Cancer: All You Wanted To Know But Were Too Shy to Ask

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September 2019
Agenda

• What is Cancer
• Causes of Cancer
• Epidemiology
• Grading and Staging
• Breast Cancer Pearls
• Prostate Cancer Pearls
• Colon Polyps/Cancer Pearls
• Leukemia/Lymphoma Pearls
• Melanoma Pearls
• Incidentalomas: Lung, Thyroid
• Case Studies
Cancer Introduction: What is Cancer

- Cancer is the second leading cause of death in the U.S. behind cardiovascular disease
- Cancer is ALREADY the number one cause of death in the insured population, due primarily to its unpredictability
- Cancer definition: The loss of normal cellular growth control
  - Just about all cells in the body grow, divide and replace the cells that die with 200 different types of cells
  - Normal cell life cycle is controlled by biochemical proteins that signal when to divide, when to stop dividing, and when to die (apoptosis)
  - If those biochemical protein signals stop working, cancer can develop
  - The development of cancer is often a multi-step process, possibly taking several years
  - With 200 normal cell types, there are 200 different types of cancers
Diagram of Normal Cell Division

The chromosomes (purple) have already replicated, and the duplicates are being pulled apart by fibers of the cell skeleton known as microtubules (green).
Development of Cancer

Genetic Causes

GENETIC ALTERATIONS

- **Chromosomal translocations** – rearrangement of portions of non-homogeneous chromosomes – ex. portion of chromosome 4 fusing with chromosome 20

- **Amplifications** – a response to a stress in environment whereby extra copies of a gene are made inside a cell

- **Point mutations** or single base modifications – single nucleotide base substitution, insertion, or deletion of genetic material; usually takes place during DNA replication
Chromosomal Translocation

Philadelphia chromosome – genetic abnormality causing Chronic Myelogenous Leukemia (CML)

BCR-ABL codes for a tyrosine kinase signaling protein that is always ON, causing the cell to divide uncontrollably.
Point Mutation

Missense Mutation – when nucleotides are replaced by another

Original DNA code for an amino acid sequence.

DNA bases

C A T C A T C A T C A T C A T C A T C A T C A T

Amino acid

His  His  His  His  His  His  His

Replacement of a single nucleotide.

C A T C A T C A T C C T C A T C A T C A T C A T

Incorrect amino acid, which may produce a malfunctioning protein.
Point Mutation

Examples of a single gene mutation

- Cystic Fibrosis
- Sickle Cell Anemia
- Tay-Sachs disease
- Phenylketonuria
- Color Blindness
- Huntington’s Disease
- p53 – Responsible for making protein that stops mutated cells from dividing
- BRCA 1 and BRCA 2 – Tumor-suppressor proteins
Known Causes of Cancer

**ENVIRONMENTAL CAUSES**

Ionizing radiation (e.g., x-rays, gamma rays, alpha rays and ultraviolet light)
Linked to:
- Skin cancer
- Lung cancer
- Bone cancer
- Liver cancer
- Leukemia
- Thyroid cancer
- Breast cancer
Development of Cancer
Intruders Into Our Normal Cells

**VIRUSES**

- Account for about 1 in 7 cancers worldwide
- 80% are caused by two DNA viruses
  - **Hepatitis B** causes hepatocellular carcinoma
  - Human papillomavirus (HPV) causes cervical cancer
- Another DNA virus, Epstein-Barr virus, has been linked to Burkitt’s lymphoma
- RNA viruses linked to cancer are HTLV-1 and HTLV-2, which can cause human T-cell leukemia
- Hepatitis C is also associated with hepatocellular cancer
- HIV is associated with Kaposi’s sarcoma
Oral sex and throat cancer: Michael Douglas HPV report spotlights "epidemic"
Chemical causes of cancer may be due to genetic damage as well as non-genotoxic causes. Examples include:

- Nitrosamines
- Polycyclic aromatic hydrocarbons
- Alkylating agents
- Vinyl chloride
- Aromatic amines
- Urethane
- Some of the chemicals found in cigarette smoke
**Pop Question #1**

Which cancers are associated with a virus?

<table>
<thead>
<tr>
<th>Options</th>
<th>Answers</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Kaposi Sarcoma</td>
<td>1. All of the above</td>
</tr>
<tr>
<td>b. Burkitt's Lymphoma</td>
<td>2. All except e</td>
</tr>
<tr>
<td>c. Chronic Myelogenous Leukemia</td>
<td>3. All except c</td>
</tr>
<tr>
<td>d. Cervical Cancer</td>
<td>4. All except b</td>
</tr>
<tr>
<td>e. Squamous Cell Ca of oropharynx</td>
<td></td>
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<tr>
<td>f. Hepatocellular carcinoma</td>
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# Leading Sites of New Cancer Cases - 2018 estimates

<table>
<thead>
<tr>
<th>Male</th>
<th>19%</th>
<th>Female</th>
<th>30%</th>
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<tr>
<td>Prostate</td>
<td>164,690</td>
<td>Breast</td>
<td>266,120</td>
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<tr>
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<td>121,680</td>
<td>Lung &amp; bronchus</td>
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<td>Colon &amp; rectum</td>
<td>75,610</td>
<td>Colon &amp; rectum</td>
<td>64,640</td>
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<td>Urinary bladder</td>
<td>62,380</td>
<td>Uterine corpus</td>
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<td>Melanoma of the skin</td>
<td>55,150</td>
<td>Thyroid</td>
<td>40,900</td>
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<td>Kidney &amp; renal pelvis</td>
<td>42,680</td>
<td>Melanoma of the skin</td>
<td>36,120</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>41,730</td>
<td>Non-Hodgkin lymphoma</td>
<td>32,950</td>
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<tr>
<td>Oral cavity &amp; pharynx</td>
<td>37,160</td>
<td>Pancreas</td>
<td>26,240</td>
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<tr>
<td>Leukemia</td>
<td>35,030</td>
<td>Leukemia</td>
<td>25,270</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>30,610</td>
<td>Kidney &amp; renal pelvis</td>
<td>22,660</td>
</tr>
<tr>
<td>All sites</td>
<td>856,370</td>
<td>All sites</td>
<td>878,980</td>
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</tbody>
</table>

- Female: Breast, Lung & bronchus, Colon & rectum, Uterine corpus, Thyroid, Melanoma of the skin, Non-Hodgkin lymphoma, Pancreas, Leukemia, Kidney & renal pelvis.
Leading Sites of Cancer Deaths – 2018 Estimates

<table>
<thead>
<tr>
<th>Male</th>
<th>Male Deaths</th>
<th>Male %</th>
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<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>83,550</td>
<td>26%</td>
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<tr>
<td>Prostate</td>
<td>29,430</td>
<td>9%</td>
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<tr>
<td>Colon &amp; rectum</td>
<td>27,390</td>
<td>8%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>23,020</td>
<td>7%</td>
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<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>20,540</td>
<td>6%</td>
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<td>Leukemia</td>
<td>14,270</td>
<td>4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>12,850</td>
<td>4%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>12,520</td>
<td>4%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>11,510</td>
<td>4%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>10,010</td>
<td>3%</td>
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<tr>
<td>All sites</td>
<td>323,630</td>
<td>100%</td>
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</table>

<table>
<thead>
<tr>
<th>Female</th>
<th>Female Deaths</th>
<th>Female %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>70,500</td>
<td>25%</td>
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<tr>
<td>Breast</td>
<td>40,920</td>
<td>14%</td>
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<tr>
<td>Colon &amp; rectum</td>
<td>23,240</td>
<td>8%</td>
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<tr>
<td>Pancreas</td>
<td>21,310</td>
<td>7%</td>
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<tr>
<td>Ovary</td>
<td>14,070</td>
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<tr>
<td>Uterine corpus</td>
<td>11,350</td>
<td>4%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>10,100</td>
<td>4%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>9,660</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>8,400</td>
<td>3%</td>
</tr>
<tr>
<td>Brain &amp; other nervous system</td>
<td>7,340</td>
<td>3%</td>
</tr>
<tr>
<td>All sites</td>
<td>286,010</td>
<td>100%</td>
</tr>
</tbody>
</table>
Worldwide Incidence of Cancer

- The four most common cancers occurring worldwide are lung, female breast, bowel and prostate cancer. These four account for around 4 in 10 of all cancers diagnosed worldwide.

- Lung cancer is the most common cancer in men worldwide. More than 1 in 10 of all cancers diagnosed in men are lung cancers; 80% due to cigarette smoking.

- Lung, breast and bowel (including anus), stomach and prostate cancers have been amongst the most commonly diagnosed worldwide since 1975.

- Worldwide, there will be 23.6 million new cases of cancer each year by 2030 (estimated).
What Do Cancers Cells Actually Do?

