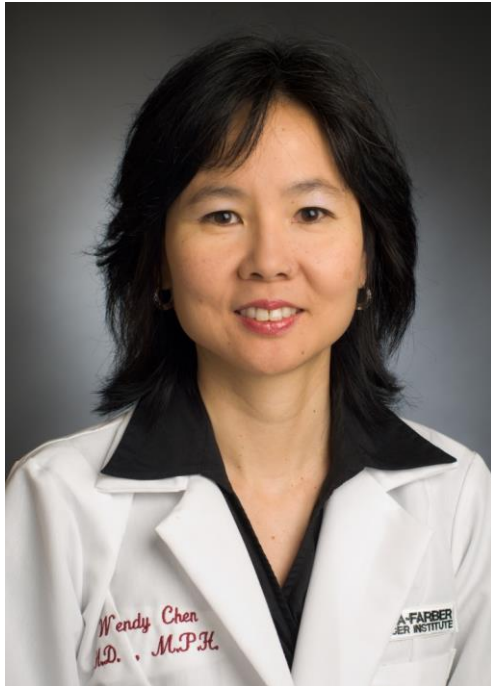


Take Home Messages

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 - Clinical focus: Breast Cancer
 - Research focus: Cancer epidemiology

Disclosures

- No financial disclosures relevant to this presentation

Learning objectives

- Review epidemiology, risk factors, and treatment for lung, breast, gastrointestinal, genitourinary, and hematologic malignancies

Breast cancer



Breast cancer

- Risk factors:
 - Age, obesity, sedentary lifestyle, alcohol, genetics
- BRCA 1/2
 - Responsible for 5-10% breast CA
 - BRCA1: lifetime risk 50-70% breast and 40-50% ovarian
 - BRCA2: lifetime risk 40-60% breast and 10-25% ovarian
 - BRCA1/2 – pancreatic, BRCA2 – male breast and pancreatic
- Prevention
 - Tamoxifen, raloxifene, and AI ↓↓ breast ca risk, but no effect on mortality
- Screening
 - Women aged 50-74 should get screening mammo every 1-2 years

Adjuvant breast cancer therapy

- **Breast cancer subtype (ER/HER2) dictate therapy**
- **Chemotherapy improves overall survival in:**
 - Triple negative
 - HER2 positive when given along with trastuzumab
 - ER positive and unfavorable gene expression profile
 - Neoadjuvant approach common with HER2 positive and triple negative breast cancer
- **Hormonal therapy:**
 - ↓↓ breast cancer mortality by 1/3
 - ↓↓ contralateral breast cancer by 1/2
 - Tamoxifen for pre or postmenopausal women
 - Ovarian suppression increasingly used
 - Aromatase inhibitors preferred for postmenopausal women
 - Duration: 5 or 10 years

Metastatic breast cancer overview

- **Survival continues to improve**
 - >1/3 alive at 5 yrs, but varies by subtype
- **Hormone receptor positive/HER2 negative**
 - Oral hormonal therapy first before chemo
- **Triple negative**
 - Chemo + immunotherapy first if tumor PDL1 positive
- **HER2 positive**
 - HER2 directed therapy followed by maintenance antibody therapy for responders
- **Antibody drug conjugates**
 - Targeted antibody linked to chemo – used for all subtypes

Lung cancer



Lung cancer epidemiology

- Leading cause of cancer death
- Smoking:
 - 80-90% of cases in smokers
 - Risk proportional to amount and duration of smoking
 - Quitting reduces risk but not to baseline
- Almost 50% patients have metastatic disease at dx
 - Survival strongly correlated with stage
- 85% of cases non-small cell lung cancer

Lung cancer screening

- 20-25% decrease in lung cancer mortality
- Consider annual low dose CT screening (need all 3)
 - Ages 50-80
 - ≥ 20 pack years
 - Current smoker or quit in past 15 years
- Follow up of radiographic findings for screening - LUNG-RADS
- Fleischner criteria for incidental nodule on scan performed for another reason

