

# Faculty/Presenter Disclosure

- **Speaker:** Dr. Kimberly Hagel
  
- **Relationships with commercial interests:**
  - Grants/Research Support: None
  - Speakers Bureau/Honoraria: None
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  - Other: None

# Disclosure of Commercial Support

- ◆ This Program is funded through AHS Operational Funding.
- ◆ This Program has not received financial support.
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- ◆ Dr. Kimberly Hagel is presenting at this Program on a voluntary basis.
- ◆ **Potential for conflict(s) of interest: None**

# Oncologic Emergencies





# Outline

- ◆ Febrile neutropenia
- ◆ Hypercalcemia of malignancy
- ◆ Spinal cord compression
- ◆ SVC syndrome

# Febrile Neutropenia

## Definition

- ◆ Fever - a single oral temp  $\geq 38.3$ , or  $\geq 38$  for more than 1 hour
  - ◆ axillary and rectal temp assessment is discouraged
- ◆ Neutropenia - ANC  $< 0.5$  cells/mm<sup>3</sup> or expected to be  $< 0.5$  during the next 48 hours.
  - ◆ Can be hard to predict. In most chemotherapy, the ANC nadir occurs between days 7-14.

## Extremely common

- ◆ Solid tumors - 10-50% of patients will develop fever during neutropenia
- ◆ Heme malignancy -  $> 80\%$  will develop fever during neutropenia.

## Neutropenic patients who aren't febrile can still have infections!

- ◆ If clinically suspect infection, treat the same as febrile neut!

# Febrile Neutropenia

- ◆ Typical sites of bacterial growth are mucosa, GI tract, and skin.
- ◆ Causes
  - ◆ Infection: ~ 50% will have documented infection. ~15% have positive blood cultures
  - ◆ Bacterial
    - ◆ ~2/3 Gram positive (Coag. neg. Staph., Staph aureus, Strept)
    - ◆ ~1/3 Gram negative (E. coli, Klebsiella, Pseudomonas, other)
    - ◆ Splenectomy (encapsulated organisms)
    - ◆ Diarrhea/recent Abx (C. diff)

# Febrile Neutropenia

- ◆ Fungal
  - ◆ Candida, Aspergillus, others
  - ◆ Usually in setting of prior Abx, profound neutropenia, BMT engraftment
- ◆ Viral
  - ◆ HSV, resp viruses, CMV esp. 1-2 months post Allogeneic BMT
- ◆ Mycobacterial
  - ◆ MAC, TB reactivation
- ◆ PCP
- ◆ Toxoplasma
- ◆ Others

# Why Cancer Patients are Predisposed to Infections

## Risk Factors for Infection

- ◆ Type of cancer (ie. Solid tumor vs. a lymphoma or acute leukemia).
- ◆ Impairments of cellular function secondary to cytotoxic or immunosuppressive drugs.
  - ◆ Depth and duration of neutropenia. (ie. >7 days of neutropenia increases risk drastically)
- ◆ Presence of indwelling plastic catheters.



# Febrile Neutropenia

- ◆ Non-infectious causes of fever
  - ◆ The malignancy itself
  - ◆ Drug fevers

# Febrile Neutropenia

## ◆ Workup:

### ◆ History and Physical

- ◆ Often unremarkable. Most of the manifestations of infections are from the immune response (cytokine release, local neutrophil activity).
- ◆ Do a thorough exam. Pay attention to indwelling lines. Avoid anything invasive like a DRE.

### ◆ Labs:

- ◆ CBC+D, lytes, Cr, BUN, liver panel
- ◆ Imaging: CXR in everyone. Everything else symptom guided.
- ◆ Cultures:
  - ◆ Blood - two cultures. If they have an indwelling catheter, need a culture from each lumen, plus a venipuncture
  - ◆ Urine
  - ◆ Others guided by symptoms - sputum, CSF, stool



# Febrile Neutropenia

- ◆ Initial Management:
  - ◆ ABCs and stabilization as necessary
  - ◆ Determine sites of possible infection ie. Catheters, lines, open lesions.
  - ◆ Risk assessment:
    - ◆ Via scoring system- MASCC
    - ◆ Low risk - Outpatient management with oral antibiotics
    - ◆ High risk - Inpatient management



**Table 3. The Multinational Association for Supportive Care in Cancer Risk-Index Score**

Characteristic	Weight
Burden of febrile neutropenia with no or mild symptoms <sup>a</sup>	5
No hypotension (systolic blood pressure >90 mmHg)	5
No chronic obstructive pulmonary disease <sup>b</sup>	4
Solid tumor or hematologic malignancy with no previous fungal infection <sup>c</sup>	4
No dehydration requiring parenteral fluids	3
Burden of febrile neutropenia with moderate symptoms <sup>a</sup>	3
Outpatient status	3
Age <60 years	2

**NOTE.** The maximum value of the score is 26. Adapted from [43]. Reproduced with permission of the American Society for Clinical Oncology.

