

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

Leukemia, Lymphoma, and Myeloma

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Hematopoiesis

- Regulation, production, & development of blood cells
 - All blood cells are derived from stem cells in the bone marrow
 - Stem cells are capable of:
 - Self-renewal
 - Differentiation
 - Proliferation
 - Maturation
 - Stem cells commit to either a LYMPHOID or MYELOID lineage
 - Cells differentiate and mature w/ the influence of growth factors

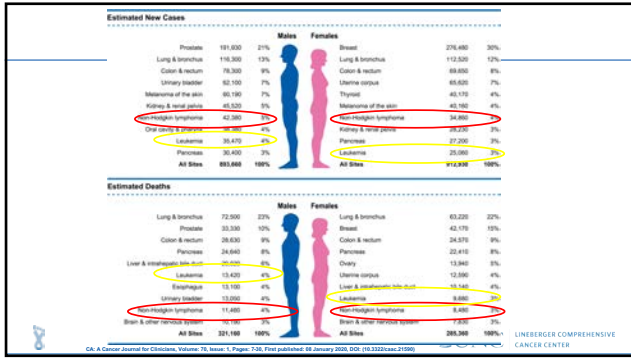
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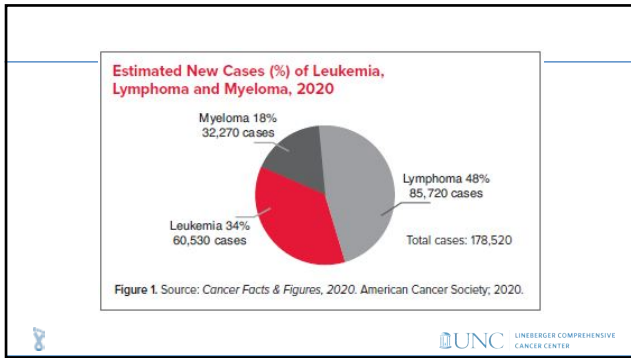
Blood cancers can develop in many different places within normal blood cell formation. The type of blood cancer that results has to do with where normal cell development is blocked. The picture shows the cell type where different blood cancers arise.

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Case Presentation #1

- 32 year old male notices an area of swelling in neck
- He presents to primary care physician (PCP) and initially this is felt to be an infection and he is given antibiotics
- He notices that this area of swelling is persisting with new swelling in his groin so he presents again to he PCP who refers him to a surgeon for a biopsy
- He has a biopsy that removes the lymph node (excisional lymph node biopsy) in his inguinal region

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What is Lymphoma?

- Cancer of the lymphocytes
- >70 types of lymphoma
- B-cell lymphoma (85%)
- T-cell lymphoma (15%)
- Aggressive and indolent subtypes

From ASH SAP 2016

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Causes of Lymphoma

- Unknown for most people
- Environmental
 - Certain chemicals suspected (eg, certain pesticides/ herbicides, agent orange)
 - High-dose radiation exposure suspected
- Immunosuppression
 - Immune deficiency (AIDS, post-organ transplant, some medications)
 - Link with autoimmune diseases
- Viral and Bacterial
 - Infections (HTLV-1 virus, EBV, *H. pylori* bacteria)

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Lymphoma Symptoms


- New mass or lump (enlarged lymph node)
 - Often painless
- B Symptoms:
 - weight loss (>10%) in 6 months
 - Fever
 - Drenching night sweats ("Do you change your clothes overnight?")
- Other: fatigue, itching, abdominal fullness/early satiety/increasing belt size, cough
- No symptoms (incidentally found on scan)

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Case Presentation, Continued

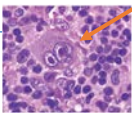
- Patient's biopsy is consistent with follicular lymphoma
- He has a PET scan which shows many enlarged and bright lymph nodes above and below the diaphragm
- He is asymptomatic from his lymphoma and would prefer not to start treatment
- Decision is made to watch and wait