Biopsy/staging

- **Tissue:**
 - Core strongly preferred to FNA
 - Genomic analysis
 - Non-bone sites strongly preferred
 - Decalcifying bone denatures DNA and interferes with IHC
- **Staging**
 - Chest CT with contrast
 - PET/CT (preferred) or bone scan
 - Brain MRI with gadolinium (preferred) or Head CT
 - Mediastinal staging for potentially resectable pts
 - Mediastinoscopy or Bronch/EBUS

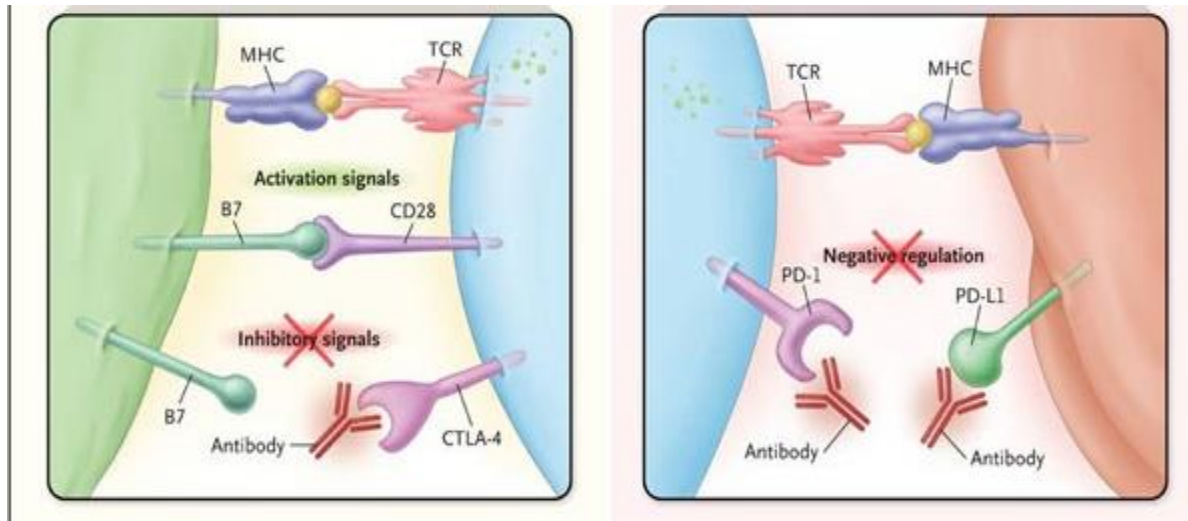
Treatment dictated by stage

NSCLC Stage	SCLC Stage	Treatment Approach
I		Surgical resection
II		Multimodality approach
III		Multimodality approach
	Limited	ChemoRT + immunoRx
IV	Extensive	Palliative systemic Rx

Targeted agents in lung cancer

- 1st targeted therapy approval EGFR TKIs in 2004
- 2025- multiple agents transformed natural history of lung cancer
 - Mutations in BRAF V600E, EGFR, HER2, KRAS G12C, MET exon 14
 - Fusions/Rearrangements – *ALK, NRG, NTRK, RET, ROS1*
 - Immunotherapy options for many
 - Not all cancers have targetable mutations

