

UNC Lineberger Cancer Network

PATIENT-CENTERED CARE

Live Webinar

Jake Stein, MD, MPH

Oncologic Emergencies

March 13

Sound Check

11:55

Start Time

12:00

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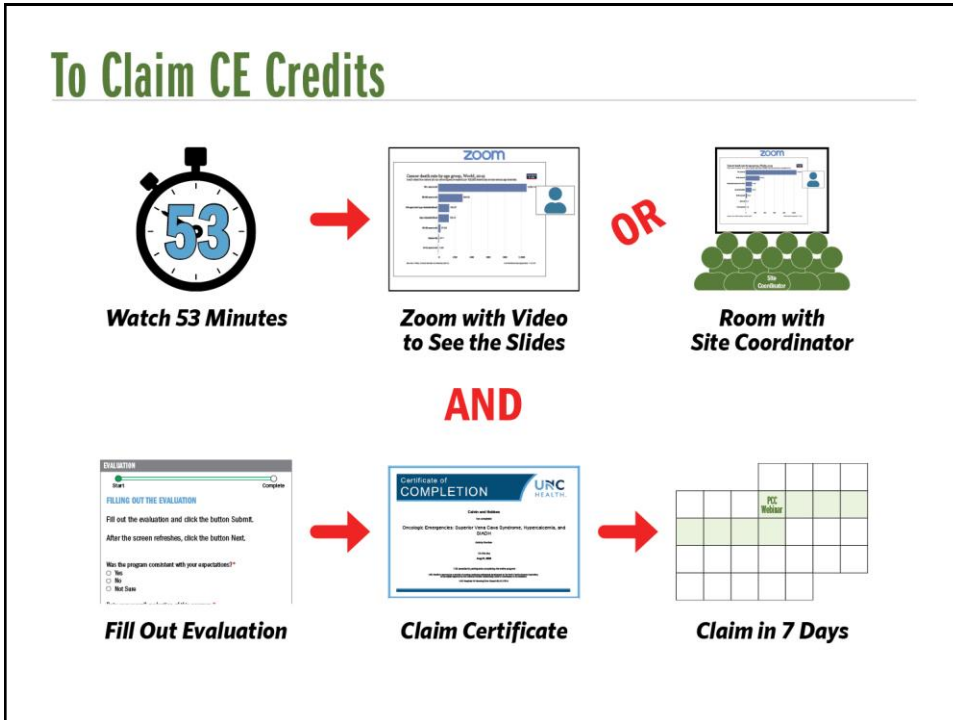
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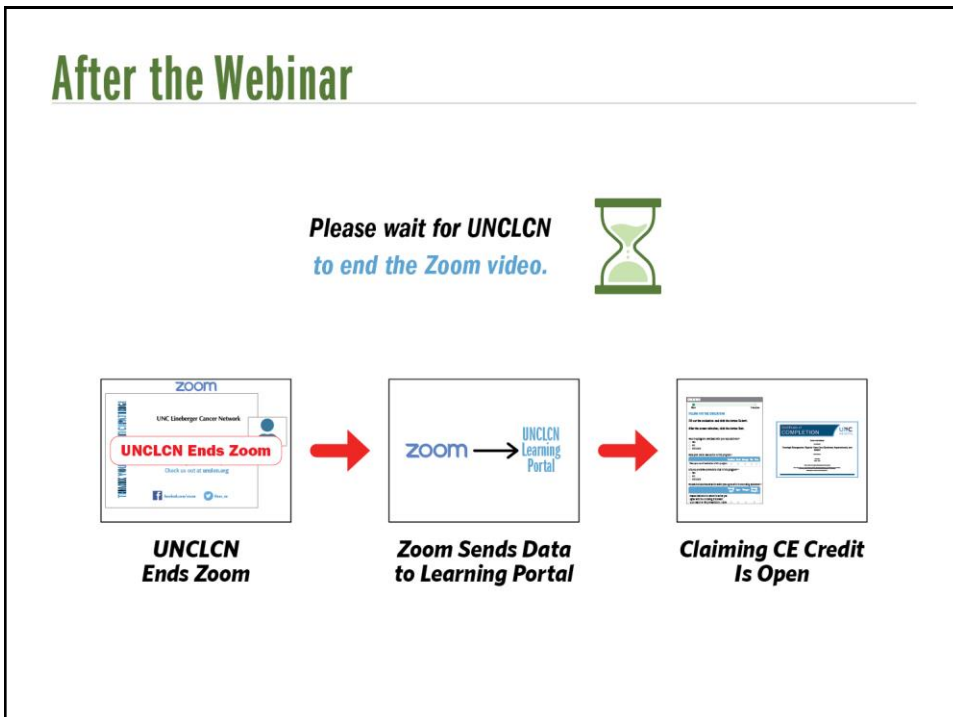
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Our Presenter

Jake Stein, MD, MPH

Jake Stein, MD, MPH is a medical oncologist with a clinical focus on caring for patients with sarcomas. These are rare and heterogeneous cancers that can affect patients of all ages, including adolescents and young adults. He has always strived to listen closely to his patients and address their concerns, while collaborating with colleagues across disciplines and bringing the highest-quality, most cutting-edge medical science to achieve the best possible outcomes for these patients. Equity is a core value for him and at a public institution like the University of North Carolina, it is our job and our privilege to provide the highest quality cancer care to all patients, regardless of their background or circumstances. My goal is to always be in partnership with my patients, navigating the complexities of a cancer journey together, side by side.

