs, pelvis, and multiple vertebrae. Currently on docetaxel chemo. Calls c/o of 1-2 weeks increasing mid-back pain. He has no weakness, radicular pain, bowel or bladder difficulties. Neurologic exam is normal.

- Order a bone scan and CT scan to look for disease progression.
- Prescribe NSAIDs and oxycodone as needed for pain.
- Obtain an MRI of the spine.
- Recommend radiation to the spine.
**Oncology pearl**

- Describe the signs and symptoms and optimal management of spinal cord compression.


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**Spinal Cord Compression**

- Must initiate treatment earlier to prevent neurologic deficits
  – Once neurologic deficits occur, often irreversible
- Usually from epidural compression from vertebral body metastases
  – Most common tumors: lung, breast, prostate, myeloma, lymphoma
  – Thoracic spine most common location

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**Symptoms**

- BACK PAIN!
  – New or worsening back pain with known vertebral mets mandates further evaluation
  – Pain may be radicular, but not always
- Weakness
  – Motor deficits more common than sensory
- Bowel and bladder symptoms occur late
- Neurologic exam may be normal
  – Key is early diagnosis
- MRI is imaging of choice

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**Treatment**

- Corticosteroids to ↓ edema
  – Only short-term benefit
    – Should not be used if diagnosis unknown
    – Typically 10 mg load then 4 mg q 6hrs
- Radiation 1st line treatment for most
- Upfront surgery reserved for:
  – Unknown diagnosis
  – Progression during or after radiation
  – Spinal instability
  – One RCT showed improved function with immediate surgery for less radiosensitive tumors with single area of compression

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**Case #3:**

62 y.o. man presents to ER with temperature of 101.4°F, malaise, and cough 15 days after receiving chemotherapy for follicular lymphoma. Physical exam is unrevealing for source. WBC is 640 cells/mm³ with 45% polys. CXR is negative. Cultures are obtained.
### Case #3:

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td>Admit patient and start ceftazidime</td>
</tr>
<tr>
<td>B.</td>
<td>Admit patient, start ceftazidime and G-CSF</td>
</tr>
<tr>
<td>C.</td>
<td>Admit patient and observe</td>
</tr>
<tr>
<td>D.</td>
<td>Discharge patient to home on oral quinolone and G-CSF</td>
</tr>
<tr>
<td>E.</td>
<td>Discharge patient to home on oral quinolone</td>
</tr>
</tbody>
</table>

### Oncology pearl

- Describe the optimal management of febrile neutropenia.


### Fever and Neutropenia

#### Fever
- Oral temperature > 38.3°C (101°F) or 38.0 °C (100.4 °F) for > 1 hr

#### Neutropenia
- Absolute neutrophil count < 500 cells/μL or ANC < 1,000 with predicted nadir of < 500 in next 48 hrs

### Fever and Neutropenia

- Risk for occult infection and mortality ↑ as ANC falls below 1,000/mm³
  - Greatest risk with ANC < 500/mm³
  - Mortality rate for solid tumors less than heme malignancies
- Growth factors (GCSF)
  - Modestly ↓ duration of neutropenia and hospitalization
  - No impact on mortality
  - No significant benefit to empiric use of GCSF in uncomplicated F & N

### Risk Factors for F&N

- Rapid decline in ANC
- Prolonged duration of neutropenia (>7-10d)
- Leukemic induction
- Uncontrolled cancer
- Hematologic cancers

### Typical infectious sources of F&N

- Catheters
- Skin
- Respiratory tract
- Sinuses
- GI tract
  - Source identified in less than 30% of cases
  - Endogenous flora in 80% of cases
**Likely Organisms**

- Gram-positive infections (60-75%)
  - *Staph epidermidis*
  - *Streptococcus*
  - *Enterococcus faecalis/faecium*
- Gram-negative rods (more likely to cause death)
  - *Pseudomonas aeruginosa*
  - *E. coli*
  - *Klebsiella pneumonia*

**Routine evaluation**

- History
- Physical exam
- CBC, chemistries, LFTs, urine analysis
- Blood/sputum/urine cultures
- CXR
- Consider directed radiology: chest/abd/sinus CT if warranted by symptoms