- Primary function of cancer cells is to metastasize – take over the universe!
  - The mechanism of metastasis is:
    - Progressive proliferation of neoplastic cells is initially supported with nutrients supplied from the primary organ microenvironment.
    - Neovascularization must take place for the tumor to grow, which is promoted by the secretion of angiogenic molecules such as endothelial growth factors (like an irrigation system).
    - Tumor cells deregulate cohesive molecules, which normally cause cells to adhere to one another; so deregulating this, allows cancerous cells to cross over into thin-walled capillaries and lymphatic channels.
    - Single tumor cells embolize through the blood or lymphatic channels and then arrest in capillary beds of these distant organs they embolize to.
    - Metastatic cells must find ways to evade destruction by the immune system.
    - Metastases must develop their own vascular network to exceed a mass of greater than 1 - 2 mm.
Neovascularization

Cancer cell

Angiogenesis

Regular Blood Vessels
Tumor Cells Deregulating Cohesive Molecules
Cancer - How Does It Kill

When growth control is lost

- Tumor enlarges invading local structures
- May move (metastasize) via blood or lymph to distant organs
How Does It Kill

Death from cancer may be due to several different events, for example:

- Invasion or destruction of a vital organ, for example:
  - Brain
  - Lungs
  - Other vital organs or structures
- Consumes the body’s nutrients and blood supply
  - Causes “wasting” – severe weight loss and malnutrition, often complicated by infection due to immunocompromised state
- Blood clots
  - Associated with hypercoagulable state - blood clots especially in those with solid tumors of the abdomen
  - Result in pulmonary embolism or stroke
- Effects of treatment
  - Severe immune system suppression with opportunistic infections
  - Damage to vital organs (heart, lungs)
  - Complications of surgery
Cancer – How it is Detected

Screening vs. Diagnostic testing

- Screening (may or may not want to postpone an offer)
  - Testing done routinely, without regard to symptoms or signs of disease
    - Mammogram for breast cancer
    - PSA tests for prostate cancer
    - Colonoscopy for colorectal cancer

- Diagnostic testing (would want to postpone any offer)
  - Testing done to evaluate a particular complaint or problem
    - A chest X-ray done on a smoker complaining of weight loss
    - A blood count done on a patient complaining of easy bruising/bleeding
    - A biopsy done to evaluate a worrisome skin lesion
Specific Radiological Tests

- Almost any type of radiology test can detect a tumor
  - Ultrasound
  - MRI
  - PET scans
  - X-rays

- Cancerous lesions typically
  - Grow more rapidly than benign lesions
  - Invade nearby structures
  - Spread to distant sites
  - Are more “metabolically active” than benign lesions
    - “Light up” on PET scan
Cancer – How is it Detected

- Radiological test can only suggest the diagnosis of cancer
- A firm diagnosis of cancer generally requires that tissue be obtained and examined by a pathologist
  - The oncologist’s motto: “No meat, no treat”
  - Usually this tissue is obtained surgically, via a biopsy
- Biopsies can be excisional, incisional, or needle
  - Excisional – the entire lesion is removed, may be intended to treat as well as diagnose
  - Incisional – only a piece of the lesion is removed, for diagnosis only
  - Needle – only a core of tissue, which can be obtained by a cutting needle, is removed
Cancer - Diagnosis

- The next step is to determine how far the cancer has spread (stage), and how fast it appears to be growing (grade)
  - In most cancers, the prognosis depends greatly on stage and grade
  - Stage cannot be determined by pathology alone, usually requires other studies (CT scans, bone scans, etc)
  - Grade is determined by pathology alone
Cancer Grade

- Grade: degree of differentiation of the tumor tissue
  - How abnormal the tumor cells look under a microscope
  - Indicator of how quickly a tumor will grow and likelihood that it will spread
  - As cells lose control over their growth, their phenotype or appearance changes from normal (similar to cell of origin) to more generic type of cell, called undifferentiated
  - Think of Mendelian genetics and how kids look like their parents… if change their DNA, they would lose any resemblance. Same goes for a cell
  - The degree of changes in appearance of cancer cells is the tumor grade
    - Low grade or Grade 1 = well differentiated = looks much like the parent cell
    - High grade or Grade 3 = poorly or undifferentiated = looks nothing like the parents
    - Grade 2 is moderately differentiated, somewhere in between low and high
Cancer Grade – an example

Well-differentiated lung cancer

Poorly differentiated lung cancer
Cancer - Grade

Chinese shar-pei
Cancer Stage

- Stage
  - How much cancer is in the body
  - Location of cancer
  - Extent of spread

*TNM is just one very common staging used*
Cancer Stage: TNM grouping

- **T**: size and extent of primary tumor
  - Tx: primary tumor cannot be excluded
  - T0: no evidence of primary tumor
  - Tis: carcinoma in situ (early cancer that has not spread to neighboring tissue)
  - T1-4: size and/or extent of the primary tumor

- **N**: involvement of lymph nodes
  - Nx: regional lymph nodes cannot be evaluated
  - N0: no regional lymph node involvement
  - N1-3: involvement of regional lymph nodes (number and/or extent of spread)

- **M**: presence or absence of distant metastasis
  - M0: no distant metastasis
  - M1: distant metastasis
TNM Groupings

- Patients with similar prognosis expectations are assigned specific stage groups
  - Stage 0
    - Carcinoma in situ with no metastatic potential, as determined by pathologic examination
  - Stage I
    - Cancers that are small or less deeply invasive, with negative nodes
  - Stage II and III
    - Cancers with increasing tumor spread or nodal extent
  - Stage IV
    - Cancers with distant metastasis at diagnosis

- Each type of cancer has its own particular definitions for the various stages

- The American Joint Committee on Cancer or AJCC is responsible for developing these staging systems (cancerstaging.org)
Staging and Grading

Conceptual Example

Grade 1

Grade 2

Grade 3

Grade 4

Stage
Stage and Grade Determine Prognosis

Prognosis

- Higher stage cancers usually have a worse prognosis

- Grade varies: In most cancers, high grade carries a worse prognosis; however in others, higher grade tumors are more susceptible to chemotherapy and radiotherapy

- Prognosis also dependent on
  - Age at diagnosis
  - Overall health status- whether any comorbidities
  - Type of treatment received
  - Molecular markers
Pop Question #2

- Which grade cancer is associated with a well differentiated cell type?

A. Grade 1  
B. Grade 3  
C. Grade 2
Pop Question #3

- Which of these TNM grouping is associated closest with stage III cancer
  A. T1N0M0
  B. T2 N0M0
  C. T2N2M0

Which of the above has a tumor size of 2 cm??
Which equates with Stage IV? T1, T2 or T4 or neither

Trick questions
REMEMBER …

- The tumor size does not correlate with any particular stage
- Depends on type of cancer so staging has different parameters for different types of cancer
Changes in Staging Criteria

The 8th Edition AJCC to come out January 2018

- Historically, staging was based solely on anatomic parameters such as the physical dimensions of the tumor or the local spread of the tumor.

- Currently, there is an increasing reliance on non-anatomic factors such as:
  - Duration of symptoms
  - Gender
  - Age
  - Health status
  - Type and grade of cancer
  - Specific biological properties of the cancer

- The challenge is to incorporate the newer non-anatomical factors into a system that retains the anatomical factors that are vital for comparison purposes with older clinical studies.
Difference Between Clinical and Pathological Staging

- **Clinical Staging**
  - Any information obtained about the extent of the cancer before initiation of definitive treatment such as surgery, radiation, surveillance or palliative care, which may be noted as \( cT \), \( cN \), \( cM \)

- **Pathological Staging**
  - Any information obtained about the spread of the cancer through completion of definitive surgery or identified within 4 months after the date of diagnosis (and prior to systemic or radiation therapy), which may be noted as \( pT \), \( pN \), \( pM \)
Additional Value of Pathological Staging

- Not all tumors are pathologically staged, for a variety of reasons (e.g., prostate cancer)

- Pathological staging is defined by all of the same diagnostic studies as clinical staging, but includes the following information from the noted sources:
  - Full surgical resection
  - Histologic examination of the surgically removed tissues

- Often need pathology reports for both initial biopsy and full surgical excision
Breast Cancer Overview

- Affects 12% of women in U.S. and less than 1% of men
- Most common malignancy diagnosed, accounting for 30% of all female cancers
- Second most common cause of cancer deaths in women
- Leading cause of death in women age 40-55
Breast Cancer

Breast cancer incidence – Worldwide
Global Statistics on Breast Cancer

- Leading cause of cancer related deaths in women in the world’s developing regions
- Incidence is still lower in developing countries overall than in the West, however death rates from the disease are higher, likely due to later diagnosis and poor access to treatment
- Breast cancer death is second to lung cancer death for women in the developed world
- Countries with highest incidence (per 100,000 women)
  - The Netherlands: 95.3
  - France: 94.6 per
  - U.S. 90.6 (white people only – other races have lower incidence)
- Countries with lowest incidence (per 100,000 women)
  - Thailand: 25.6
  - Algeria: 29.8
  - India: 30.9
Risk Factors