Immunotherapy in lung cancer



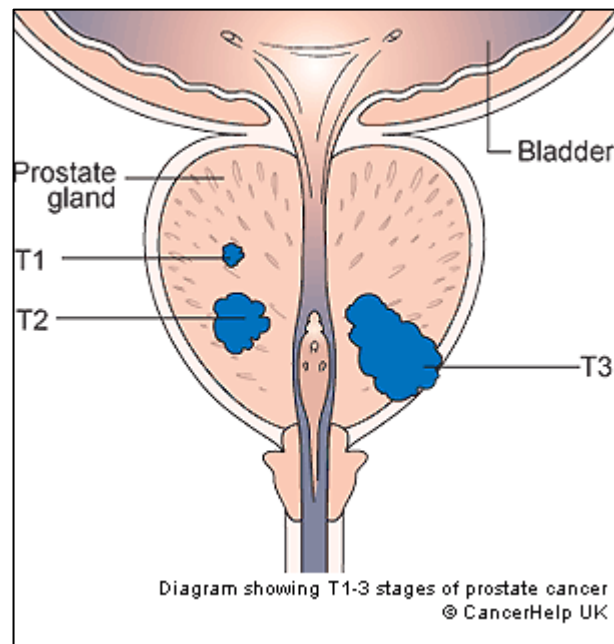
Ribas, NEJM 2012

Can be used with or without chemotherapy

Careful monitoring and attention to immunotoxicity

- Can occur in any organ system at any time

Genito-urinary cancer



Prostate cancer epidemiology

- 299,010 new cases per year (1 in 7 men)
- 35,250 deaths per year
- Risk factors:
 - Age
 - Family history
 - African American
 - BRCA 1/2, Lynch syndrome

Prostate cancer screening

American Urologic Association (AUA)

- < age 40 - No routine screening
- Age 40-54 years at average risk – no routine screening
- Age 55-69 - shared decision-making with physicians
- Age 70+ (or life expectancy < 10 years) – no routine screening

US Preventive Services Task Force 2018

- Age 55- 69 – shared decision making with physicians
- Age 70+ - recommend against screening

American Cancer Society

Discuss screening with

- ≥age 50 with 10 yr life expectancy
- Discuss age ≥45 for African Americans and men with 1st degree relative dx < age 65
- Discuss age ≥40 for those with multiple 1st degree relatives dx < age 65

Treatment Options

Active surveillance



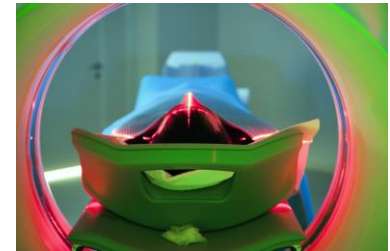
Gleason Score <7 ,
PSA <10
 $<T2b$
 $<1/3$ bx cores
positive

Surgery



High cure
rate in GS ≤ 7
Surgery for
select cases
of GS 8-10

Radiation



+/- ADT
Androgen
Deprivation
therapy

Weighing Toxicity

Surgery	Radiation	ADT
• Surgical complications - Wound healing - Infection - Anesthesia risks • Erectile dysfunction • Urinary Incontinence	• Irritative urinary Sx • Bowel dysfunction • Erectile dysfunction • Risk of second cancer	• Hot flashes • Fatigue • Weight gain • Bone density loss • Loss of libido • Emotional changes • Metabolic insults: insulin resistance • ?Cardiac toxicity

- Surgery: radical prostatectomy (robotic, open, laparoscopic)
- Radiation: external beam, brachytherapy
- Androgen deprivation therapy: GnRH agonist or antagonist +/- antiandrogen

Current Treatment of Castration-resistant Prostate Cancer

Androgen deprivation therapy backbone of 1st line treatment

**Second line
Androgen blockade:**

- Abiraterone
- Enzalutamide

Bone-targeted:

- Radium-223
- Antiresorptives

**Immunotherapy:
Sipuleucel-T**

Chemotherapy

- Docetaxel
- Cabazitaxel

PARP inhibitors:

- Rucaparib
- Olaparib

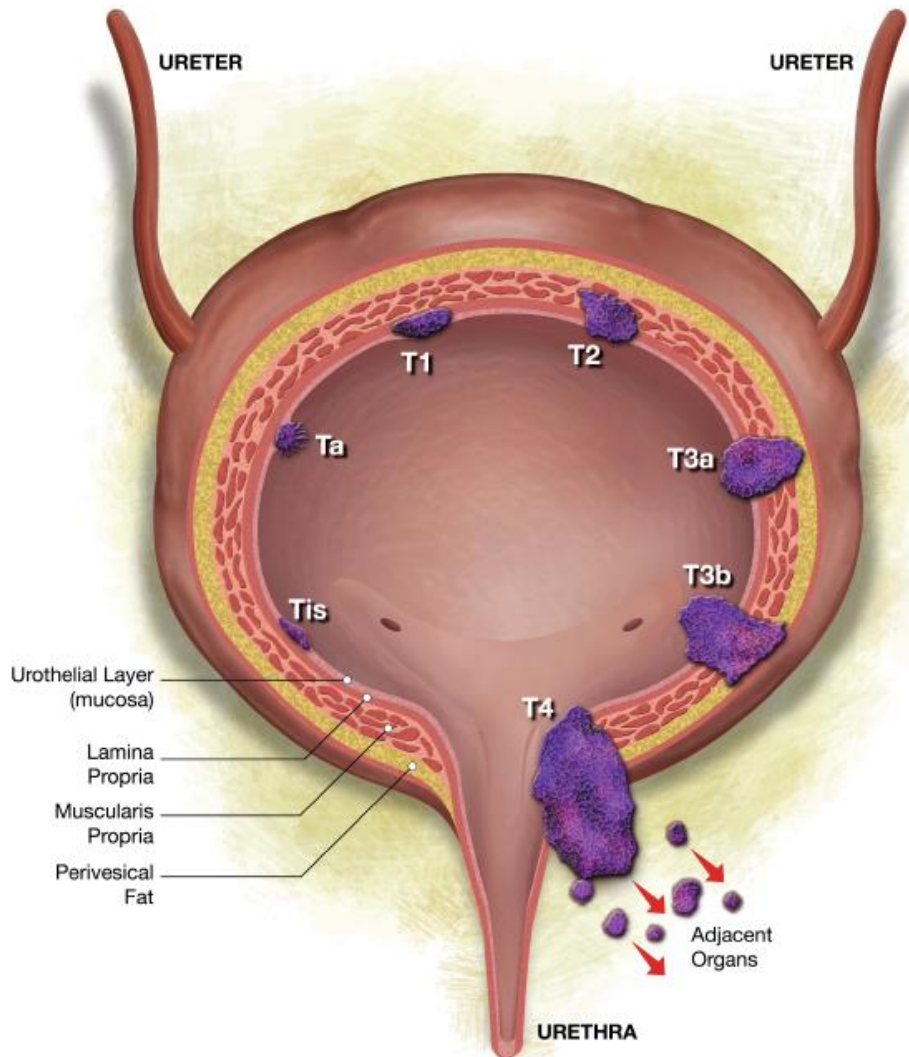
Bladder cancer epidemiology

- 80,470 cases per year in the US (3 to 1 M/F)
- Median age 73-74
- 17,670 deaths per year
- Risk factors
 - Age
 - Tobacco
 - Occupational exposures
 - Parasitic infection of bladder
 - Cyclophosphamide or arsenic
 - Male
 - Family history
 - Race
- 50-60% superficial disease
- 90% urothelial or transitional cell

Presentation

- Hematuria : gross or microscopic
- UTI like symptoms
 - Frequency, dysuria
- If no infection:
 - Refer for cystoscopy
 - Urine cytology
 - Possible imaging with CT