<sup>a</sup> Burden of febrile neutropenia refers to the general clinical status of the patient as influenced by the febrile neutropenic episode. It should be evaluated on the following scale: no or mild symptoms (score of 5); moderate symptoms (score of 3); and severe symptoms or moribund (score of 0). Scores of 3 and 5 are not cumulative.

<sup>b</sup> Chronic obstructive pulmonary disease means active chronic bronchitis, emphysema, decrease in forced expiratory volumes, need for oxygen therapy and/or steroids and/or bronchodilators requiring treatment at the presentation of the febrile neutropenic episode.

<sup>c</sup> Previous fungal infection means demonstrated fungal infection or empirically treated suspected fungal infection.

# Treat Febrile Neutropenia

## Initial antibiotics

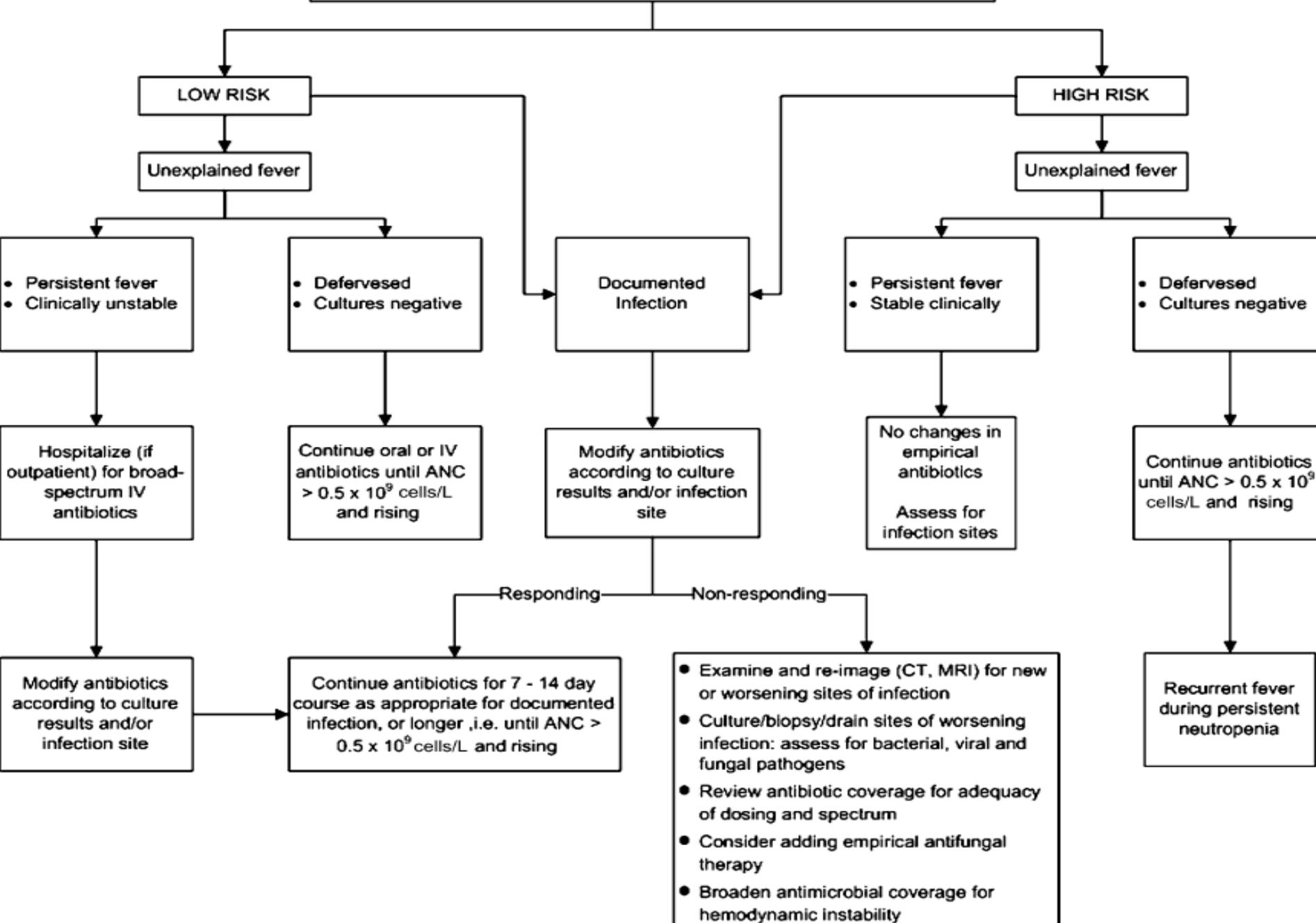
- As soon as possible - goal is to start within 2 hours
- Need broad coverage - gram +, gram -, including pseudomonas
  - First choice - pip-tazo
  - Other options: cefepime, imipenem, meropenem
- Oral regimens (typically for low risk patients)
  - amox-clav + cipro, clinda + cipro, levo monotherapy
- If pen allergic?
  - clinda+cipro
  - vanco+cipro
  - vanco+aztreonam