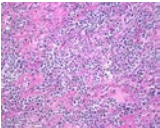
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Type of Lymphoma: Aggressive


- More often symptomatic at presentation (but not always!)
- Curable in many cases (even stage IV)
- Often progresses quickly if not responding to treatment
- **Diffuse Large B cell Lymphoma** – most common type
- **Classical Hodgkin lymphoma**- younger patients - high cure rate
- **Burkitt lymphoma** – VERY fast growing



Reed-Sternberg Cell



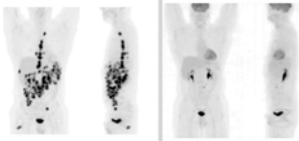
Diffuse Large B Cell Lymphoma



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Lymphoma Diagnostic Tests


- Lymph Node Biopsy:
 - NEVER: Fine-Needle Aspirate
 - ADEQUATE: Core-Needle Biopsy
 - BEST: Surgical Excision
- PET/CT Scan




From lymphoma-action.org.uk


TYPES OF BIOPSIES

Fine-Needle Aspirate 

Core-Needle Biopsy 

Surgical Biopsy 

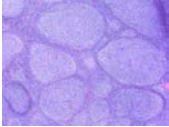
National breast cancer foundation, inc., 2015




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Types of Lymphoma: Indolent

- Often asymptomatic at presentation
- Slow growing
- Generally not considered curable but often long life expectancy (chronic disease)
- Older patients on average
- In some cases, can watch and wait instead of starting treatment
- Follicular lymphoma – most common subtype





Follicular Lymphoma



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Case Presentation: Treatment


- Over the next year, he notes that the lymph nodes are continuing to grow and causing discomfort because they are getting so big
- He also notes increasing fatigue
- Decision is made to start combination chemotherapy to treat his lymphoma



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Lymphoma Treatment



- Observation (may be appropriate for indolent lymphomas)
- Radiation – usually if localized disease
- Chemotherapy – traditional chemotherapy (combination chemotherapy), immunotherapy, new targeted drugs
- Clinical trials



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Side Effects of Treatment

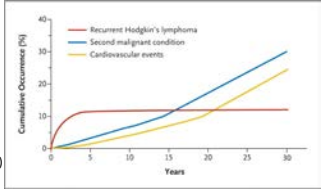


- Fatigue
- Hair loss (for some chemotherapy)
- Nausea/Vomiting
- Mucositis/mouth sores
- Infections
- Low blood counts – need for blood or platelet transfusions
- Neuropathy
- Cardiac toxicity
- Pulmonary toxicity

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Lymphoma Survivorship Issues



- Concern about relapse
- Depression and anxiety
- Fatigue or cognitive deficits
- Cardiac – heart failure, coronary artery disease
 - Modifying cardiac risk factors (quit smoking, etc.)
- Lungs – from chemotherapy or radiation
- Bone marrow – side effects from chemotherapy leading to second cancers (leukemia, etc.)
- Other cancers (breast or lung from radiation)

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Case Presentation #2

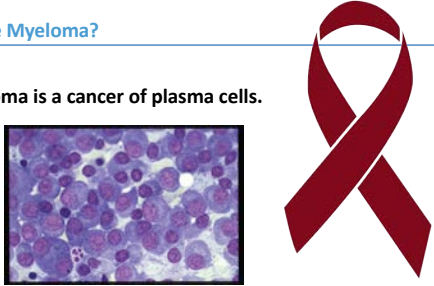
- A 67 year old woman presents with a 3 month history of progressive back pain and a 2 week history of lower extremity weakness.
- Labs are significant for anemia, hypercalcemia, and elevated creatinine (renal dysfunction).
- An MRI of her spine shows a vertebral body mass with extension into the T12 epidural space and leading to spinal cord compression.
- Bone marrow biopsy shows sheets of atypical plasma cells.

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What is Multiple Myeloma?