He is also a health services researcher, and his work focuses on how to optimize care delivery systems to improve the quality of cancer care for all patients, especially those who have been traditionally underserved. This involves understanding the gaps and barriers within our current delivery systems, followed by the development and testing of interventions to improve those systems. Some of his current projects involve evaluating how to improve the delivery of precision medicine for patients with advanced cancer, developing predictive models to determine what patients are at high risk for complications from cancer therapy and how to reduce that risk, and how to make sarcoma care for young people better aligned with their goals and needs.

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Our Presenter

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Our Presenter

- 5.** Jake Stein, MD, MPH, a medical oncologist caring for patients with sarcoma - a group of rare and heterogeneous cancers.

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Our Presenter

5. Jake Stein, MD, MPH, a medical oncologist caring for patients with sarcoma - a group of rare and heterogeneous cancers.
4. He has a particular interest in caring for young people with cancer and how to improve their care and outcomes.

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Sample Poll Everywhere Question

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An oncologic emergency is an acute health problem caused by the cancer or its treatment and requires immediate treatment.

(A) True 0%

(B) False

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This activity has been planned and implemented under the sole supervision of the Course Director, Stephanie Wheeler, PhD, MPH, in association with the UNC Office of Continuing Professional Development (CPD). The course director received research support from AstraZeneca (ended June 2023) and Pfizer Medical Foundation (ended December 2023). These financial relationships have been mitigated. CPD staff have no relevant financial relationships with ineligible companies as defined by the ACCME.

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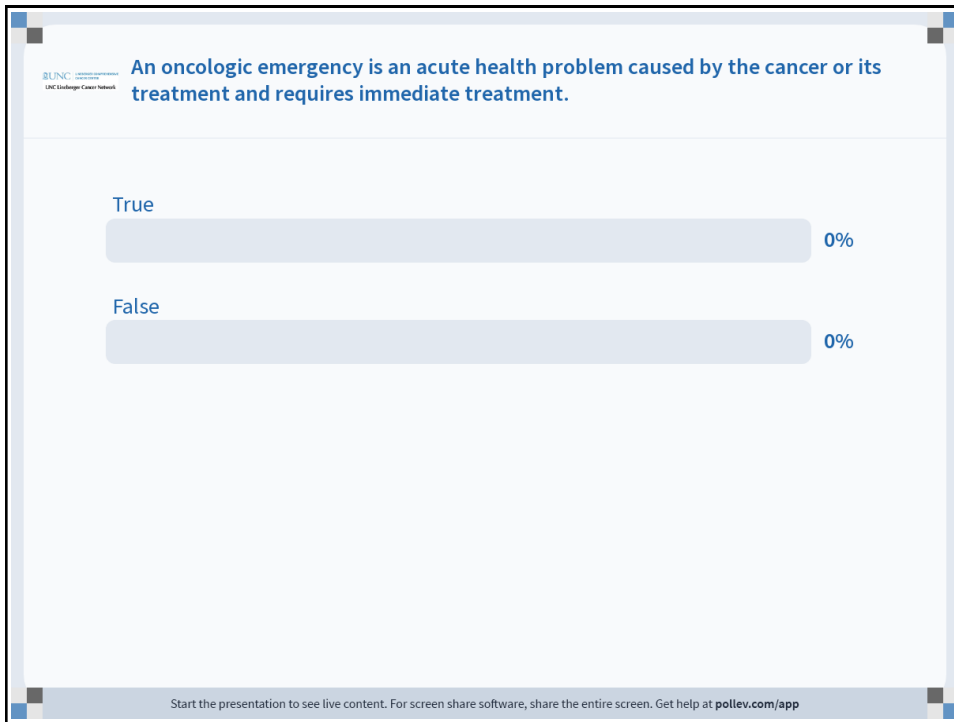
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Oncologic Emergencies

Jacob Stein, MD/MPH
Assistant Professor
Division of Oncology
Bone and Soft Tissue Oncology Program



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Overview/Objectives

- Identify the most common oncologic emergencies.
- Describe key elements to diagnosis common oncologic emergencies.
- Recognize critical aspects of oncologic emergency management.



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Case 1

A 75-year-old man with a recent diagnosis of lung cancer presents to the ER with back pain. He also mentions that he has had several falls in the past week, and his feet feel “clumsy.” MRI spine shows a vertebral body mass with extension into the epidural space and compression of the spinal cord with associated cord edema.

What is the most appropriate next step in management?