- **BRCA-1 or BRCA-2 mutations**
  (2.9% Caucasians, 10% of Ashkenazi, 3.5% Hispanic, 0.5% Asian Americans for BRCA1)
- Family history of breast or ovarian cancer
- Personal history of prior breast, endometrial or ovarian cancer
- **Increasing age**
- Nulliparity or late age at first pregnancy (age over 30)
- Absence of breast feeding
- Early menarche
- Late menopause
- Hormone replacement therapy
- **Hyperplasia, multiple papillomatosis, sclerosing adenosis, fibroadenomas with proliferative change and atypical hyperplasia**
- Radiation to breast area
- **No added risk for fibrocystic breast disease, simple fibroadenomas without proliferative change, duct ectasia and solitary papillomas**
Recommendations on Screening

- American Cancer Society 10/15 revised their guidelines from age 40 to recommend routine screening at age 45 annually until age 55 then every 2 years and as long as life expectancy is 10 years or longer

- American College of Ob/GYN continue to recommend starting age 40 annually

- US Preventive Task Force, Canadian Task Force and American College of Physicians recommend beginning age 50 every 2 yrs through age 74

- American College of Radiology continue to recommend routine screening age 40 until life expectancy is 5-7 more years

- For HIGH RISK individuals, suggest annual starting age 25 with alternating annual MMG and MRI as well as clinical exam every 6 months … and consider BRCA testing
BI-RADS

- Breast Imaging-Reporting and Data System
  - BI-RADS 0: incomplete; further imaging or information is required, such as compression or magnification views or ultrasound
  - BI-RADS I: negative; no suspicious findings
  - BI-RADS II: benign findings, such as fibroadenomas, lipomas or simple cysts
  - BI-RADS III: probably benign, short interval (6 month) follow up suggested
  - BI-RADS IV: abnormality suspicious for malignancy
    - BI-RADS IVa – low level of suspicion for malignancy
    - BI-RADS IVb – intermediate suspicion for malignancy
    - BI-RADS IVc – moderate level of suspicion for malignancy
  - BI-RADS V: highly suggestive of malignancy; action should be taken
  - BI-RADS VI: known biopsy-proven malignancy
Diagnostic Tests: SLN Dissection

- Has become the standard over last 15 years, replacing the Axillary Lymph Node dissection ... here is why:
  - More accurate and can pick up micrometastasis ... which ultimately causes upstaging
  - Less morbidity with SLN than ALND: ex. Lymphedema 2% with SLN as compared to 13% with ALND
  - Conclusion from multiple large studies suggests SLND should be performed on all women less than 70 with clinically negative nodes
Newer Staging Strategy

TNM Staging System – what has been added?

- Tumor – size
- Regional lymph nodes
- Metastasis

<table>
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<tr>
<th>Micrometastasis and Isolated Tumor Cells</th>
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</thead>
<tbody>
<tr>
<td>pN0(i+) means isolated tumor cells no greater than 0.2 mm and are prognostically similar to node negative</td>
</tr>
<tr>
<td>pN1mi refers to micrometastasis and would think worse prognosis, however this class has only slight increase in recurrence rate</td>
</tr>
<tr>
<td>Data on SLN indicates that there was 0% additional positive nodes with ITC; 27% had additional positive node for mi</td>
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## Breast Cancer Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Tis</td>
<td>No evidence of invasive tumor</td>
</tr>
<tr>
<td></td>
<td>T\textsubscript{1}N\textsubscript{0}M\textsubscript{0}</td>
<td>Tumor ≤ 2 cm</td>
</tr>
<tr>
<td></td>
<td>T\textsubscript{1}mic</td>
<td>≤ 0.1 cm</td>
</tr>
<tr>
<td></td>
<td>T\textsubscript{1}a</td>
<td>&gt; 0.1 cm - 0.5 cm</td>
</tr>
<tr>
<td></td>
<td>T\textsubscript{1}b</td>
<td>&gt; 0.5 cm - 1 cm</td>
</tr>
<tr>
<td></td>
<td>T\textsubscript{1}c</td>
<td>&gt; 1 cm - 2 cm</td>
</tr>
<tr>
<td>IIA</td>
<td>T\textsubscript{0}-T\textsubscript{1}N\textsubscript{1}M\textsubscript{0}</td>
<td>Tumor ≤ 2 cm with metastasis to a moveable ipsilateral axillary node or nodes or Tumor ≤ 5 cm without node involvement</td>
</tr>
<tr>
<td>IIB</td>
<td>T\textsubscript{2}N\textsubscript{1}M\textsubscript{0}</td>
<td>Tumor ≤ 5 cm with metastasis to a moveable ipsilateral axillary node or nodes or Tumor &gt; 5 cm without node involvement</td>
</tr>
<tr>
<td>IIA</td>
<td>T\textsubscript{3}N\textsubscript{0}M\textsubscript{0}</td>
<td>Tumor ≤ 5 cm with metastasis to a moveable ipsilateral axillary node or nodes or Tumor &gt; 5 cm without node involvement</td>
</tr>
<tr>
<td>IIIA</td>
<td>T\textsubscript{0}-T\textsubscript{2}N\textsubscript{2}M\textsubscript{0}</td>
<td>Tumor ≤ 5 cm with metastasis to ipsilateral node or nodes, either moveable or fixed to one another or other structures or Tumor &gt; 5 cm with a moveable ipsilateral node or nodes</td>
</tr>
<tr>
<td>IV</td>
<td>Any T, any N, M\textsubscript{1}</td>
<td>Distant metastasis</td>
</tr>
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### AJCC Staging – Prior Staging

<table>
<thead>
<tr>
<th>When T is…</th>
<th>And N is…</th>
<th>And M is…</th>
<th>The Stage Group is…</th>
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<tbody>
<tr>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
<td>0</td>
</tr>
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<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>IA</td>
</tr>
<tr>
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<td>M0</td>
<td>IB</td>
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You will see that the noted AJCC prior staging can be either IA or IB in the new AJCC 8th edition.
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# AJCC 8th edition Prognostic Staging Groups

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Note: The stage groupings are based on the combination of TNM, Grade, HER2, ER, and PR status.
Anatomical Staging versus New Prognostic Staging

Can see the clinical implications here

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Oncotype DX: Important Prognosticator

Require Tissue Evaluation

Oncotype DX

- Standard of Care
- Looks at 21 genes; provides recurrence score or RS
- Predicts likely benefit of chemotherapy
- Predicts risk of distant recurrence
- Score is from 0-100
Oncotype DX Is Part of AJCC Prognostic Stage Group

- Oncotype DX applicable only for assigning prognostic stage group to patients with T1-2 N0M0
  - ER Positive
  - HER 2 Negative

Oncotype DX score of <11, in above, no matter the grade or PR status, stage is IA
If score is >11, then prognostic stage is only based on anatomical and biomarkers

Future may include other multigene panels
Morbidity

- **Chemotherapy effects:**
  - Neurotoxicity - peripheral neuropathy from certain chemo agents such as Cisplatinum
  - Plexopathy can be permanent
  - Cardiomyopathy from Trastuzimab
  - Cardiomyopathy from Adriamycin
  - In 2012 study of 12,500 women, 6-11% of older women had CHF and 20% had cardiomyopathy with Trastuzimab plus anthracylcine

- **Surgical complications:**
  - Chest wall and breast complications-seromas, fat necrosis, recurrent skin infection
  - Reduced arm mobility
  - Lymphedema 2% in SLN and 13% in axillary lymph node
Morbidity (Continued)

- Radiation therapy effects:
  - Premature CAD, especially left-sided breast radiation
  - Secondary malignancies: increase risk for esophageal and lung cancer as well as sarcomas, leukemias, myelodysplastic syndrome
    - Occurs within 5-7 years post treatment in 1.5% of patients

- General or other related adverse effects:
  - Long-term effects for primary therapy include cognitive dysfunction, fatigue, insomnia, pain and debilitating menopausal symptoms
  - Pulmonary – cough, dyspnea
  - Fatigue
  - Chemo brain-real or Memorex
Pop Question #4

Which 2 statements are true.

- There is an increase risk of breast cancer with fibrocystic breast disease
- The risk for breast cancer increases with increasing age
- Breast feeding increases the risk for breast cancer
- Early menarche (early age of menses) is associated with increased risk for breast cancer

1. a and c
2. b and d
3. b and c
Pop Question #5

Morbidity related to breast cancer treatment includes:

a. Premature CAD especially with left breast radiation
b. Cardiomyopathy related to Trastuzimab and Adriamycin
c. Peripheral neuropathy due to Cisplatinum
d. Fat necrosis

1. a, b and c are correct
2. a and c are correct
3. all of the above
Pop Question #6

Which biological, histological or other information is associated with more favorable risks? Discuss as a group.