# Treat Febrile Neutropenia

- ◆ Indications for vancomycin?
  - ◆ sick patient (hemodynamically unstable)
  - ◆ specific clinical syndromes: soft tissue, line infection, pneumonia
  - ◆ Previous MRSA infections and known colonization
  - ◆ Blood cultures positive for Gram positive bacteria before sensitivities are available



Day 2-4 after empirical antibiotic therapy



# Treat Febrile Neutropenia

- ◆ Antifungal indications
  - ◆ Documented infection
  - ◆ If persistently febrile >4 days of appropriate antibiotics, *and* expected duration of neutropenia >7 days.
- ◆ Evidence of oral or esophageal mucositis – Send swab for HSV culture and add antiviral coverage.
- ◆ G-CSF
  - ◆ Not indicated to treat febrile neutropenia
    - ◆ documented to shorten duration of neutropenia and hospitalization
    - ◆ no mortality benefit
    - ◆ expensive
    - ◆ painful
    - ◆ can cause fevers
  - ◆ Prophylaxis
    - ◆ primary - if risk of feb neut >20% (some adjuvant breast regimens)
    - ◆ secondary - curative regimens

# Febrile Neutropenia

- ◆ Duration of treatment:
  - ◆ Recovery of ANC  $>500$  so as long as patient is stable.
  - ◆ Further investigations may be warranted for patients with normal counts but persistent febrile episodes.
- ◆ Antibiotic prophylaxis
  - ◆ Indicated if profound and prolonged neutropenia expected
    - ◆ ANC  $<0.1$  and  $>7$  days.
  - ◆ Mostly heme patients or transplants
  - ◆ use cipro or levofloxacin

# Febrile Neutropenia

◆ Questions?



# Hypercalcemia of malignancy

- ◆ Definition: Hypercalcemia caused by a cancer
- ◆ Causes:
  - ◆ PTHrP - NSCLC
  - ◆ Increased conversion of vitamin D- lymphoma
  - ◆ Bone mets with increased osteoclast activity - myeloma, breast/lung/renal/lymphoma/leukemia.
  - ◆ Ectopic PTH- rare; a few cases in the literature

# Hypercalcemia of malignancy

## ◆ Grading of Hypercalcemia:

- ◆ Mild: Asymptomatic with serum Ca less than 3mmol/L
- ◆ Moderate: Asymptomatic with a serum Ca between 3-3.5mmol/L
- ◆ Severe: Symptomatic or greater than 3.5 mmol/L

## ◆ Clinical symptoms:

- ◆ Stones - kidney/biliary
- ◆ Bones - bone pain
- ◆ Groans - abdo pain, nausea, constipation
- ◆ Psychic overtones - depression, confusion, coma
- ◆ Also get polyuria (nephrogenic DI), pancreatitis, dysrhythmia