**Treatment**

**Empiric antibiotics:** broad spectrum with gram positive and gram negative coverage (especially *Pseudomonas*)

- 3rd generation cephalosporin (ceftaz or cefepime)
  - May depend upon local hospital bacteriology
- Alternatives:
  - Imipenem cilastatin or meropenem
    - Higher rate C.diff colitis than cephalospoin
  - Beta-lactam allergy: Quinolone with gram pos
    - <1% cross-reactivity between 3rd generation ceph and PCN/1st gen cephalosporin

**Vancomycin for F & N**

- Empiric initial use does not improve morbidity or mortality
- Encourages development of vancomycin resistant *Enterococcus*
- Reserve for high suspicion of line/skin infection, mucositis, h/o MRSA, severe PCN allergy along with quinolone or aztreonam

**“Low risk” F & N**

- Outpatient Empiric Antibiotic Treatment still controversial (e.g. Cipro + Amox/Clav)
  - anticipated duration of neutropenia < 7 days
  - solid tumor
  - clinically stable
  - no major morbidities
  - adequate oral intake and social supports
  - malignancy responding to current treatment
  - 24/7 access to health care for monitoring

**Case #4:**

45 y.o. female with mantle cell lymphoma admitted day 9 after chemotherapy with F & N. Her fever resolved promptly with institution of empiric antibiotics. One day later, blood cultures grow *E. coli* sensitive to amoxicillin. ANC is currently 246.
### Case #4:

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td>Stop IV antibiotics and discharge her on p.o. amoxicillin.</td>
</tr>
<tr>
<td>B.</td>
<td>Continue IV antibiotics until ANC &gt; 500.</td>
</tr>
<tr>
<td>C.</td>
<td>Obtain echocardiogram to evaluate for endocarditis</td>
</tr>
<tr>
<td>D.</td>
<td>Stop IV antibiotics and start amoxicillin, but continue to observe her for 48 hours in hospital.</td>
</tr>
</tbody>
</table>

### F & N – part 2

- When can antibiotics be stopped or changed?  
  - Only when BOTH fever and neutropenia have resolved  
  - If ANC > 500 and afebrile and source isolated => complete course of abx for infection  
  - If ANC>500 and afebrile and no source isolated=> discontinue abx

### Case #5:

57-year-old woman with metastatic lung cancer is brought to the emergency room with confusion. Serum calcium is 17.2 mg/dl and creatinine is 2.0 mg/dl. Four liters of normal saline and IV furosemide are administered. What is the next most appropriate therapeutic intervention that should be undertaken first?

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td>Another 2 liters normal saline infusion IV and furosemide</td>
</tr>
<tr>
<td>B.</td>
<td>Pamidronate, 90 mg IV, infused over 24 hours</td>
</tr>
<tr>
<td>C.</td>
<td>Zoledronate, 4 mg IV, infused over 15 minutes</td>
</tr>
<tr>
<td>D.</td>
<td>Calcitonin</td>
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<tr>
<td>E.</td>
<td>Chemotherapy for lung cancer</td>
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</table>

### Oncology pearl

- Describe optimal management of hypercalcemia.


### Hypercalcemia

- Occurs in up to 20% of patients with cancer  
  - Both solid tumors and leukemia  
  - Most common: breast, lung, myeloma  
    - Incidence among pts with metastatic breast and myeloma may be decreasing with routine use of bisphophonates  
  - Hypercalcemia Rx important for palliation, but long-term control requires effective anti-cancer therapy
Causes of Hypercalcemia

- Humoral hypercalcemia of malignancy
  - Tumors secrete PTHrP
  - Most common cause
- Local osteolytic hypercalcemia
  - Mainly in breast, myeloma, and lymphoma
- 1,25 (OH)2D-production by tumor
  - Rare and occurs only in lymphoma
- Ectopic PTH
  - Extremely rare – isolated case reports

Drug therapy for hypercalcemia

- Inhibit osteoclastic bone resorption
  - Bisphosphonates (2-4 days for max effect)
  - Calcitonin (immediate; tachyphylaxis in 2-3d)
- Increase urinary calcium excretion
  - Normal saline to volume replete then add loop diuretic (immediate effect)
- Decrease intestinal absorption
  - Glucocorticoids
    - More helpful in 1,25 (OH)2D lymphoma pts
- Dialysis
  - Only in rare circumstances – e.g. CHF does not allow aggressive volume repletion or oliguric renal failure

Bisphosphonates for hypercalcemia

- 1st line treatment after volume repletion and loop diuretic
  - Oral agents much less potent so not used for hypercalcemia Rx
- Zolendronate vs. Pamidronate
  - Zolendronate faster infusion (15 min vs 2 hrs)
    - Lower mean nadir calcium (9.8 vs 10.8 mg/dl)
    - Higher proportion normocalcemic at day 10 (88% vs 70%)
  => Clinical difference modest, zolendronate more expensive

Case #6

Which of the following pairs a proven cancer prevention action and the cancer it prevents?