1. ER positive
2. HER 2 positive
3. Low oncotype DX score of 10
4. Grade 3
5. Triple negative (ER, PR and HER 2 negative)
6. Sentinel node with micrometastasis
7. Sentinel node with isolated tumor cells
8. Diagnosis of cancer after age 50
Prostate Cancer

- Signs of prostate cancer include a weak flow of urine or frequent urination or stop and go, blood in urine or semen, pain with urination, trouble emptying the bladder completely and back, hip or pelvic pain
- Tests that examine the prostate and blood are used to detect (find) and diagnose prostate cancer
- Most are adenocarcinomas
- Risk factors
  - Older age
  - Family history
  - Ethnicity
Epidemiology

Percent of New Cases by Age Group: Prostate Cancer

Prostate cancer is most frequently diagnosed among men aged 65-74.

Median Age At Diagnosis

66

SEER 18 2010-2014, All Races, Males
Epidemiology

Percent of Deaths by Age Group: Prostate Cancer

The percent of prostate cancer deaths is highest among men aged 75–84.

U.S. 2010–2014, All Races, Males
Prostate Testing

- Digital rectal exam (DRE)
- Prostate-specific antigen (PSA) test
- Transrectal ultrasound (TRUS)
- Transrectal MRI
- Transrectal biopsy
Historical Review: Digital Rectal Exam – 1904

Hugh Hampton Young, M.D.

Promoted the use of digital rectal exam for prostate cancer screening  NOTE 60% Stage T4!!! An UW PEARL

- 60% Stage T4
- 20% Stage T3
- 20% Stage T2
The Gleason Score:

- Pathologist looks at the slides and rates as follows:
  - Most common cell pattern seen is given a score of 1 (well-differentiated) to 5 (poorly differentiated)
  - Second most common cell pattern seen if given a score on the same scale
  - The two scores are added
- Example: Gleason “3+4=7” (most common pattern is 3, second most common is 4) – which is actually a better prognosis than “4+3=7”
Prostate Cancer Grading

Gleason’s Pattern

1. Small, uniform glands
2. More stroma between glands
3. Distinctly infiltrative margins
4. Irregular masses of neoplastic glands
5. Only occasional gland formation
Newer Grading for Prostate Cancer Emerging

Gleason 7 made up of 3+4 or 4+3 with prognostic differences. Likewise there is prognostic difference between Gleason 8 and Gleason 9 and 10

New Grading in use currently along side Gleason Scoring

- Grade Group 1 = Gleason 6 (or less)
- Grade Group 2 = Gleason 3+4=7
- Grade Group 3 = Gleason 4+3=7
- Grade Group 4 = Gleason 8 (4+4, 3+5, 5+3)
- Grade Group 5 = Gleason 9-10 (4+5, 5+4, 5+5)

And remember… Grade reflects behavior… Think of spring break. The worse the behavior, the worse the consequences!!
Prostate Cancer Clinical Staging

- **T1a:** Found incidentally on TURP, <5%, Normal DRE
- **T1b:** Found incidentally on TURP, >5%, Normal DRE
- **T1c:** Found on TRUS – NBP for an elevated PSA, Normal DRE
- **T2a:** Palpable nodule on DRE, <½ of one lobe
- **T2b:** Palpable nodule on DRE, >½ of one lobe
- **T2c:** Palpable nodule bilaterally on DRE, both lobes
- **T3a:** Palpable outside the prostate but not seminal vesicles
- **T3b:** Palpable outside the prostate invading seminal vesicles
- **T4:** Locally invading the sphincter, rectum, bladder or pelvic wall
# Prostate Cancer Risk Groups: Stage, Grade and PSA

<table>
<thead>
<tr>
<th>Risk Profile</th>
<th>Criteria†</th>
<th>Approximate Proportion of Newly Diagnosed Cases‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Favorable</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very Low Risk</td>
<td>• T1c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gleason score 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PSA &lt; 10 ng/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Fewer than 3 biopsy cores positive, ≤50% cancer in any core</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PSA Density &lt; 0.15 ng/ml/cc</td>
<td>35%</td>
</tr>
<tr>
<td>Low Risk</td>
<td>• T1 or T2a</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gleason score 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PSA &lt; 10 ng/ml</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>• T2b-T2c or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gleason score 7 or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PSA 10-20 ng/ml</td>
<td>33%</td>
</tr>
<tr>
<td>High</td>
<td>• T3a or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gleason score 8-10 or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• PSA &gt; 20 ng/ml</td>
<td>32%</td>
</tr>
</tbody>
</table>

†Adapted from Mohler, J., et al., *Prostate cancer, Version 3.2012: featured updates to the NCCN guidelines*. J Natl Compr Canc Netw, 2012. 10(9): p. 1081-7. and based on T stage, Gleason score, PSA, PSA density, number and percentage of biopsy cores with cancer; T1c (non palpable cancer), T2a (minimally palpable cancer in one lobe), T2b-T2c (substantial palpable cancer felt to be localized to prostate gland), T3a (palpable cancer thought to have extended beyond the prostate gland).

### AJCC 8th Edition Prostate Cancer Prognostic Groups

<table>
<thead>
<tr>
<th>AJCC</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Gleason Score</th>
<th>PSA</th>
<th>Grade Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>cT1a-c, cT2a</td>
<td>N0</td>
<td>M0</td>
<td>≤6</td>
<td>&lt;10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>pT2</td>
<td>N0</td>
<td>M0</td>
<td>≤6</td>
<td>&lt;10</td>
<td>1</td>
</tr>
<tr>
<td>IIA</td>
<td>cT1a-c, cT2a</td>
<td>N0</td>
<td>M0</td>
<td>≤6</td>
<td>≥10 &lt;20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>cT2b-c</td>
<td>N0</td>
<td>M0</td>
<td>≤6</td>
<td>&lt;20</td>
<td>1</td>
</tr>
<tr>
<td>IIB</td>
<td>T1-2</td>
<td>N0</td>
<td>M0</td>
<td>7 (3+4)</td>
<td>&lt;20</td>
<td>2</td>
</tr>
<tr>
<td>IIC</td>
<td>T1-2</td>
<td>N0</td>
<td>M0</td>
<td>7 (4+3)</td>
<td>&lt;20</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>T1-2</td>
<td>N0</td>
<td>M0</td>
<td>8</td>
<td>&lt;20</td>
<td>4</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1-2</td>
<td>N0</td>
<td>M0</td>
<td>≤8</td>
<td>≥20</td>
<td>1-4</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3-4</td>
<td>N0</td>
<td>M0</td>
<td>≤8</td>
<td>Any</td>
<td>1-4</td>
</tr>
<tr>
<td>IIIC</td>
<td>Any T</td>
<td>N0</td>
<td>M0</td>
<td>9 or 10</td>
<td>Any</td>
<td>5</td>
</tr>
<tr>
<td>IVA</td>
<td>Any T</td>
<td>N1</td>
<td>M0</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>N0</td>
<td>M1</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
</tbody>
</table>
Approaches to Prostate Cancer Treatment

From Indolent Prostate Cancer to Lethal Prostate Cancer

- Watchful Waiting
- Active Surveillance
- Immediate Treatment
Definition of Active Surveillance and Watchful Waiting

- **Active Surveillance** is also called “Active monitoring”. The aim is to properly time curative treatment or the active decision not to treat the patient immediately. Treatment is held up until a predefined threshold is reached that prompts treatment. This takes into account the patient’s life expectancy into consideration. Treatment options are intended to be curative.

- **Watchful Waiting** is also known as “symptom guided treatment”. This was the pre-PSA screening era’s form of conservative management of prostate cancer until the development of local or systemic progression. At this point the patient would be treated palliatively with TURP or hormonal therapy or radiotherapy for palliation of metastatic lesions.