- A. Biopsy of the epidural mass
- B. Corticosteroids followed by radiation therapy
- C. Platinum based chemotherapy
- D. Radiation therapy alone



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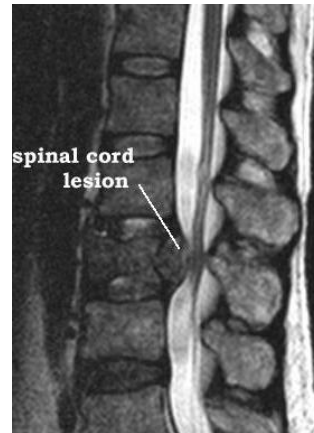
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SPINAL CORD COMPRESSION

- Occurs in up to 5% of all patients with cancer, 20% of those with spinal mets
- Most common: breast, lung, prostate
- Also seen in lymphoma, renal cell, multiple myeloma
- Associated with poor prognosis
- CRITICAL to diagnose and treat ASAP
 - Neurological status at presentation and rapidity of onset predict outcome



http://www.aboutcancer.com/spinal_cord_anatomy.htm

Lawton, et al, 2019, JCO. Assessment and Management of Patients With Metastatic Spinal Cord Compression: A Multidisciplinary Review
 Gould Rothberg BE, et al. Oncologic emergencies and urgencies: A comprehensive review. CA Cancer J Clin. 2022. <https://doi.org/10.3322/caac.21727>

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Etiology

- Usually due to direct extension from spinal bony mets
- Can occur from destruction of cortical bone causing vertebral body collapse and displacement of bony fragments into the spinal canal
- Most common in thoracic spine (70%) due to smaller available free space within thoracic canal
 - Lumbosacral spine (20%)
 - Cervical spine (10%)

Lawton, et al, 2019, JCO. Assessment and Management of Patients With Metastatic Spinal Cord Compression: A Multidisciplinary Review
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Symptoms of SCC

- Back pain (~90%) -> often first presenting symptom
- ****This is why back pain in a cancer patient is a “red flag” and merits prompt imaging****
- Weakness (35-75%)
- Sensory loss
- Bowel, bladder dysfunction (late finding)
- Gait ataxia

Lawton, et al. 2019. JCO. Assessment and Management of Patients With Metastatic Spinal Cord Compression: A Multidisciplinary Review
Gould Rothberg BE, et al. Oncologic emergencies and urgencies: A comprehensive review. CA Cancer J Clin. 2022. <https://doi.org/10.3322/caac.21727>



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Diagnosis

- Early recognition is essential
- **MRI is imaging modality of choice**
- Recommendation is to image the entire spine as many patients have multiple sites of disease
- Often sensory level affected does not correspond to area of suspected cord compression

Lawton, et al. 2019. JCO. Assessment and Management of Patients With Metastatic Spinal Cord Compression: A Multidisciplinary Review
Gould Rothberg BE, et al. Oncologic emergencies and urgencies: A comprehensive review. CA Cancer J Clin. 2022. <https://doi.org/10.3322/caac.21727>



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Treatment

- Immediate dexamethasone
 - Increases likelihood of ambulation post treatment, improves pain scores
 - Typical dosing: 10mg IV x1 followed by 16mg daily in divided doses (ie, 4mg q6hrs)
- Opiate analgesics
- Prompt neurosurgery and rad-onc consultation (even in the middle of the night!)
 - Surgery + XRT improved outcomes (ability to ambulate) over XRT alone



Patchell 2005 Lancet, Vecht, Neurology 1989, Sorenson, Eur J Cancer 1994



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Case 2

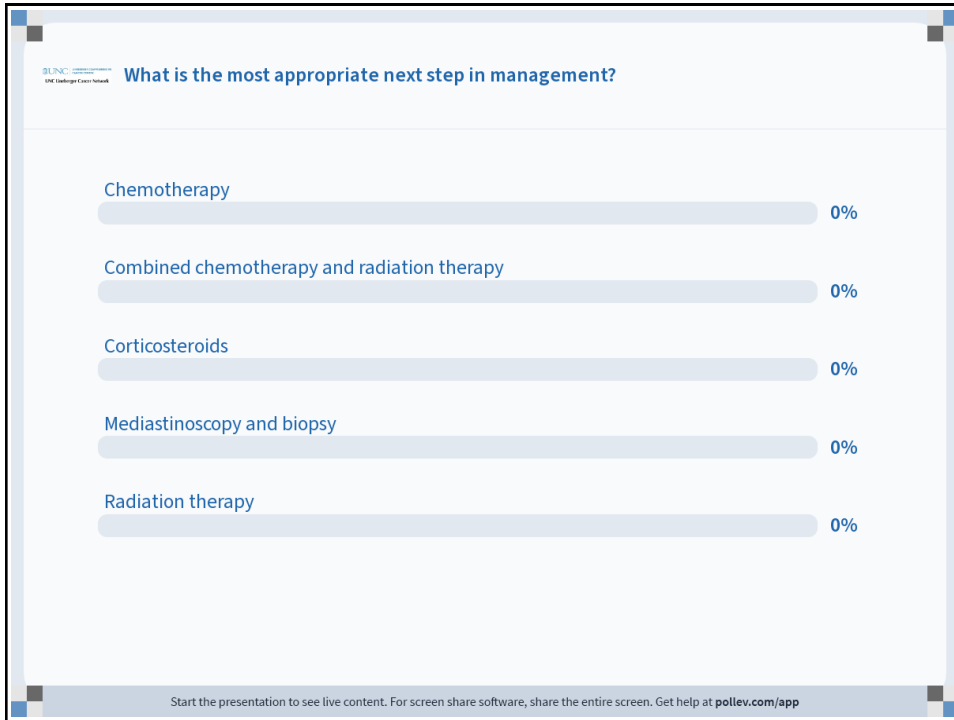
A 54-year-old man presents with facial swelling and cough. Vital signs show normal temperature, BP 160/95, HR 106, RR 20, O₂ sat 92% on room air. Exam reveals facial plethora as well as bilateral jugular venous distention. CT scan of the chest demonstrates a LUL mass with compression of the SVC in addition to mediastinal lymphadenopathy.