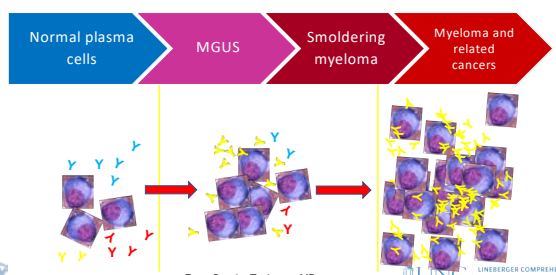
- Multiple myeloma is a cancer of plasma cells.



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When plasma cells act up...



From Sascha Tuchman, MD

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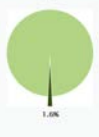
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Multiple Myeloma Epidemiology

- Incurable but survival improved from 2-3 years to 10+ years
- Primarily disease of elderly – median age of 70 at diagnosis

Common Types of Cancer	Estimated New Cases 2015	Estimated Deaths 2015
1. Breast Cancer (female)	211,840	40,290
2. Lung and Bronchus Cancer	221,200	158,040
3. Prostate Cancer	220,800	27,540
4. Colon and Rectum Cancer	132,700	49,700
5. Bladder Cancer	74,000	16,000
6. Melanoma of the Skin	73,870	9,940
7. Non-Hodgkin Lymphoma	71,850	19,790
8. Thyroid Cancer	62,450	1,950
9. Kidney and Renal Pelvis Cancer	61,560	14,080
10. Endometrial Cancer	54,870	10,170
14. Myeloma	26,850	11,240


Myeloma represents 1.0% of all new cancer cases in the U.S.




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Myeloma Symptoms: CRAB



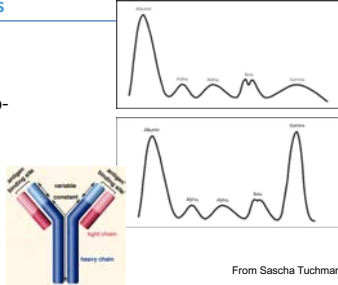
- HyperCalcemia- **lethargy, confusion, constipation**
- Renal Insufficiency
- Anemia
- Bone Lesions
 - Bone pain due to lytic lesions
 - Spinal cord compression from retropulsed bone fragments from vertebral body compression fractures or from plasmacytomas




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Myeloma Diagnostic Tests

- Tests for monoclonal protein (serum protein electrophoresis/immunofixation, serum free light chains)
- Checking for organ damage
 - Skeletal survey for bone involvement
 - Labs to check for anemia, calcium, renal dysfunction




From Sascha Tuchman, MD



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Case Presentation, Continued

- Patient with spinal cord compression urgently treated with steroids and radiation.
- She was discharged from the hospital to rehab and continued to improve her strength and mobility.
- She was started on chemotherapy for her multiple myeloma and her disease has been well controlled.





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Myeloma Treatment

- Incurable
- General course of progressively shorter durations of remission until death due to uncontrolled disease
- Most therapy is outpatient
- Intensity of therapy is up and down over course of a pt's journey with myeloma
 - Ranges from one pill once a day to stem cell transplant

From Sascha Tuchman, MD



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Side Effects of Treatment

- Bortezomib: peripheral neuropathy, orthostatic hypotension, diarrhea/constipation
- Carfilzomib: dyspnea, HTN, CHF, rarely tumor lysis
- Immunomodulators: cytopenias, diarrhea, rash
- Steroids: Insomnia, mood changes, sugars
- Daratumumab: Infusion reactions

* Typical chemotherapy side effects (alopecia, severe nausea, etc.) are largely history. *



From Sascha Tuchman, MD

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Case Presentation

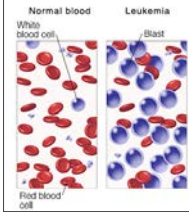

- Mr. O, a 63 year old man, presents to his local ED with a dog bite on his hand. Routine labs (including a CBC w/ differential) show a white blood cell count of 150k, hemoglobin of 7.4, platelets of 43k, and some blast cells in his peripheral blood.
- In obtaining a health history, the patient explains that he has been really tired for the last month and has had some bleeding in his gums, but he had not thought much about it and had been putting off going to his doctor.
- He is admitted to the hospital for an emergent workup and treatment.