Now we use the terms pretty much interchangeably
Prostate Cancer - Treatment

Radiation

- Radiation will kill the tumor cells and shrink the prostate, but since the gland is still present, the PSA will fall but perhaps not to zero
- The PSA often falls initially, then “bounces” (cause unknown) then continues to decline and reaches a steady state
- PSA bounce can be for up to 1-2 years
- Failure to decline below 1.0 may indicate treatment failure, whereas a sudden rise during follow up (except for the “bounce”) may indicate recurrence
Colon Cancer
Progression of Early Stage 0 to Stage IV
Colon Cancer Staging
Colon Cancer Staging
# TNM Staging for Colon Cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIC</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1–T2</td>
<td>N1/N1c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td>IIIB</td>
<td>T2–T4a</td>
<td>N1/N1c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2–T3</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1–T2</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td>IIIC</td>
<td>T4a</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3–T4a</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N1–N2</td>
<td>M0</td>
</tr>
<tr>
<td>IVA</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
</tr>
</tbody>
</table>

**Primary Tumor (T)**

- **TX**: Primary tumor cannot be assessed
- **T0**: No evidence of primary tumor
- **Tis**: Carcinoma in situ: intraepithelial or invasion of lamina propria
- **T1**: Tumor invades submucosa
- **T2**: Tumor invades muscularis propria
- **T3**: Tumor invades through the muscularis propria into pericolorectal tissues
- **T4a**: Tumor penetrates to the surface of the visceral peritoneum
- **T4b**: Tumor directly invades or is adherent to other organs or structures

**Regional Lymph Nodes (N)**

- **NX**: Regional lymph nodes cannot be assessed
- **N0**: No regional lymph node metastasis
- **N1**: Metastasis in 1–3 regional lymph nodes
- **N1a**: Metastasis in one regional lymph node
- **N1b**: Metastasis in 2–3 regional lymph nodes
- **N1c**: Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
- **N2**: Metastasis in 4 or more regional lymph nodes
- **N2a**: Metastasis in 4–6 regional lymph nodes
- **N2b**: Metastasis in 7 or more regional lymph nodes

**Distant Metastasis (M)**

- **M0**: No distant metastasis
- **M1**: Distant metastasis
- **M1a**: Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node)
- **M1b**: Metastases in more than one organ/site or the peritoneum
Colon Polyps: Which Are Underwriting Concerns

- Hyperplastic Polyps
- Inflammatory Polyps  Usually no risk for colon cancer

Adenomas or adenomatous polyps such as tubular and villous. Most concern for villous adenomas as highest risk to develop cancer. Next worse is tubulovillous. Sessile serrated polyps concerning.

Polyposis type syndromes: High risk of colon cancer
- Lynch Syndrome I and II
- Familial Adenomatous Polyposis  Autosomal Dominant disorders
- Gardner’s Syndrome
Hematologic Cancers
Leukemias

<table>
<thead>
<tr>
<th>Acute Leukemia</th>
<th>Chronic Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Leading cancer death in age &lt;35</td>
<td>▪ Chronic Myelogenous Leukemia (CML) think of Philadelphia chromosome</td>
</tr>
<tr>
<td>▪ Acute Myelogenous Leukemia</td>
<td>▪ CLL – Older-age leukemia</td>
</tr>
<tr>
<td>▪ Acute Lymphoblastic Leukemia median age 10</td>
<td>▪ Stage CLL with RAI system as in earlier slide</td>
</tr>
<tr>
<td>▪ Clonal neoplastic cells that proliferate in bone</td>
<td></td>
</tr>
<tr>
<td>marrow, causing bone marrow failure</td>
<td></td>
</tr>
</tbody>
</table>
Chronic Lymphocytic Leukemia Staging

**Rai stage 0:** Lymphocytosis and no enlargement of the lymph nodes, spleen, or liver, and with near normal red blood cell and platelet counts.

**Rai stage I:** Lymphocytosis plus enlarged lymph nodes. The spleen and liver are not enlarged and the red blood cell and platelet counts are near normal.

**Rai stage II:** Lymphocytosis plus an enlarged spleen (and possibly an enlarged liver), with or without enlarged lymph nodes. The red blood cell and platelet counts are near normal.

**Rai stage III:** Lymphocytosis plus anemia (too few red blood cells), with or without enlarged lymph nodes, spleen, or liver. Platelet counts are near normal.

**Rai stage IV:** Lymphocytosis plus thrombocytopenia (too few blood platelets), with or without anemia, enlarged lymph nodes, spleen, or liver.
Hematologic Cancers

Hodgkin’s Lymphoma

Key Points

- B cell lymphocyte tumor characterized by the Reed-Sternberg cell
- Bimodal peak incidence: age 15-35 and less frequent increase >45
- Strong evidence that infectious agent is contributing cause (EBV)
- Genetic component also (identical twin of affected has 99-fold increase risk)
- Most relapses will occur within 2 years after completion of therapy but can be up to 13 yrs post RX
- Long term complications dictated by type of treatment
  - Chemo associated with 1-3% risk of acute leukemia w/in 5-10 years
  - Radiation associated with solid tumors depending on radiation field
  - Thyroid, lung, breast, colon, bone
  - Mantle radiation (radiation above the diaphragm) associated with CAD
Hodgkin’s Staging and Survival

- Staging based on:
  - History
  - Physical exam
  - CXR, CT scans of chest, abdomen and pelvis
  - Bone marrow biopsy
  - Other staging from staging laparotomy (splenectomy, liver and all major lymph nodes)
  - “B” symptoms associated with advanced disease-60% have stage III or IV

- 10-year survival according to stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>80-92%</td>
</tr>
<tr>
<td>II</td>
<td>75%</td>
</tr>
<tr>
<td>III</td>
<td>60% (approximately)</td>
</tr>
<tr>
<td>IV</td>
<td>40% (approximately)</td>
</tr>
</tbody>
</table>
# Hematologic Cancers

## Non Hodgkin’s Lymphoma

### Key Points

- 6th most common cause of cancer related deaths in U.S. with average age at DX 42
- 5 times more common than Hodgkin’s
- Etiology: congenital and acquired immunodeficiency states – including those on immunosuppressive; infective agents such as HIV, EBV, Herpes, H.Pylori; autoimmune disorders such as RA, SLE, Sjogrens; chemicals such as herbicides, radiation and prior chemo
- Indolent types such as B cell lymphoma can be controlled but not often cured – act like chronic lymphocytic leukemia
- Some are extremely indolent AND resistant to therapy
- Some aggressive if caught at stage I or II and treated can be curable (they just soak up the chemo and DIE)
- Aggressive can be cured but succumb to the risk of secondary cancers later in life, which explains higher rating
Non Hodgkin’s Lymphoma

Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Involvement of single lymph node of a single extralymphatic organ or site</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Involvement of 2 or more lymph nodes on the same side of diaphragm or localized involvement of an extralymphatic organ or site</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Involvement of lymph node regions on both sides of diaphragm or localized involvement of an extralymphatic organ or site or spleen or both</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Diffuse or disseminated involvement of one or more extralymphatic organs with or without associated lymph node involvement</td>
</tr>
</tbody>
</table>

Identification of the presence of absence of symptoms should be noted with each stage designation. A = asymptomatic, B= fever, sweats or weight loss > 10% body weight
Non Hodgkin’s Lymphoma

Survival

<table>
<thead>
<tr>
<th>Prognostic Factors</th>
<th>Better Prognosis</th>
<th>Worse Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Age &lt;60</td>
<td>Age &gt;60</td>
</tr>
<tr>
<td>LDH</td>
<td>LDH normal</td>
<td>LDH abnormal</td>
</tr>
<tr>
<td>Ann Arbor</td>
<td>Ann Arbor State I or II</td>
<td>Ann Arbor Stage III or IV</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>Symptomatic</td>
<td></td>
</tr>
<tr>
<td>Small size of tumor</td>
<td>Bulky tumor (as defined by pathologist)</td>
<td></td>
</tr>
<tr>
<td>Small number of nodes</td>
<td>Large number of nodes</td>
<td></td>
</tr>
<tr>
<td>No extranodal involvement</td>
<td>Extranodal involvement</td>
<td></td>
</tr>
</tbody>
</table>
Melanoma

Risk Factors

- Light skin
- History of multiple atypical nevi
- Previous history of melanoma
- Multiple dysplastic nevi
- Family history of melanoma
- History of sunburn or extensive exposure to the sun between the ages of 10 - 24
## Anatomical Staging of Melanoma

**Notice Melanoma Deals with Depth or Thickness and Ulceration status and Mitosis**

<table>
<thead>
<tr>
<th>Stage</th>
<th>T Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>T1s</td>
<td>Melanoma in situ, Atypical melanocytic dysplasia, or Hutchinson’s Freckle</td>
</tr>
<tr>
<td>IA</td>
<td>T1a</td>
<td>Melanoma ≤ 1.0 mm in thickness, Clark’s level II or III, <strong>without</strong> ulceration, and mitosis &lt; 1/mm²</td>
</tr>
<tr>
<td>1B</td>
<td>T1b</td>
<td>Melanoma ≤ 1.0 mm in thickness, Clark’s level IV or V, <strong>with</strong> ulceration or mitosis</td>
</tr>
<tr>
<td></td>
<td>T2a</td>
<td>Melanoma 1.01 – 2.0 mm in thickness <strong>without</strong> ulceration</td>
</tr>
<tr>
<td>IIA</td>
<td>T2b</td>
<td>Melanoma 1.01 – 2.0 mm in thickness</td>
</tr>
<tr>
<td></td>
<td>T3a</td>
<td>Melanoma 2.01 – 4.0 mm in thickness <strong>without</strong> ulceration</td>
</tr>
<tr>
<td>IIB</td>
<td>T3b</td>
<td>Melanoma 2.01 – 4.0 mm in thickness <strong>with</strong> ulceration</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>Melanoma &gt; 4.0 mm in thickness <strong>without</strong> ulceration</td>
</tr>
<tr>
<td>IIC</td>
<td>T4b</td>
<td>Melanoma &gt; 4.0 mm in thickness <strong>with</strong> ulceration</td>
</tr>
<tr>
<td>III</td>
<td>Any T, any N M0</td>
<td>Any T, with lymph node involvement</td>
</tr>
<tr>
<td></td>
<td>Any T, N2c</td>
<td><strong>Satellite or in-transit metastasis</strong></td>
</tr>
<tr>
<td>IV</td>
<td>Any T, any N M1</td>
<td>Any T, with metastasis</td>
</tr>
<tr>
<td>Any</td>
<td>Any T</td>
<td>Elevated LDH</td>
</tr>
</tbody>
</table>
Melanoma: Clark’s Classification (level of invasion)

- **Level I**: Lesions involving only the epidermis (in situ melanoma); not an invasive lesion
- **Level II**: Invasion of the papillary dermis but does not reach the papillary-recticular dermal interface
- **Level III**: Invasion fills and expands the papillary dermis but does not penetrate the reticular dermis
- **Level IV**: Invasion into the reticular dermis but not into the subcutaneous tissue
- **Level V**: Invasion through the reticular dermis into the subcutaneous tissue
Growth Patterns of Melanoma Subtypes

- **Melanoma in situ** is a non-invasive melanoma with little risk of metastasis, but capable of local recurrence.