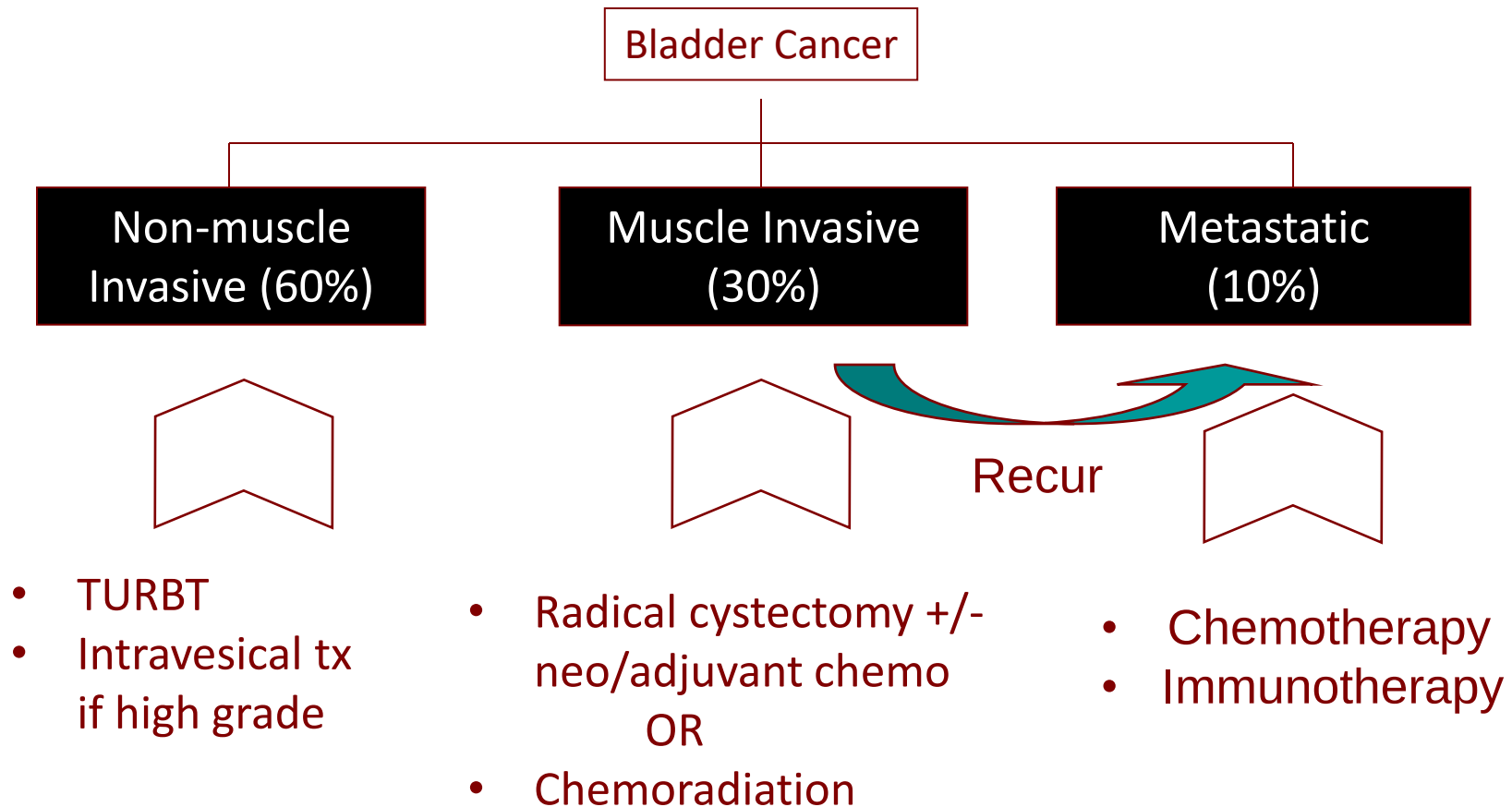
Staging of Bladder Cancer



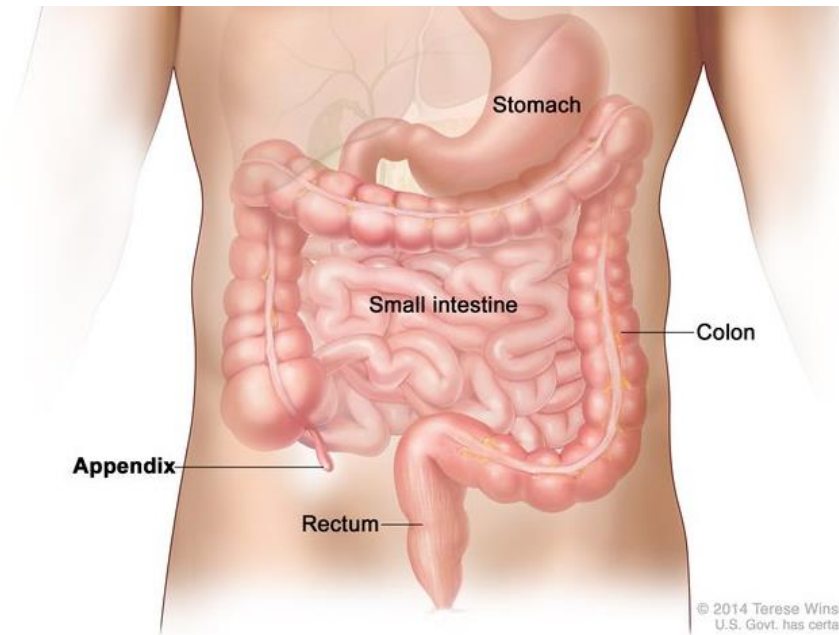
- T1: superficial, non-invasive
- T2: muscle invasion; path specimen must have muscularis propria
- T3: into/thru periesicular fat
- T4a: invades prostate, seminal vesicles, uterus, or vagina,
- T4b: invades pelvic/abd wall