What is the most appropriate next step in management?

- A. Chemotherapy
- B. Combined chemotherapy and radiation therapy
- C. Corticosteroids
- D. Mediastinoscopy and biopsy
- E. Radiation therapy



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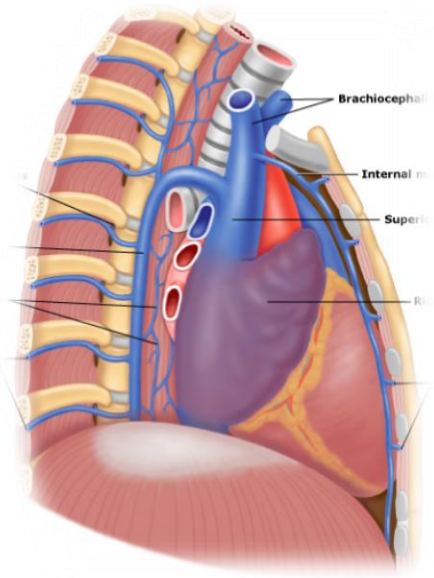
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SVC SYNDROME

- Caused by SVC occlusion
- Low pressure vessel with thin walls amid critical anatomic structures
- Symptoms are due to venous distension and pressure behind the obstruction





Azizi et al. JACC Cardiovasc Interv. 2020 https://link.springer.com/chapter/10.1007/978-3-030-67123-5_22

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Etiology

- Non-malignant causes
 - Catheter related
 - Pacemaker leads
 - Infectious (TB, syphilis, fibrosing mediastinitis)
- Malignancy-related SVC
 - NSCLC: 50%, portends poor prognosis
 - SCLC: 25%
 - NHL: 10%

 Azizi et al. JACC Cardiovasc Interv. 2020


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Presentation

- Can be subacute or quite rapid, depending on degree of collateralization
- Facial, neck, and upper extremity swelling
- Dilated chest veins
- Dyspnea, cough, hoarseness
- Headache, confusion, or lethargy



Azizi et al. JACC Cardiovasc Interv. 2020



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Pemberton's Sign



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Diagnosis

- **CT chest with contrast** is imaging of choice
- MR venography is a potential alternative
- Prompt Mediastinoscopy vs CT guided biopsy
- **Usually can delay treatment while obtaining tissue diagnosis since treatment guided by tumor type** (i.e. R-CHOP vs platinum-based chemotherapy)



Azizi et al. JACC Cardiovasc Interv. 2020



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Treatment

- **Emergent if stridor/respiratory compromise or lethargy/coma**
- Endovascular stent placement or thrombolysis are emergent therapy options (VIR consult)
- Radiotherapy: benefit in 72 hours
- Chemotherapy: benefit in 1-2 weeks
- Steroids: Only if laryngeal edema or known steroid responsive cancer
- Diuretics: Unclear benefit



Azizi et al. JACC Cardiovasc Interv. 2020



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Case 3

An 85-year-old woman presents with fatigue, lethargy and constipation. She has advanced breast cancer with bony metastases. She does not have previous medical history aside from her cancer.