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What is leukemia?

- Leukemia is a malignant disorder of blood cells and lymphatic tissues, most commonly involving white blood cells (WBCs)
 - Categorized based on which type of WBC is involved (lymphocyte or myeloid cells) & whether the illness is developing quickly (acute) or slowly (chronic)
- Blasts = precursors to mature, circulating blood cells
 - In leukemia, there are more blasts because the cells are not maturing correctly
 - Do NOT function properly
 - Block production of normal cells
 - Grow and survive better than normal cells

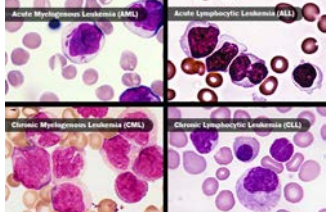



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Types of Leukemia

	MYELOID LINEAGE (affects granulocytes – from myeloid stem cells)	LYMPHOID LINEAGE (affects lymphocytes – from lymphoid stem cells)
ACUTE (blast cells)	Acute Myelogenous Leukemia (AML)	Acute Lymphocytic Leukemia (ALL)
CHRONIC (mature but dysfunctional cells)	Chronic Myelogenous Leukemia (CML)	Chronic Lymphocytic Leukemia (CLL)



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Epidemiology of Leukemia


	ACUTE		CHRONIC	
	AML	ALL	CML	CLL
Incidence (new cases expected in 2020)	19,940	6,150	8,450	21,040
Average Age at Diagnosis	68 years old	15 years old	64 years old	70 years old
5-Year Survival	25% (>20 years old) 67% (<20 years old)	37% (>20 years old) 89% (<20 years old)	69%	85%

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Risk Factors for Leukemia



- Age
- Gender
- "Pre-leukemia": MDS or MPN
- Exposure to radiation
 - Previous XRT treatment
 - Work exposure
 - Environmental radiation
- Chemical exposure
 - Chemo – especially alkylating agents
 - Benzene
 - Formaldehyde
 - Pesticides – ex. Agent Orange in Vietnam
- Cigarette smoking
- 1st degree relative w/ leukemia
- Viruses
 - Human T-cell leukemia virus type 1 (HTLV-1) associated with adult T-cell leukemia
- Genetic d/o
 - Down syndrome
 - Turner syndrome
 - Bloom syndrome
 - Klinefelter syndrome
 - Fanconi anemia
 - Ataxia telangiectasia



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Symptoms of Leukemia

- **Head and neck:** pale mucous membranes, bleeding gums, lymphadenopathy
- **Abdomen:** hepatomegaly, splenomegaly
- **Neurologic:** headache, papilledema, meningismus, abnormal cranial nerve responses
- **Respiratory:** abnormal lung sounds if pneumonia is present
- **Cardiovascular:** tachycardia, murmurs
- **Musculoskeletal:** joint pain and inflammation
- **Integumentary:** bruising, ecchymosis, petechiae, leukemia cutis lesions
- **Lymph nodes:** cervical, supraclavicular, axillary, mediastinal, or inguinal lymphadenopathy
- **Genitourinary:** urinary tract infections, hematuria, testicular mass, menorrhagia

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Leukemia Diagnostic Tests

Labs




- CBC w/ differential
- Liver function tests
- Uric acid, BUN, Creatinine

Lumbar puncture (CSF studies)

- Increased protein
- Decreased glucose
- Presence of leukemia cells

Bone marrow core biopsy & aspiration



- Cell morphology
- Immunophenotype
- Cellularity
- Cytogenetic analysis
- "Karyotyping" & "fluorescence in situ hybridization (FISH)" are tests used to identify certain changes in chromosomes and genes.