Key that biopsy includes muscle

Spectrum of Bladder Cancer



Gastrointestinal cancer



Esophageal cancer

- **Risk factors:**
 - **SCC:** alcohol, tobacco, prior RT
 - **Adeno:** Barrett's, reflux, obesity
- **Localized disease**
 - Neoadjuvant chemo RT->surgery->immunoRx
 - Peri-op chemo -> surgery-> chemo
- **Metastatic disease**
 - Median survival 7-14 months
 - 1st line therapy usually platinum based chemo
 - Esophageal/GE junction adeno treated like gastric

Gastric cancer

- **Risk factors**
 - H.pylori, salted meats, nitrates, smoking , occupation, E cadherin mutation
- **Localized disease**
 - Surgery + post-op chemo/RT or
 - Chemo-> surgery-> chemo
- **Palliative chemo for metastatic disease**
 - 1st line chemo usually platinum-based combo
 - ImmunoRx with chemo for selected pts
 - If HER2 positive – trastuzumab or trastuzumab deruxtecan

Pancreatic cancer

- **Risk factors:**
 - DM, obesity, smoking, hereditary (germline testing rec)
- **Localized disease (15% of patients):**
 - surgery with adjuvant chemo/RT
 - 15% survive 5 years
- **Locally advanced:**
 - Chemotherapy + RT or chemo RT
- **Metastatic disease:**
 - Combination chemo
 - Median survival < 12 months

Colorectal cancer

- **Risk factors:**
 - Increase risk: family hx, IBD, Diabetes, smoking, obesity, western diet
 - Decrease risk: screening, exercise, vit D, ASA, NSAIDS, calcium
- **Hereditary Familial syndromes (5% cases):**
 - Familial Adenomatous Polyposis
 - Hereditary Non Polyposis Colorectal Cancer