# Hypercalcemia of malignancy

- ◆ Usually found in patients who present with delirium
- ◆ Workup for hypercalcemia
  - ◆ PTH, PO<sub>4</sub>, calcium, albumin
    - ◆ PTHrP- expensive and slow to obtain
  - ◆ GIM/metabolic investigations
    - ◆ Urea, creatinine, lytes, Mg, liver panel, urinalysis
- ◆ Chest X-ray; other symptom-guided imaging

# Hypercalcemia of malignancy

- ◆ Management:
  - ◆ ABCs
  - ◆ IV fluids - NS 250-500cc/hr
    - ◆ Lasix only if fluid overloaded
  - ◆ Bisphosphonates
    - ◆ Pamidronate/zolendronic acid
      - ◆ Takes ~12 hours for onset. Peak effect 4-7 days. Effect persists for ~4 weeks
  - ◆ Calcitonin
    - ◆ Used for severe hypercalcemia (>4), while awaiting bisphosphonates to take effect
      - ◆ Takes 1-2 hours to start working, lasts 6-8 hours
      - ◆ Nasal calcitonin no longer available

# Hypercalcemia

- ◆ Steroids
  - ◆ Only for lymphoma or granulomatous disease
  - ◆ Usually 40mg prednisone daily
- ◆ Dialysis for refractory cases
- ◆ Treat underlying malignancy

# Hypercalcemia

1.60F presents with history of known breast cancer to your clinic with a calcium of 2.96. Other than adequate hydration, which of the following treatments is most appropriate?