A. Tobacco cessation and bladder cancer
B. Hepatitis C vaccine and hepatocellular carcinoma
C. Decreasing fat consumption and breast cancer
D. Human papilloma virus and uterine cancer

Oncology pearl

- Recognize important epidemiologic associations for cancer

Important associations

<table>
<thead>
<tr>
<th>Tobacco</th>
<th>Ionizing Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Hodgkin's</td>
</tr>
<tr>
<td>Bladder</td>
<td>Breast</td>
</tr>
<tr>
<td>Lung</td>
<td>Lung</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
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</tbody>
</table>

Infectious causes

- Hepatitis B and C => hepatocellular cancer
- Epstein-Barr virus =>post-transplant lymphoma and nasopharyngeal cancer
- Human papilloma virus => cervical and anal cancer
Case #7:

53 year-old man with Burkitt’s lymphoma begins induction chemotherapy. He starts on allopurinol and hydration. Four days later, his creatinine has increased from 1.0 to 5.4 mg/dL. Urine output is 20 cc over the last 24 hours. Labs include K+ 6.0, Ca 6.1, PO4 8.3, uric acid 15.0. He complains of muscle cramps and paresthesias.

Case #7:

A. Rasburicase, aggressive IV hydration, alkalinize urine, kayexelate.
B. Aggressive IV hydration, alkalinize urine, kayexelate, IV calcium.
C. Dialysis
D. Rasburicase, furosemide, kayexelate, oral calcium.

Oncology pearl

• To recognize and treat tumor lysis syndrome.

Tumor lysis syndrome

• Large tumor burden with rapid cell kill
• More common with aggressive leukemia and lymphomas, e.g. Burkitt’s
  – Uncommon with solid tumors
  – Risk highest during induction chemo when tumor burden greatest
• Fatal complications include arrhythmias and renal failure
• Oliguria poor prognostic sign

Laboratory abnormalities

• Serum potassium > 6.0 mg/dL
• Serum uric acid > 8 mg/dL
• Serum phosphate ≥ 4.5 mg/dL
• Serum calcium < 7 mg/dL

Management

• Prophylaxis/prevention key
  – Allopurinol and aggressive hydration to maintain urine output
• Treatment
  – Rasburicase - recombinant urate oxidase
    • Converts uric acid to allantoin which is more soluble in urine than uric acid
• Dialysis if oliguric or persistent metabolic abnormalities or severe symptoms
Case #8:

32 y.o. man in good health presents for routine physical exam. His mother died of colon cancer at 37, and his 39 y.o. brother was just diagnosed with colon cancer. Physical examination and fecal occult blood test are negative. Labs are normal.

What do you recommend?

A. Colonoscopy now and, if negative, every 10 years.
B. Sigmoidoscopy now and, if negative, every 5 years.
C. Annual fecal occult blood testing
D. Prophylactic colectomy
E. Genetic counseling with screening recommendations to take place after that has been performed.

Oncology pearl

- Describe appropriate colorectal cancer screening for different populations.

Screening for colorectal cancer

- Risk assessment to determine screening
  - Average risk
    - Age 50 or older without personal or family history of colorectal cancer or adenoma
  - Increased risk
    - Personal history of polyps or colorectal cancer
    - Family history of polyps or colorectal cancer
    - History of inflammatory bowel disease
      - Risk greater with pancolitis,
      - Start screening ~10 yrs after disease onset

Screening for average risk

Beginning at age 50
- Annual high sensitivity Fecal Occult Blood Test or annual Fecal Immunochemical Test
  - Single FOBT in office with digital rectal exam not acceptable
- Flex sig q 5 yrs
- Double contract barium enema q 5 yrs
- Colonoscopy q 10 yrs
- CT colonography ("virtual colonoscopy") q 5 yrs
- Stool DNA test (?interval)