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Case Presentation, Continued



- Mr. O received a bone marrow biopsy to confirm a diagnosis of leukemia. He is started on Hydroxyurea to lower his white blood cell count.
- The results come back a couple of days later. He is diagnosed with Acute Myeloid Leukemia.

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Leukemia Treatment

- Hydroxyurea (to lower WBC count)
- IV Chemotherapy – most given in the hospital
- Chemotherapy injections
- Oral chemotherapy
- Immunotherapy
- Lumbar punctures with intrathecal chemotherapy
- Radiation (less common)
- Blood transfusions
- Bone marrow/stem cell transplant
- Palliative care
- Hospice

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AML Treatment

Special consideration: treatment for older adults or patients who have failed multiple treatments:
Hypomethylating Agent (HMA) + Venetoclax



Induction

- High doses of chemotherapy to eradicate leukemia cells – **AGGRESSIVE TREATMENT**
- Multiple-drug regimen (standard of care: 7+3)
- Usually Cytarabine + anthracycline (Doxorubicin, Daunorubicin, Idarubicin, Mitoxantrone)
- Vyxeos for t-AML
- **GOAL:** Induce a remission (<5% blasts in marrow)

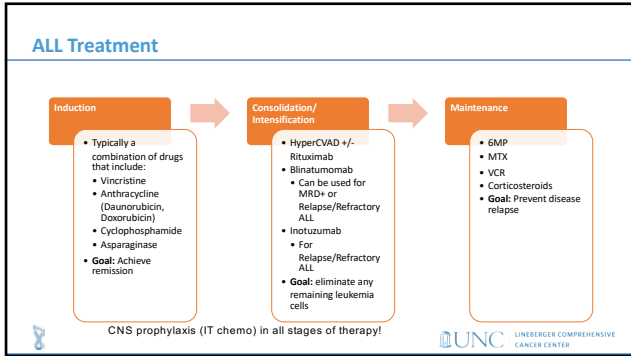
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Consolidation

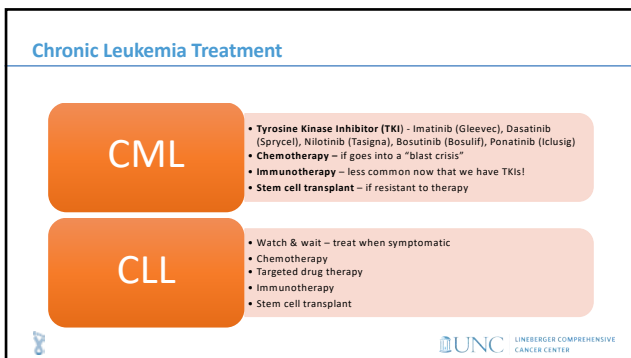
- Aims to eliminate remaining leukemia cells
- Ex: HIDAC (High dose Cytarabine)

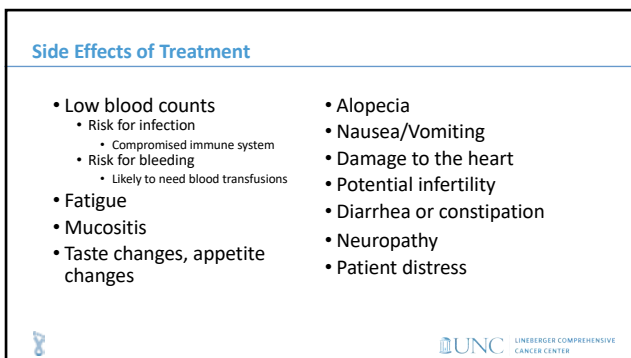
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Cancer Treatment: It takes a village!

Oncologist (& NPs/Pas)	Nurse Navigator	Palliative Care	Comprehensive Cancer Support Program	PT/OT/Rec Therapy
Nutrition	Adolescent & Young Adult Program	Bone Marrow Transplant	Financial Counselors	Psychiatry
Infectious Disease	Hospice	Infusion Center	Inpatient team	Pharmacists
Social Work	Interventional Radiology	XRT	Nursing staff	& more!



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Questions?



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