Colorectal Cancer Screening

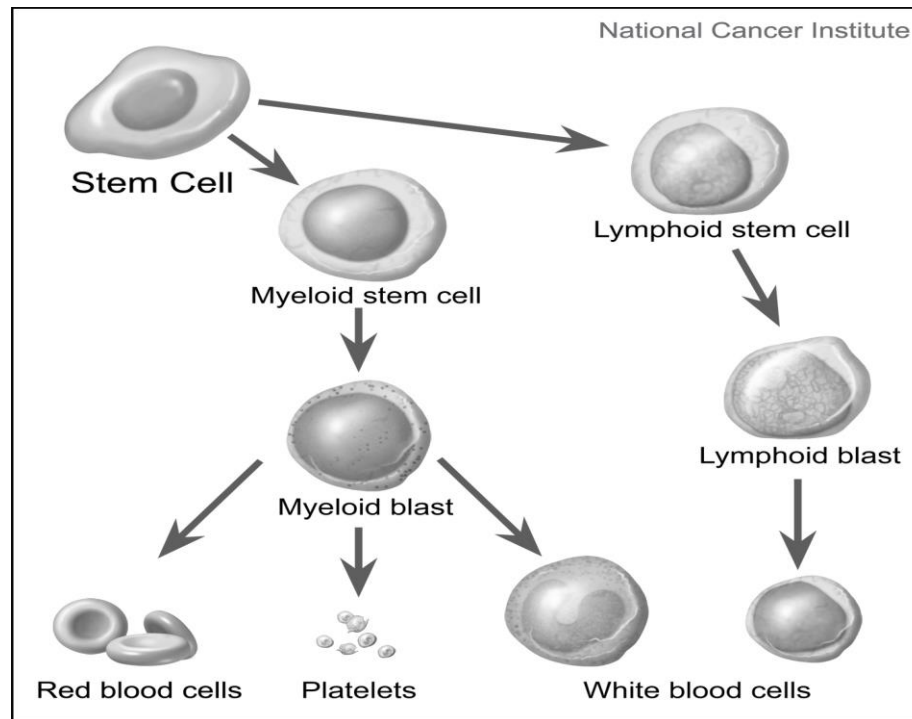
- American Cancer Society recommendations for average risk
- Consider screening age 45, routine screening 50 and older
- Options
 - Structural exams
 - Flexible sigmoidoscopy every 5 years*
 - Colonoscopy every 10 years
 - CT colonography (virtual colonoscopy) every 5 years *
 - Stool based tests
 - Fecal occult blood test (FOBT) every year *
 - Fecal immunochemical test (FIT) every year *
 - Stool DNA test every 3 years*

***Colonoscopy should be done if test results positive**

Colorectal cancer treatment

Stage	Colon	Rectal	5 yr survival
I (T₁-T₂, N₀, M₀)	Surgery only	Surgery only	>90%
II (T₃-T₄, N₀, M₀)	Surgery +/- Chemotherapy	Chemoradiation → Surgery → Chemotherapy OR Surgery → Chemoradiation & Chemotherapy	70-85%
III (T_{any}, N₊, M₀)	Surgery → Chemotherapy		30-70%
IV (T_{any}, N_{any}, M₁)	Chemotherapy +/- Surgery	Chemotherapy +/- Surgery	8-10%

Hematologic cancers



Myelodysplastic syndrome

- Heterogeneous in presentation and risk of progression
- Risk factors: age, prior chemo/RT
- Presents with cytopenias (anemia most common)
- Need bone marrow bx with karyotype for dx
- Prognosis – IPSS - % blasts, cytogenetics, # of cytopenias
- Treatment
 - Supportive care
 - Azacitidine, decitabine, lenalidomide, luspatercept
 - Curative : allogenic stem cell transplant

Chronic Myeloid Leukemia

- **Myeloproliferative disorder defined by Philadelphia chromosome t(9;22)**
 - **Presents with leukocytosis and splenomegaly**
- **Natural history**
 - **Chronic phase ->accelerated phase->blast phase**
- **Treatment**
 - **Tyrosine kinase inhibitors transformed prognosis**
 - **Imatinib, dasatinib, nilotinib, bosutinib, ponatinib, asciminib**
 - **Life expectancy approaches age matched population**

Acute Myeloid Leukemia

- **Risk factors**
 - Age, prior chemo/RT, pre-existing MDS
- **Prognosis:**
 - Age, cytogenetics (favorable vs unfavorable), mutations (favorable vs unfavorable)
- **Treatment**
 - Intensive induction chemotherapies
 - Consolidation - chemo or allogeneic transplant depending on risk
 - >75 years old – targeted therapies (e.g. FLT3, IDH1, BCL2)

Plasma cell disorders

Monoclonal gammopathy of unknown significance

- M protein <3 g/dL
- Clonal plasma cells in bone marrow <10%
- No myeloma-defining events
- Risk of progression to MM 1% per year

Smoldering myeloma

- M protein ≥ 3 g/dL (serum) or ≥ 500 mg/24 hrs (urine)
- Clonal plasma cells in bone marrow $\geq 10\%$ to 60%
- No myeloma-defining events
- Heterogeneous disease