- **Superficial Spreading Melanoma (SSM)** constitutes about 70% of melanomas. They usually initially develop slowly and often start in brown junctional nevi. They are generally flat lesions and develop any time after puberty.

- **Nodular melanomas** constitute about 15 - 30% of melanomas. They are more aggressive than SSMs and usually develop in middle age, on the trunk, head and neck. They are often blue-black in color, but may be red, purple, or amelanotic. They tend to grow vertically rather than horizontally.

- **Lentigo Maligna Melanoma (LMM)** constitutes about 15% of melanomas. They are characterized by a long in situ phase. LMM does not metastasize as often as other melanomas. They are usually seen on the face of older females.

- **Acral Lentiginous Melanoma (ALM)** constitutes about 5% of melanomas. They occur on the hands, the soles of the feet, or under nail beds. This is a relatively uncommon type of melanoma in Caucasians, but is seen with much greater frequency in Asians, Hispanics and Blacks. They generally occur in older people and are more aggressive than LMMs and are more likely to metastasize.
Lung Cancer

• Can arise from many cell types in the lungs, causing several types of cancer
  o Small cell lung cancer (20%)
  o Non-small cell – includes adenocarcinoma, squamous cell cancer and other types (80%)

• A very common form of cancer (about 15% of all cancers)

• The leading cause of cancer deaths in the US

• Causes
  o Smoking – about 87% of cases in the US are related to smoking
  o Radon – first discovered to be a causative agent in uranium mine workers

• More common with advancing age, with usual age around 55-60

• Symptoms
  o Coughing, hemoptysis
  o Weight loss

• Diagnosis
  o Strongly suggested by radiological tests and history
  o Confirmed by biopsy or at surgery
Lung Cancer

- **Staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1 N0 M0</td>
<td>Tumor 3.0cm or less</td>
</tr>
<tr>
<td>IB</td>
<td>T2 N0 M0</td>
<td>Tumor larger than 3.0cm, or with certain other features</td>
</tr>
<tr>
<td>IIA</td>
<td>T1 N1 M0</td>
<td>Tumor 3.0cm or less with nearby positive nodes</td>
</tr>
<tr>
<td>IIB</td>
<td>T2 N1 M0</td>
<td>Tumor larger than 3.0cm with nearby positive nodes</td>
</tr>
<tr>
<td></td>
<td>T3 N0 M0</td>
<td>Tumor invades nearby structures without positive nodes</td>
</tr>
<tr>
<td>III</td>
<td>Tany Nany M0</td>
<td>Any other T/N stage without distant metastasis</td>
</tr>
<tr>
<td>IV</td>
<td>Tany Nany M1</td>
<td>Any case with distant metastasis</td>
</tr>
</tbody>
</table>

- The above staging is used for non-small cell lung cancer only (most common type)
- Small cell has only 2 stages
  - Limited: confined to one side of the chest
  - Extensive: not confined to one side of the chest

For non small cell, stage is strongly correlated with survival
- Stage 1: 57% five yr survival
- Stage IV: 2% five yr survival
Lung Cancer

- **Mortality concerns**
  - A very deadly cancer
  - Early stages have better survival but only 15% of cases are diagnosed in Stages I or II

- **Morbidity concerns**
  - Survivors may have chronic shortness of breath due to lung resection or other treatments
  - Potential also exists for other smoking-related illnesses like COPD or CAD
Underwriting Concerns

What to do with those incidental lung nodules … the bain of our existence

- Radiology reports are key: pulmonologist’s gospel – always look for any old images to compare to

- In general, what constitutes an appropriate surveillance of nodules is stability for 2+ years … this would suggest benign

- In general, ANY lung density 3+ cm is named a MASS and should be considered malignant until proven otherwise

- Solitary nodule 6mm or less DO NOT mandate any follow up in low-risk individual

- What constitutes low risk: younger age, nonsmoker, no workplace exposure, no fam hx, no personal hx cancer and no suspicious radiographic characteristics
What Constitutes Low-Risk Pulmonary Nodules?

- These are features that can possibly allow immediate favorable consideration for underwriting
  1. Diffusely or heavily calcified granulomas
  2. Nodules with central calcification (bull’s-eye nodules)
  3. Nodules with laminated calcification rings
  4. Popcorn calcification within nodule - these are usually hamartomas and benign
  5. Pleural-based nodules
What Constitutes High-Risk Pulmonary Nodules?

- Upper-lobe nodules more worrisome than lower-lobe
- Spiculated vs. lobulated
- Ground glass
- Note: nonsolid, partially solid or ground-glass nodules may require longer follow up to exclude indolent adenocarcinoma
- And of course, smoking history, older age, fam history, personal history of lung disorders, and any constitutional symptoms … what are those?
- A cool tool is the SPN calculator. You plug in age, sex, size, whether solid, partial-solid or nonsolid or ground glass, nodule count and if family history lung cancer, personal history emphysema and get the probability of nodule being diagnosed as cancer within 2-4-year follow up. Just Google it.
# Terrific Tools Regarding Solitary Pulmonary Nodules


## Prior Probability of Malignancy

The prior odds of malignancy can be subjectively estimated or based on the prevalence of malignancy in your patient population with solitary pulmonary nodules. The latter will vary by geographic location (due to histoplasmosis) or vary by referral pattern (tertiary care hospital vs clinic).

Enter a number from 1-100%: 50

## Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50-59</td>
</tr>
<tr>
<td>Smoking (Pk-Yrs)</td>
<td>&lt;30 Pk-yrs</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>Absent</td>
</tr>
<tr>
<td>Hx Prev Malig</td>
<td>Absent</td>
</tr>
</tbody>
</table>

## Radiographic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size (cm)</td>
<td>0-1 cm</td>
</tr>
<tr>
<td>Location</td>
<td>Lower</td>
</tr>
<tr>
<td>Growth Rate</td>
<td>Not Known</td>
</tr>
<tr>
<td>Cavity Wall Thickness</td>
<td>Not Cavitated</td>
</tr>
<tr>
<td>Edge</td>
<td>Spiculated</td>
</tr>
<tr>
<td>Calcification</td>
<td>None</td>
</tr>
</tbody>
</table>

## Additional Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contrast Enhancement</td>
<td>&gt;15 HU</td>
</tr>
<tr>
<td>PET</td>
<td>Not Performed</td>
</tr>
</tbody>
</table>

Calculate Probability of Malignancy

The Probability of Malignancy is: 93%
## Likelihood Ratios for Lung Nodule Characteristics

<table>
<thead>
<tr>
<th><strong>AGE</strong></th>
<th><strong>SIZE</strong></th>
<th><strong>CAVITY WALL THICKNESS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29yrs</td>
<td>0.05</td>
<td>Not Cavitated</td>
</tr>
<tr>
<td>30-39yrs</td>
<td>0.24</td>
<td>1 5-15mm 0.72</td>
</tr>
<tr>
<td>40-49yrs</td>
<td>0.94</td>
<td>&lt;4mm 0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;16mm 38</td>
</tr>
<tr>
<td><strong>SMOKING (Pk-Yrs)</strong></td>
<td></td>
<td><strong>LOCATION</strong></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>0.05</td>
<td>Upper/Middle 1.22</td>
</tr>
<tr>
<td>&lt;30 Pk-Yrs</td>
<td>0.24</td>
<td>Lower 0.66</td>
</tr>
<tr>
<td>&gt;40</td>
<td>1.90</td>
<td></td>
</tr>
<tr>
<td><strong>HEMOPTYSIS</strong></td>
<td></td>
<td><strong>EDGE</strong></td>
</tr>
<tr>
<td>Absent</td>
<td>1.0</td>
<td>Lobulated 0.74</td>
</tr>
<tr>
<td>Present</td>
<td>5.08</td>
<td>Spiculated 5.54</td>
</tr>
<tr>
<td><strong>HX PREV MALIG</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Prev Malig</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Prev Malig</td>
<td>4.95</td>
<td></td>
</tr>
<tr>
<td><strong>GROWTH RATE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not Known</td>
<td>1</td>
<td>Malignant 3.4</td>
</tr>
<tr>
<td>Benign</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td><strong>CONTRAST ENHANCEMENT</strong></td>
<td></td>
<td><strong>PET</strong></td>
</tr>
<tr>
<td>SUR &lt;2.5</td>
<td>0.04</td>
<td>&lt;15 HU 0.04</td>
</tr>
<tr>
<td>SUR &gt;2.5</td>
<td>2.32</td>
<td>&gt;15 HU 2.32</td>
</tr>
</tbody>
</table>
### Fleischner 2017 Guideline for Pulmonary Nodules