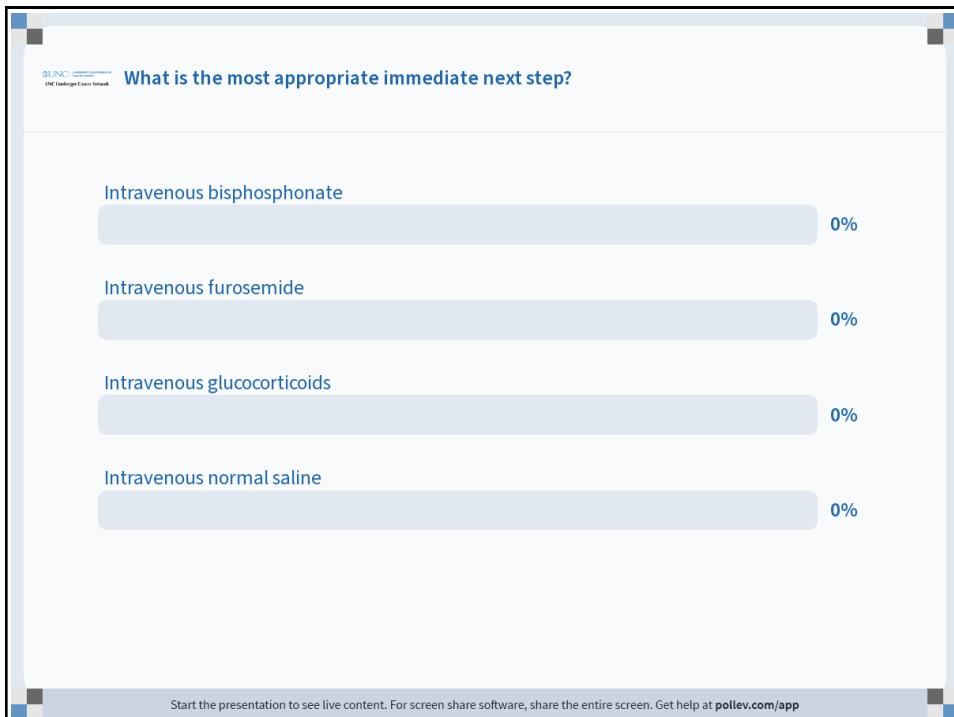
Labs are notable for an elevated calcium to 15.1.

What is the most appropriate immediate next step?

- A. Intravenous bisphosphonate
- B. Intravenous furosemide
- C. Intravenous glucocorticoids
- D. Intravenous normal saline



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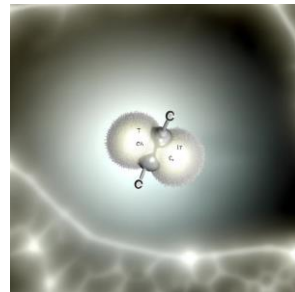
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- C. Intravenous glucocorticoids
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HYPERCALCEMIA

- Most common cause among inpatients is cancer
 - Malignancy diagnosed in >33% of all patients who present to ED with hypercalcemia
- Affects ~20% of cancer patients
 - ~50% die within 1 month



Vakiti et al, StatPearls, 2024. Clines, Curr Opin Endocrin, 2011 18:339-346;
image generated by ChatGPT4 image generator, 3/4/2024.

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Pathophysiology

- Tumor secretion of PTHrP (Humoral hypercalcemia of malignancy) (~80%)
 - PTHrP increases osteoclastic bone resorption and enhances calcium resorption through renal tubules
- Local bone destruction (i.e. bone mets) -> local release of cytokines, osteoclast activating factors (~20%)
- 1,25-dihydroxy vitamin D production (<1%)
 - Increases calcium absorption in gut and osteoclast activity
- Ectopic secretion of PTH (<1%)

Vakiti et al, StatPearls, 2024. Clinics, Curr Opin Endocrin, 2011 18:339-346;



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Malignancies associated with hypercalcemia

Osteolytic metastases:
Breast cancer
Multiple myeloma
Lymphoma
Leukemia
Humoral hypercalcemia (PTHrP):
Squamous cell carcinomas
Renal carcinomas
Bladder carcinoma
Breast cancer
Ovarian carcinoma
Non-Hodgkin lymphoma
CML
Leukemia
Lymphoma
1,25-dihydroxyvitamin D:
Lymphoma (Non-Hodgkin, Hodgkin, lymphomatosis/granulomatosis)
Ovarian dysgerminomas
Ectopic PTH secretion:
Ovarian carcinoma
Lung carcinomas
Neuroectodermal tumor
Thyroid papillary carcinoma
Rhabdomyosarcoma
Pancreatic cancer

<https://www.uptodate.com/contents/hypercalcemia-of-malignancy-mechanisms>



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Symptoms

- Weakness, fatigue
- Polyuria, polydipsia (nephrogenic DI)
- GI symptoms (abdominal pain, nausea, vomiting, constipation)
- Psychiatric symptoms (memory loss, apathy)
- Bone pain
- “Stones, bones, groans, psychiatric overtones”

Vakiti et al, StatPearls, 2024. Clinics, Curr Opin Endocrin, 2011 18:339-346;



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Diagnosis

- Serum lab value does not necessarily account for acuity or degree of symptoms
 - Mild < 12 mg/dl
 - Moderate 12-14 mg/dl
 - Severe > 14 mg/dl
- Remember to use ionized or corrected calcium

Vakiti et al, StatPearls, 2024. Clinics, Curr Opin Endocrin, 2011 18:339-346;



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Treatment

- **Fluids:** NS at initial rate of 200-300 cc/h
 - Loop diuretics only if fluid overload, CHF, or renal failure
- **Bisphosphonates**
 - Block osteoclastic bone resorption, delayed onset (24-48h)
 - Zoledronic acid 4 mg over 15 min or pamidronate
- **Calcitonin (SubQ or IM)**
 - Early onset of action: hours, but short duration (48h)
 - Can help temporize while bisphosphonates take effect
- Consider steroids if increased calcitriol production
- Consider HD for patients w/ neurological symptoms, calcium >18, renal failure, CHF



Vakiti et al, StatPearls, 2024. Clines, Curr Opin Endocrin, 2011 18:339-346;



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Case 4

A 26-year-old man presents with 2 weeks of rapidly enlarging cervical lymphadenopathy, abdominal distention and fever.