Screening if family history

- Increased risk: One 1st degree relative with history of colorectal cancer > age 50 or 2 or more 2nd degree relatives with colon cancer
  - Begin screening at age 40 or 10 years before youngest age of diagnosis then follow standard screening intervals
### High risk for screening (HNPCC)

- **Amsterdam criteria** (all criteria)
  - At least 3 relatives (2 must be FDR) with history of colorectal cancer
  - At least one relative <50 at diagnosis
  - At least 2 successive generations affected
- **Bethesda criteria**
  - FDR with colon cancer < 45 or adenoma < 40
  - Two HNPCC-related cancer (endometrial, small intestine, ovarian, gastric)

### Screening for high risk

- Familial adenomatous polyposis
  - Consideration of colectomy
- HNPCC
  - Colonoscopy q1-3 yrs beginning age 20-25
- Personal history of colorectal cancer
  - Colonoscopy at 1, 3, then q 5 yrs
- Personal history of polyps
  - Depends upon number and type of polyps (tubular vs villous, high grade vs low grade dysplasia)

### Case #9:

Which of the following patients has resectable non-small cell lung cancer?

- **A.** 10 cm RLL mass with ipsilateral mediastinal and subcarinal LN involvement.
- **B.** 2 cm LUL mass with ipsilateral hilar and supraclavicular LN involvement.
- **C.** 2 cm RUL mass with ipsilateral hilar LN involvement and small malignant pleural effusion.
- **D.** 4 cm RLL mass with positive ipsilateral mediastinal LN and invasion of carina
- **E.** 2 cm LLL mass with positive contralateral hilar LN, but negative contralateral mediastinal LN

### Oncology pearl

- Identify which patients with non-small cell lung cancer are operable.

### Lung cancer staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>M1</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
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<tr>
<td>T3</td>
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<tr>
<td>T4</td>
<td>IIIB</td>
<td></td>
<td></td>
<td></td>
<td>IV</td>
</tr>
</tbody>
</table>

### Lung cancer staging - nodes

- **N1** – ipsilateral peribronchial or hilar
- **N2** – ipsilateral mediastinal or subcarinal
- **N3** – contralateral mediastinal or hilar, ipsilateral or contralateral scalene, or supraclavicular LN
**Lung cancer staging - tumor**

- **T3** – Tumor of any size extending into chest wall, diaphragm, mediastinal pleura, or pericardium *without* involving heart, great vessels, trachea, esophagus, vertebrae, main stem bronchus, or carina; separate tumor nodule in same lobe
- **T4** – Tumor of any size involving heart, trachea, esophagus, vertebrae, or carina; separate tumor nodule in different ipsilateral lobe
- Malignant pleural/pericardial effusion M1

**Know which patients are resectable**

*Patient must be able to breathe after surgery!*

- Lobectomy is preferred procedure
- Predicted post-operative FEV-1 > 750 cc measured using quantitative ventilation and perfusion scanning and PFT’s
- Rough assessment: climb one flight of stairs without stopping

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**Case #10**

A 62 y.o. man has a PSA of 3.9 on routine check. He has no urinary symptoms. On digital rectal exam, the prostate appears of normal size without any abnormalities. What would you advise next for this patient?

- Repeat PSA
- Ultrasound-guided biopsy of prostate
- Free PSA test
- CT scan of abdomen and pelvis and bone scan

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**Oncology pearl**

- Discuss options after prostate cancer screening

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**Prostate cancer screening**

- **PSA ≥ 4.0** => generally consider biopsy
- **PSA 2.5-4.0**
  - Repeat PSA since PSA may fluctuate
  - 44% of men with PSA > 4.0 had normal PSA at subsequent visit
  - PSA velocity (increase over time) may help predict cancer risk
  - %free PSA may guide decision for biopsy in men with PSA 4-10
    - Cancer has lower %free PSA

www.nccn.org
### Case #11:

A 40 y.o. woman with a strong family history of breast cancer is considering taking tamoxifen for chemoprevention. She calls to discuss potential side effects of the medication. She reports she does not want to experience premature menopause, weight gain or depression.