#### Solid Nodules

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Size</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk¹</td>
<td>No routine follow-up</td>
<td>CT at 6–12 months, then consider CT at 18–24 months</td>
</tr>
<tr>
<td>High risk¹</td>
<td>Optional CT at 12 months</td>
<td>CT at 6–12 months, then CT at 18–24 months</td>
</tr>
<tr>
<td><strong>Multiple</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk¹</td>
<td>No routine follow-up</td>
<td>CT at 3–6 months, then consider CT at 18–24 months</td>
</tr>
<tr>
<td>High risk¹</td>
<td>Optional CT at 12 months</td>
<td>CT at 3–6 months, then at 18–24 months</td>
</tr>
</tbody>
</table>

Nodules <6 mm do not require routine follow-up, but certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A). Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
## Fleischner 2017 Guideline for Pulmonary Nodules

### SubSolid Nodules

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Size</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ground glass</td>
<td>No routine follow-up</td>
<td>CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years. In certain suspicious nodules &lt; 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).</td>
</tr>
<tr>
<td>Part solid</td>
<td>No routine follow-up</td>
<td>CT at 3–6 months to confirm persistence. If unchanged and solid component remains &lt; 6 mm, annual CT should be performed for 5 years. In practice, part-solid nodules cannot be defined as such until ≥ 6 mm, and nodules &lt; 6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥ 6 mm should be considered highly suspicious (recommendations 4A-4C).</td>
</tr>
<tr>
<td>Multiple</td>
<td>CT at 3–6 months. If stable, consider CT at 2 and 4 years.</td>
<td>CT at 3–6 months. Subsequent management based on the most suspicious nodule(s). Multiple &lt; 6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).</td>
</tr>
</tbody>
</table>
Pop Quiz: Which characteristic(s) of a lung nodule are associated with a higher risk of cancer?

1. Upper lobe nodule
2. Calcified
3. Popcorn appearance
4. Partial solid
5. Spiculated

A. 1, 4, 5
B. 2, 3, 4
C. All of them

Which can you almost always assume is benign, with no need for any surveillance?
Thyroid Nodules

- Detected in 50-60% of healthy individuals
- Vast majority are benign
- Most are asymptomatic
- Multiple nodules does not necessarily mean all are benign – the risk of cancer is similar in those with solitary and in those with multiple nodules
Clinical Risk Markers for Thyroid Cancer

- History of head and neck irradiation
- Personal or family history of medullary or papillary thyroid carcinoma, parathyroid tumor or pheochromocytoma or MEN type 2
- Growth of the nodule
- Nodule ≥ 2 cm
- Cervical adenopathy or abnormal neck lymph nodes
- Thyroid nodule described as hard, fixed, firm or causing tracheal deviation
- Persistent dysphonia, dysphagia or dyspnea
### Ultrasound Risk Markers for Thyroid Cancer

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>(risk of malignancy ~1%)</td>
<td>(risk of malignancy 5-15%)</td>
<td>(risk of malignancy 50-90%)</td>
</tr>
<tr>
<td>▪ Purely cystic</td>
<td>▪ Isoechoic with central vascularity</td>
<td>▪ Marked hypoechogenicity</td>
</tr>
<tr>
<td>▪ Mostly cystic with reverberating artifacts</td>
<td>▪ Isoechoic with central vascularity</td>
<td>▪ Microcalcifications</td>
</tr>
<tr>
<td>▪ Isoechoic spongiform</td>
<td>▪ Isoechoic with indeterminate hyperechoic spots</td>
<td>▪ Irregular (spiculated) margins</td>
</tr>
<tr>
<td></td>
<td>▪ Isoechoic with elevated stiffness</td>
<td>▪ More tall than wide</td>
</tr>
<tr>
<td></td>
<td>▪ Calcified rim which is continuous</td>
<td>▪ Interrupted calcified rim</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Extracapsular growth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>▪ Suspicious regional lymph nodes</td>
</tr>
</tbody>
</table>

---

Recommendations for Fine Needle Aspiration (FNA)

- **Nodules < 0.5 cm**: monitor only regardless of ultrasound appearance
- **Nodules 0.5-1 cm**: may consider FNA or watchful waiting depending on clinical setting and patient preference. Biopsy recommended specifically if:
  - Subcapsular or paratracheal lesion
  - Suspicious lymph nodes or extrathyroid spread
  - Positive personal or family history of thyroid cancer
  - Suspicious clinical features
- **Biopsy is recommended for**
  - High-risk lesions \( \geq 1 \text{ cm} \)
  - Intermediate risk lesions > 2 cm
  - Low-risk lesions only when > 2 cm and increasing in size or associated with a risk history

Recommendations for Follow Up

- **Nodules nondiagnostic by FNA**
  - If cystic or predominantly (>50%) cystic, and no suspicious clinical or ultrasound features: follow up clinically and with ultrasound
  - Others: consider repeat FNA or other means of tissue sampling

- **Nodules benign by FNA**
  - No suspicious clinical or ultrasound features: repeat clinical and ultrasound follow up in 12 months; if unchanged, repeat ultrasound follow up after 24 months
  - With suspicious clinical or ultrasound features: a repeat FNA is recommended

Pop Quiz: Which characteristics of thyroid nodule carry higher risk of malignancy?

a. Isoechoic
b. Microcalcifications
c. Wider than tall
d. Markedly hypoechoic

1. Both a and c
2. Both b and d
3. All excluding d
4. All excluding a
Another Pop Quiz or Pause to Reflect on a Case

Case:

- 45-year-old male with prior history of Hodgkin’s treated a decade ago with chemo and radiation to subclavicular nodes
- Presents with incidental findings of hypoechoic, irregular left thyroid nodule measuring 1.5 cm. FNA performed showing nondiagnostic findings.

How would you rate case: standard, substandard or decline?
Cancer Case Studies
Breast Cancer Case #1

55 year old female dentist applying for $500,000 of term life insurance

- Mother with breast cancer at 50, she is still alive.
- BRCA testing (-).
- Because of this family history, she started screening mammography at age 40 and in August, 2006 suspicious calcifications were noted prompting a biopsy that showed infiltrating ductal breast cancer.
- She had a lumpectomy & sentinel node bx:
  - Final path: 1.6 cm high grade infiltrating ductal breast cancer, clear margins, Grade 3, ER (-), PR (-), Her 2/neu ab (+); nodes (-). Dx: T1c,N0, M0.
- She was treated at Johns Hopkins receiving 6 months of chemotherapy completing treatment in April, 2007.
- She is followed yearly with mammograms which have been normal.

How would you assess the risk?
Case 1 (Continued)

Risk Issue: Early stage breast cancer in young female >10 yrs ago s/p optimal treatment and without recurrence.

- Favorable Factors:
  - Young age
  - BRCA (-)
  - Early stage breast cancer
  - Her 2/neu ab +
  - Appropriate treatment & follow-up

- Unfavorable Factors:
  - Young age
  - High grade histology
  - Hormone receptors (-)

- Risk Assessment: Life – Standard to Low Substandard

Would it matter if there was an Oncotype DX score on this case?
55 year old female dentist applying for $500,000 of term life insurance

• Mother with breast cancer at 50, she is still alive. BRCA testing (-).
• Because of this family history, she started screening mammography at age 40 and in August, 2006 suspicious calcifications were noted prompting a biopsy that showed infiltrating ductal breast cancer.
• She had a lumpectomy & sentinel node bx:
  o Final path: 1.6 cm high grade infiltrating ductal breast cancer, clear margins, ER (-), PR (-), Her 2/neu ab (+); nodes (-). Dx: T1c,N0, M0.
• She was treated at Johns Hopkins receiving 6 months of chemotherapy completing treatment in April, 2007.
• Her treatment was complicated by CHF d/t a drug-induced cardiomyopathy that has resolved. Most recent echo WNL. (Or maybe not an echo, but probnp is 30)
• She is followed yearly with mammograms which have been normal.