VS: 39C, BP 90/60, HR 115 and RR 24. He has significant cervical and axillary LAD. Spleen is palpable and a firm abdominal mass.

Hgb 10.5, WBC 65k, 35% PMNs and 65% atypical lymphs, Plt 90K

Cr 3.8, LDH 12,000, Phos 9.9, K 6.6, Uric acid 18.6

A lymph node biopsy reveals Burkitt lymphoma.

Which is the most appropriate immediate next step in treatment?

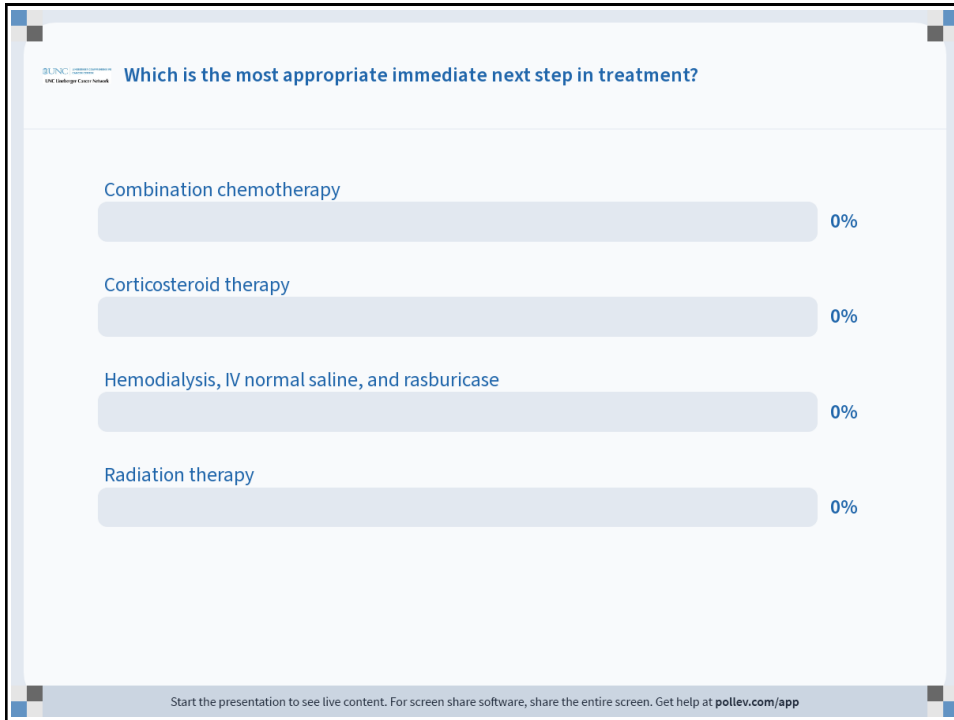
- A. Combination chemotherapy
- B. Corticosteroid therapy
- C. Hemodialysis, IV normal saline, and rasburicase
- D. Radiation therapy



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TUMOR LYSIS SYNDROME

- Most common in aggressive heme malignancies
 - High-grade lymphoma, AML, ALL
 - Occasionally seen after treatment of solid tumors
- Massive release of intracellular contents from malignant cells -> leads to metabolic derangements

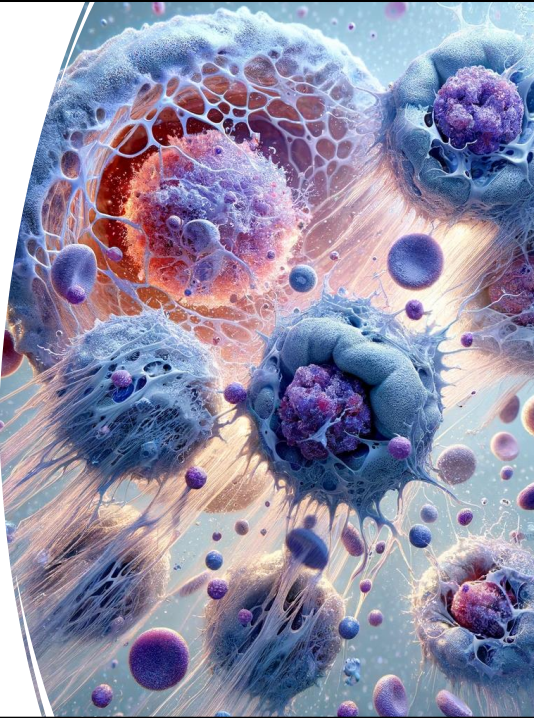




Image courtesy of ChatGPT image generator, 3/4/2024

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Laboratory Abnormalities

- Hyperkalemia
 - Life-threatening arrhythmias
- Hyperuricemia
 - Crystallize in renal tubules -> obstructive uropathy
 - Can lead to acute renal failure
- Hyperphosphatemia
 - Leads to hypocalcemia, tetany, seizures, arrhythmias

Gould Rothberg BE, et al. CA Cancer J Clin. 2022.