**A.** Advise that tamoxifen causes none of these side effects  
**B.** Recommend raloxifene instead  
**C.** Recommend exemestane instead  
**D.** Advise that tamoxifen may cause weight gain and depression, but not premature menopause  
**E.** Recommend that she wait until after menopause to take tamoxifen

### Breast cancer chemoprevention

- **Age 60 or older**  
- **Personal history of lobular carcinoma in situ or atypical hyperplasia**  
- **Age 35-59 with 5 yr predicted risk of breast cancer >1.66% (Gail model)**  
  
  http://www.cancer.gov/bcrisktool/  

  => Both tamoxifen and raloxifene FDA approved for chemoprevention

### Oncology pearl

- Counsel women regarding the risks and benefits of chemoprevention for breast cancer  

### Tamoxifen

- Although tamoxifen causes hot flashes and menopausal symptoms => it does not cause premature menopause  
  - May increase fertility  
- Placebo-controlled RCT of tamoxifen  
  - ↓ risk of breast cancer by 50%  
  - ↑ vaginal discharge and bleeding  
  - ↑ endometrial cancer, thromboembolism, and cataracts  
  - Weight gain/depression same as placebo

### Raloxifene

- STAR trial: tamoxifen vs raloxifene  
  - Initial report: Tam and raloxifene equivalent against breast cancer (published in JAMA)  
  - 2010 update: Raloxifene less effective against invasive breast cancer  
    - ↓↓ uterine cancer and thromboembolic risk  
- No data on efficacy or safety among premenopausal women  
- Both tamoxifen and raloxifene improve bone density in postmenopausal women
### Exemestane

- **MAP-3: exemestane vs. tamoxifen**
  - Aromatase inhibitors only effective in postmenopausal women
  - Same study population as tamoxifen trial but also included DCIS
  - At 35 mths, 0.19 vs 0.55% annual incidence of invasive breast cancer (HR 0.35, p=0.002)

### Case #12

45 y.o. premenopausal women has severe hot flashes during the day and frequent night sweats. She has a history of a stage I breast cancer diagnosed two years ago treated with lumpectomy and radiation. She is now on tamoxifen. Which of the following is the best choice for treating her hot flashes?

- A. Venlafaxine
- B. Amitriptyline
- C. Lorazepam
- D. Soy protein
- E. Fluoxetine

### Oncology pearl

- Counsel cancer survivors regarding hot flash treatment and recognize possible drug interaction from CYP2D6 inhibition


### Hot flash treatment

- Placebo-controlled RCT key since placebo has 25-30% response rate
- RCTs show 30-50% ↓ in frequency and intensity of hot flashes with:
  - SSRI’s (paroxetine, fluoxetine)
  - SNRI’s (venlafaxine)
  - Gabapentin
  - Clonidine

=> No consistent effect of soy protein, black cohosh

### CYP2D6 and tamoxifen

- Tamoxifen depends upon conversion by cytochrome P450 2D6 into endoxifen, a more active metabolites
- CYP2D6 inhibition leads to lower endoxifen levels
  - ~5-10% Caucasians “poor metabolizers”
  - Both fluoxetine and paroxetine strongly inhibit CYP2D6
    - SNRI’s do not inhibit CYP2D6
  - Clinical significance still debated
Match chromosomal abnormalities with the cancer

| 1. t(15;17)  | A. Better prognosis AML |
| 2. t(11;22)  | B. Ewing's Sarcoma |
| 3. Isochrome 12p | C. Testicular Germ cell |
| 4. 11q23     | D. Follicular lymphoma |
| 5. Monosomy 7 | E. Topoisomerase exposure |
| 6. t(9;22)   | F. AML from prior alkylator/radiation |
| 7. t(14;18)  | G. CML |
| 8. t(8;21)   | H. Mantle cell lymphoma |
| 9. t(8;14)   | I. APML |
| 10. t(11;14) | J. Burkitt's lymphoma |

Match chromosomal abnormalities with the cancer

| 1. t(15;17) = APML |
| 2. t(11;22) = Ewing's sarcoma |
| 3. Isochrome 12p = Testicular germ cell |
| 4. 11q23 = Topoisomerase |
| 5. Monosomy 7 = AML from prior alkylator/radiation |
| 6. t(9;22) = CML |
| 7. t(14;18) = Follicular lymphoma |
| 8. t(8;21) = Better prognosis AML |
| 9. t(8;14) = Burkitt's lymphoma |
| 10. t(11;14) = Mantle cell lymphoma |

Summary

- Study what is important for the internist to know (and a little bit of trivia)
  - Know your oncologic emergencies
  - Cancer risk assessment
  - Screening recommendations
  - Common issues among common cancers