Would this scenario alter the rating?
Breast Cancer Case #2

67 year old female radiologist applying for $5,000,000 WL

- In 2008, she had an abnormal mammogram with suspicious calcifications noted in the left upper quadrant of her right breast; biopsy showed DCIS.
- She underwent a lumpectomy which confirmed a single, grade 2, 12 mm DCIS with clear wide margins, ER (+), PR (+), HER2 (-). No comedonecrosis.
- She just completed 10 years of tamoxifen.
- She is followed closely with yearly mammograms; her most recent this year was BIRADS 2.

How would you assess the risk?
Case 2 (Continued)

Risk Issue: DCIS in older woman

- Favorable Factors:
  - Older age applicant
  - DCIS – small, single lesion & without comedonecrosis
  - Optimal treatment with surgery with wide clear margins
  - Good follow-up without recurrence

- +/- Prognostic Factor:
  - Hormone receptors (+)

- Unfavorable Factors:
  - Grade 2

- Risk Assessment: Life – Standard
Cancer Case Studies

Case Study #3

- 55 year old male
  Amount: $300,000
- Ceding Company Offer: Unknown
- Insurance Labs: Normal
- Disclosed: Routine office visit 3-6 months ago, high cholesterol
- APS: Four years ago – screening colonoscopy with 3 small polyps and 1 large polyp removed. Per pathology report, small polyps described as hyperplastic, while the large polyp described as a tubular adenoma with moderate atypia.
  
  Four months later, an additional colonoscopy was done to fully remove the large polyp, however the operative report indicates unable to snare safely. They did remove two additional specimens though – one being a hyperplastic polyp and the other showing serrated adenoma with mild atypia.
  
  Two months later, a transanal excision was done to remove the rectal mass. Pathology showed serrated adenoma with mild-moderate atypia.
  
  One year later, his doctor notes discussing removal of the persistent polyp.
- Six months later, an office visit notes a history of villous adenoma.
- No additional operative reports or pathology reports in the APS.
Cancer Case Studies

Case Study #4

- **47 year old male**
  - Amount: $500,000

- **Ceding Company Offer**: Unknown

- **Insurance Labs**: Hemoglobin A1c 7.7, AST 62, ALT 109, HCV negative, cotinine negative

- **Disclosed**: Anxiety for many years, stable on Effexor. Diabetes for 4 years on 2 meds.

- **APS**: Never smoked, but World Trade Center exposure. Complained of several weeks of dyspnea (2 months prior to application).

- **CT scan (2 months prior to application)**: No emphysema or bronchiectasis. No definite interstitial lung disease. Mild localized subpleural reticular and ground glass opacity in the medial right lower lobe favored to represent subsegmental atelectasis. A solitary subpleural 5 x 3 mm nodule is present in the left lower lobe – likely postinflammatory in nature, however somewhat indeterminate in appearance. A follow up chest CT in one year is recommended to ensure stability.
Cancer Case Studies

Case Study #5

- **46 year old male**
  Amount: $100,000

- **Ceding Company Offer**: Postpone

- **Insurance Labs**: Total cholesterol 216, HDL 39, cotinine negative

- **Disclosed**: Seizure disorder, on Keppra. Last seizure 4 years ago. Sleep apnea, no treatment. CXR due to cough 6-12 months ago, on promethazine as needed.

- **APS**: Never smoked. Complained of a chronic cough 10 months prior to application. Physical exam negative. Chest CT revealed mild parenchymal scarring in both lungs. No adenopathy. There was a 5mm ground-glass nodule in the left-upper lobe, which is stable when compared to the 2010 examination.

- The report for the 2010 CT scan not included in the APS.
Cancer Case Studies

Case Study #6

- **64 year old male**
  Amount : $150,000

- **Ceding Company Offer**: Unknown

- **Insurance Labs**: PSA < .04

- **Disclosed**: Prostate removed 7 years ago, non-cancerous

- **APS**: Office visit 7 years ago notes history of prostate cancer. No pathology, but it says 9 years ago, prostate biopsy showing a small focus of adenocarcinoma, Gleason 6. Patient chose watchful waiting. Currently wants to have prostatectomy. Prostatectomy was done showing extensive BPH, acute and chronic prostatitis, extensive atrophy with small gland acinar hyperplasia with focal atypical changes suggestive but not definitive for adenocarcinoma.

- Follow-up PSA(s) have been < .1
Cancer Case Studies

Case Study #7

- **69 year old female**
  Amount: $215,249

- **Ceding Company Offer**: Unknown

- **Disclosed**: Melanoma 5-10 years ago

- **APS**: Seven years ago – wide excision: melanoma, superficial spreading, 0.65mm, Clark’s level III/IV, ulceration absent, mitotic index 1; notes original punch biopsy with 1.0mm invasion (original biopsy path not included).

- Four years ago – less than 50 nevi
- Three years ago – whole body scan ok
- Two years ago – stable derm checkup
- One year ago – no recurrence
Cancer Case Studies

Case Study #8

- **64 year old male**
  Amount: $1,000,000

- **Ceding Company Offer**: Unknown

- **Disclosed**: Prostate cancer 2009; father died from lung cancer and had history of Hodgkin’s

- **Insurance Labs**: PSA .01

- **APS**: Seven years ago PSA at 5.7 and 18.3

- Six years ago – PSA at 6.5, free PSA of 18%; prostate needle biopsy with findings of Gleason 3+3 on one specimen; placed on surveillance only

- Four years ago PSA at 6.6 and 6.9; Prostate needle biopsy: Gleason 3+4 and bilateral Gleason 3+3

- Three years ago – prostatectomy: left apex small acinar adenocarcinoma, Gleason 3+4, 15% tumor grade, <5% grade 5, extensive intraepithelial neoplasia, T2cNxMx; past medical history of lung of cancer in 1985

- Two years ago – PSA at 0.0008

- History of benign carcinoid 1980s
Cancer Case Studies

Case Study #9

- **53 year old female**
  Amount: $160,000

- **Ceding Company Offer:** Decline

- **Insurance Labs:** Normal

- **Exam:** 5.1 and 157 pounds

- **Disclosed:** Breast cancer 2011, depression for 4 years

- **APS:** 5 years ago - needle biopsy showed invasive ductal carcinoma and ductal carcinoma in situ; lumpectomy then done showing invasive ductal carcinoma, moderately differentiated 0.7cm, also some DCIS

  Additional lumpectomy done showing residual invasive ductal carcinoma, moderately differentiated, 2.1cm, also some DCIS, both the carcinoma and DCIS extended to superior margin of resection; underwent additional resection for additional margins which was negative; staging T2N0, Ila; chemo started; pulmonary nodules found on CT and all <5mm.

- Three years ago – weight at 170, CT with no new nodules

- One year ago – weight at 155
Cancer Case Studies

Case Study #10

- **53 year old male**
  Amount: $1,523,000

- **Ceding Company Offer**: Unknown

- **Insurance labs**: Uric acid at 7.3

- **Disclosed**: Partial nephrectomy 2010 due to cancer; father with lymphoma and sister with breast cancer

- **APS**: Three years ago - CT showed bilateral renal cysts, one complex renal cyst has enhancing component “worrisome for neoplasm” and interval increase in size when compared to CT two years prior

- Office visit one year ago notes history of pT1a, low grade, cystic renal cell carcinoma

- Current CT notes bilateral renal cysts are unchanged

- Renal cancer pathology report not included
Cancer Case Studies

Case Study #11

- 75 year old female
  Amount: $250,000
- **Ceding Company Offer**: Standard, looking for preferred
- **Insurance Labs**: AST 34, otherwise normal
- **Exam**: 5.1 and 112 pounds
- **Disclosed**: benign pancreatic cyst 2012
- **APS**: Three years ago - intermittent abdominal discomfort; new findings of 2.2cm pancreatic cyst by CT
- **EGD**: normal stomach, 16mm septated cystic lesion pancreatic head- fine needle biopsy done, pancreatic parenchymal abnormalities consisting of hyperechoic strands noted in the entire pancreas – await path; path reported completed and no malignant cells
- Two years ago – MRI of abdomen and showed stable lesion; MD reviewed MRI and opinion is that she has a side branch IPMN (intraductal papillary mucinous neoplasm), which has a low-grade malignant potential
Cancer Case Studies

Case Study #12

- **58 year old female**
  Amount: $100,000

- **Ceding Co. Offer**: Standard with $7.50 flat extra/3 years

- **Insurance Labs**: protein/creatinine ratio at 700mg/g, repeat protein/creatinine ratio at 422mg/g

- **Disclosed**: Father died from liver cirrhosis, mother died from breast cancer; annual exam (no medical history of concern admitted)

- **APS**: One year ago – right breast nodule on mammogram

  Right breast nodule core biopsy path: invasive ductal carcinoma, grade 1; an additional review of the specimen raised the possibility of sclerosing adenosis – excisional biopsy suggested; morphological features are worrisome but the lesion is P63, SMM-HC, and D240 positive, strongly suggestive of sclerosing adenosis.

- **Right breast mass excision path**: sclerosing adenosis