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Risk Factors for TLS

- *High grade lymphoma
 - Burkitt's lymphoma
- *ALL with WBC $\geq 100,000$
- *AML with WBC $\geq 50,000$
- High tumor cell proliferation rate
- Chemosensitivity
- Large tumor burden: Bulky disease, WBC $\geq 50,000$, or pre-tx LDH $> 2x$ ULN
- Dehydration
- Pre-existing CKD

Gould Rothberg BE, et al. CA Cancer J Clin. 2022.



Coiffier, B. Journal of Clinical Oncology, 2008



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Management

- Prevention: If high or intermediate risk
 - Allopurinol: Decreases uric acid formation
 - IVF
 - Consider rasburicase
- Treatment: FLUIDS
- Rasburicase: Degrades uric acid to allantoin
 - Consider if pre-existing hyperuricemia
 - Relative contraindication: G6PD deficiency -> can lead to hemolysis and methemoglobinemia
- Treat electrolyte abnormalities
- HD in severe cases



Puri et al, J Community Hosp Intern Med Perspect. 2020. Cairo.M, Coiffier, et.al. BJH 149:578-586, 2010





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Fig 1. Purine catabolism pathway

Coiffier, B. et al. *J Clin Oncol*; 26:2767-2778 2008

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Case 5

A 28-year-old previously healthy woman presents with 3 weeks of progressive fatigue, dyspnea on exertion, and easy bruising. T 37.2C, BP 124/78, HR 106, RR 22. O2 sat 83% on RA, improved to 95% on 4L. Exam reveals petechiae, ecchymoses, pallor. Mild cervical lymphadenopathy. Crackles in bilateral lung bases, no peripheral edema. No hepatosplenomegaly.

Hb 7.4, WBC 108,400 (ANC 400), Plt 18,000
 BUN 24, Cr 1.1
 Normal PT, PTT, elevated fibrinogen, D-dimer
 Peripheral blood smear - blasts

Which of the following is the most appropriate treatment?

- A. Imatinib
- B. Induction chemotherapy
- C. Leukapheresis
- D. Rituximab

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Which of the following is the most appropriate treatment?

- Imatinib 0%
- Induction chemotherapy 0%
- Leukapheresis 0%
- Rituximab 0%

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LEUKOSTASIS

- Presenting symptoms:
- Pulmonary: dyspnea, hypoxia, infiltrates
- Neurologic: AMS, vision changes, headache, tinnitus
- Fever in up to 80%
- Spontaneous TLS and DIC






Image courtesy of chatGPT4
image generator: 3/13/2024

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Hyperleukocytosis/Leukostasis

- Hyperleukocytosis = WBC >100k
- Leukostasis = increased viscosity, white cell plugs in the microvasculature due to blasts being less deformable, endothelial activity
- Most common with AML
- Can also see in ALL, CML in blast crisis
- Rare in CLL and CML in chronic phase

Schiffer et al. UptoDate. 2024

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Treatment

- One week mortality of 20-40% if untreated
- Treatment:
 - Hydroxyurea for cytoreduction (in asymptomatic patients) or induction chemotherapy
 - Leukapheresis if symptomatic -> involves MICU admission, line placement, transfusion med input
 - IV hydration and allopurinol for TLS prophylaxis
 - **Avoid PRBC transfusions prior to leukoreduction, if possible**

Schiffer et al. UptoDate. 2024



3/13/2024



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Case 6

You receive a phone call at 2:30am on a Thursday night. A 24-year-old man with a recent diagnosis of DLBCL reports that he awoke to some mild chills, and his temperature is 100.7. He recently was discharged from the hospital after his first cycle of R-CHOP. He received G-CSF on the day prior to D/C.

Tonight, he reports that he has felt in his usual state of health. No new cough, shortness of breath, abdominal pain, nausea, diarrhea, headache, dysuria. He lives very far away in rural NC. He is quite worried about flu and COVID and does not want to come to the hospital if it can be avoided.

What is the best course of action?

- A. Send a message to his nurse navigator for an infusion visit tomorrow
- B. As long as he feels fine, he can go back to sleep and not worry about it
- C. Advise him to drive up to UNC for admission
- D. Order a prescription for levofloxacin at his local 24-hour pharmacy and encourage good PO intake, advise hospital admission if he feels any worse
- E. Recommend that he immediately present to his local ER for evaluation



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What is the best course of action?