Multiple myeloma

- Underlying plasma cell proliferative disorder
- AND**
- 1 or more myeloma-defining events:
- ≥ 1 CRAB* feature
 - Clonal plasma cells in bone marrow $\geq 60\%$
 - Serum free light chain ratio ≥ 100
 - >1 MRI focal lesion

***C**: Calcium elevation (>11 mg/dL or >1 mg/dL higher than ULN)

R: Renal insufficiency (creatinine clearance <40 mL/min or serum creatinine >2 mg/dL)

A: Anemia (Hb <10 g/dL or 2 g/dL $<$ normal)

B: Bone disease (≥ 1 lytic lesions on skeletal radiography, CT, or PET-CT)

Treatment of plasma cell disorders

Monoclonal gammopathy of unknown significance

- Observation with close monitoring

Smoldering myeloma

- Observation with close monitoring
- If high risk=> *possible* myeloma drugs
- If bone loss => bone modifying agents

Multiple myeloma

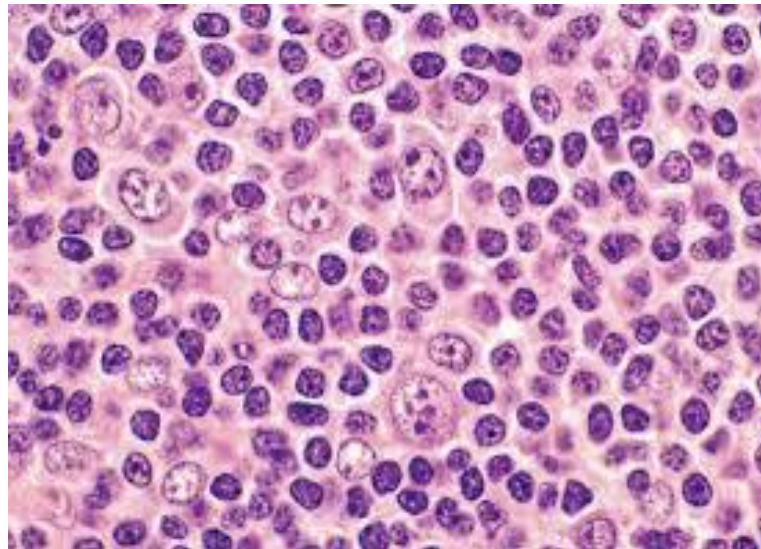
- Transplant candidate
 - Induction=> Transplant=> Consolidation=> Maintenance
- Non-transplant candidate
 - Induction=> Maintenance

- Revised International Staging system for multiple myeloma – β 2 microglobulin, albumin, FISH, and LDH
- Median Overall survival 83 months for II and 43 months for III

Complications

- Bone disease/hypercalcemia
- Hyperviscosity
- Recurrent infections
- Renal failure: hypercalcemia, myeloma kidney, hyperuricemia, plasma cell infiltration, pyelonephritis, amyloid
- Cardiac failure: amyloid, hyperviscosity, anemia
- Anemia: bone marrow involvement, renal dysfunction, low endogenous erythropoietin
- Neuropathy: sensory $\pm$ motor, amyloid, anti-myelin Ab

Lymphomas



Non-Hodgkin's lymphoma

	Indolent	Aggressive	Highly aggressive
Survival untreated	Years	Months	Weeks
Response to chemotherapy	Not curable	Curable	Curable
Example	Follicular lymphoma	Diffuse large B-cell lymphoma	Burkitt lymphoma

NHL diagnosis

- Supraclavicular > cervical/axillary > inguinal
- Excisional biopsy when possible
 - Or CT guided core needle
- Send for pathology, immunohistochemistry, flow cytometry, cytogenetics
- Work up – PET-CT +/- bone marrow biopsy

Hodgkin lymphoma

- **Stage I and II Disease**
 - Chemo +/- RT
 - 85%-90% cured with initial chemo
- **Stage III and IV Disease**
 - Chemotherapy always required
 - Usually with brentuximab (anti CD30 antibody drug conjugate)
 - Role of radiation therapy to sites of bulky disease uncertain
 - 75% cured with initial therapy depending on risk

Thank You!