Option	Percentage
Send a message to his nurse navigator for an infusion visit tomorrow	0%
As long as he feels fine, he can go back to sleep and not worry about it	0%
Advise him to drive up to UNC for admission	0%
Order a prescription for levofloxacin at his local 24-hour pharmacy and encourage ...	0%
Recommend that he immediately present to his local ER for evaluation	0%

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Case 6

You receive a phone call at 2:30am on a Thursday night. A 24-year-old man with a recent diagnosis of DLBCL reports that he awoke to some mild chills, and his temperature is 100.7. He recently was discharged from the hospital after his first cycle of R-CHOP. He received G-CSF on the day prior to D/C. Tonight, he reports that he has felt in his usual state of health. No new cough, shortness of breath, abdominal pain, nausea, diarrhea, headache, dysuria. He lives very far away in rural NC. He is quite worried about flu and COVID and does not want to come to the hospital if it can be avoided.

What is the best course of action?

- Send a message to his nurse navigator for an infusion visit tomorrow
- As long as he feels fine, he can go back to sleep and not worry about it
- Advise him to drive up to UNC for admission
- Order a prescription for levofloxacin at his local 24-hour pharmacy and encourage good PO intake, advise hospital admission if he feels any worse
- Recommend that he immediately present to his local ER for evaluation**

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NEUTROPENIC FEVER

- Fever: oral temp $\geq 38.4\text{C}$ or $\geq 38.0\text{C}$, sustained over 1 hour
- Neutropenia: ANC < 500 or expected to decrease
- Critical to evaluate patient and start antibiotics ASAP

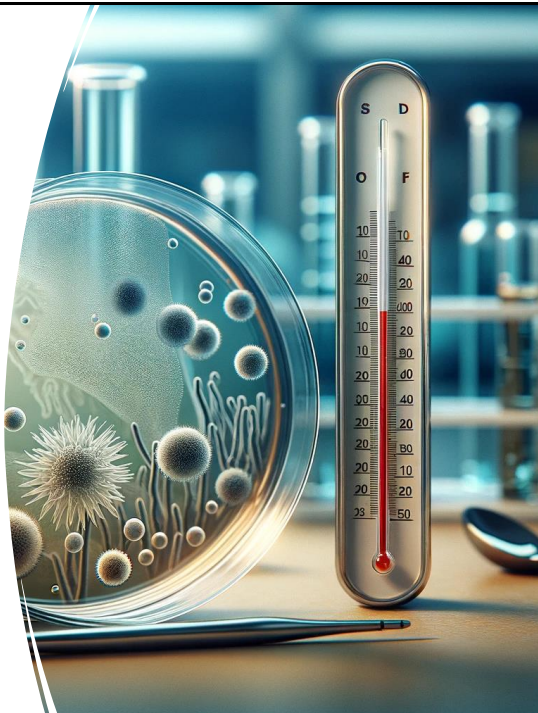



Image courtesy of chatGPT4
image generator: 3/13/2024


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Neutropenia

- Risk of neutropenic fever depends on depth and duration of neutropenia and comorbidities
- Generally due to myelosuppressive chemotherapy
 - Solid tumors: duration of neutropenia < 5 days
 - Heme malignancies: can last > 14 days
 - BMT: can be months
 - Highest risk usually 5-10 days after chemo
- Can also occur w/o chemo or at presentation in heme malignancy or if marrow involvement
- New AML is functionally neutropenic
- Remember to check diff


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Approach to Patient with Neutropenic Fever

- Thorough physical exam
 - Skin, oral cavity, line sites
 - Abdomen (typhlitis), perianal area (not DRE)
- Labs
 - CBC diff, CMP
 - UA and culture
 - Blood cultures (if CVC, at least 1 from line)
 - COVID-19 PCR
 - “Sepsis Bundle”
- CXR
- Further workup guided by sx/exam



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Neutropenic Fever Treatment

- Rapid treatment CRITICAL!
- Anti-pseudomonal coverage (**cefepime**) for all patients
- Vancomycin
 - Suspected catheter-related infection
 - Skin or soft tissue infection
 - Hemodynamic instability
- Use zosyn if c/f anaerobes, carbapenem if c/f ESBLs
- Consider adding antifungal if persistent fever after 4-7 days of broad spectrum coverage without clear source



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Thank you!

Never be afraid to speak up or ask for help if you are concerned about a patient. Identifying these emergencies early and reacting quickly can save lives.



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Thank you!

Jacob.stein@unchealth.unc.edu



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Questions/Comments?

Nobody has responded yet.

Hang tight! Responses are coming in.

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Thank You . . .

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The Telehealth Team

Tim Poe – Director

Veneranda Obure – Technology Support Specialist **Andrew Dodgson**, DPT – Continuing Education Specialist

Jon Powell, PhD – Continuing Education Specialist **Patrick Muscarella** – Technology Support Technician

Oliver Marth – Technology Support Technician **Lindsey Reich**, MA – Public Communication Specialist

Barbara Walsh, DNP, MPH, MSN, RN – Nurse Planner

The song *Back Rhodes* written and performed by **Don Poe**

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