- A. Bisphosphonate
- B. Calcitonin
- C. Lasix
- D. Prednisone

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# Spinal cord compression

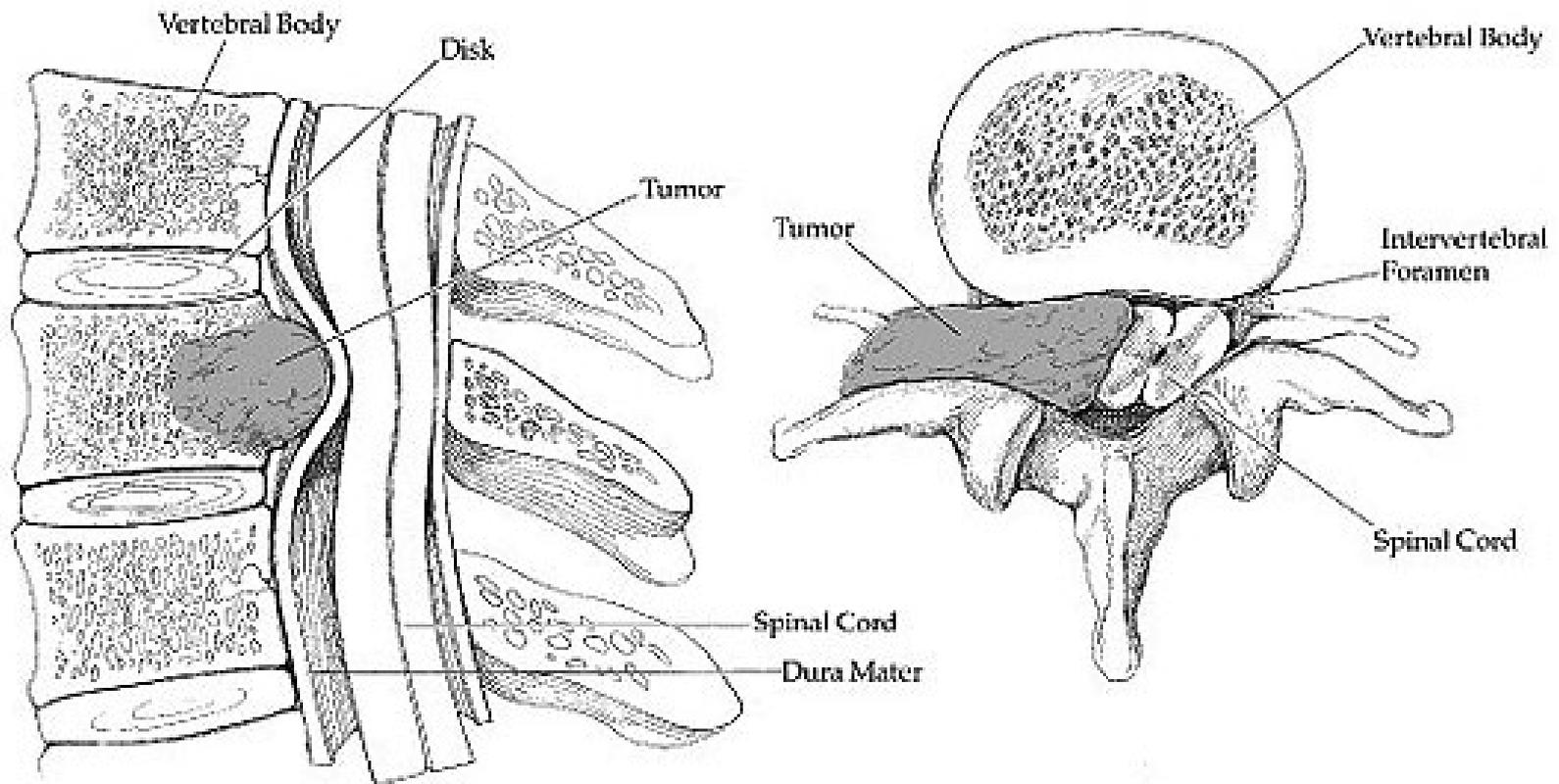
## ◆ Definition

- ◆ Compression of the dural sac and its contents (spinal cord and/or cauda equina) by an extradural tumor mass.

## ◆ Frequency

- ◆ One study showed 2.5% of patients who died of cancer were treated for cord compression at one point during their illness.

# Spinal cord compression



# Spinal cord compression

- ◆ Clinical features:
  - ◆ Pain: >90% (can be local or radicular)
    - ◆ worse with laying down, sneezing, coughing, valsalva
  - ◆ Sensory loss: 50%
  - ◆ Motor loss: 50%
  - ◆ Bowel/bladder dysfunction: 25%
- ◆ T spine most commonly affected; then L spine, then C spine
- ◆ Factors predictive of cord compression
  - ◆ Inability to walk
  - ◆ Increased reflexes
  - ◆ Compression # on plain film
  - ◆ Known bone mets
  - ◆ Bone mets for >1 year duration
  - ◆ Age <60

# Spinal cord compression

- ◆ Investigations
  - ◆ Gold Standard test - MRI of the whole spine
    - ◆ ~30% of patients will have asymptomatic cord compression at other levels.
    - ◆ Who to image?
      - ◆ Everyone with neurologic symptoms
      - ◆ T-spine pain
      - ◆ New or different pain
      - ◆ Persistent pain despite conservative measures
      - ◆ Pain aggravated by supine position
  - ◆ Other tests:
    - ◆ Plain film:
      - ◆ May be compression # or lytic lesion
    - ◆ CT:
      - ◆ Will likely see bony mets

# Spinal cord compression

- ◆ Management:
  - ◆ Steroids
    - ◆ Who:
      - ◆ All - reduces vasogenic edema, causes significant pain palliation and improves neurologic outcomes
      - ◆ Can consider avoiding in patients who have good motor function
    - ◆ How much:
      - ◆ Dexamethasone 10mg followed by 4mg qid. Higher doses have been studied with trend towards better functional outcomes with high dose, but significantly more adverse effects (GI bleed, psychosis). Most physicians use lower dos
    - ◆ How long:
      - ◆ Duration of RT, then taper over several weeks.
  - ◆ Need to consider adverse effects of steroids
    - ◆ Monitor blood sugars, consider GERD prophylaxis.

# Spinal cord compression

## ◆ Radiation

### ◆ All patients

- ◆ even those with “radioresistant” tumors (melanoma, RCC)
- ◆ can consider those who have had prior radiation to the area

## ◆ Surgery

### ◆ Controversial, no definite indications

### ◆ Relative indications for surgery:

- ◆ For diagnostic purposes/pathology
- ◆ Previously radiated segment
- ◆ Progressive pain/disability during RT
- ◆ Spinal instability

# Spinal cord compression

- ◆ Prognosis:
  - ◆ mortality linked to underlying malignancy
  - ◆ functional status depends on pretreatment function
    - ◆ Ability to walk after treatment
      - ◆ asymptomatic - 80%
      - ◆ mild myelopathy - 50%
      - ◆ paraplegic - 5%

# Spinal cord compression

What is the earliest sign of spinal cord compression from metastatic cancer?

- A. Motor changes
- B. Sensory changes
- C. Back pain
- D. Bowel/bladder dysfunction

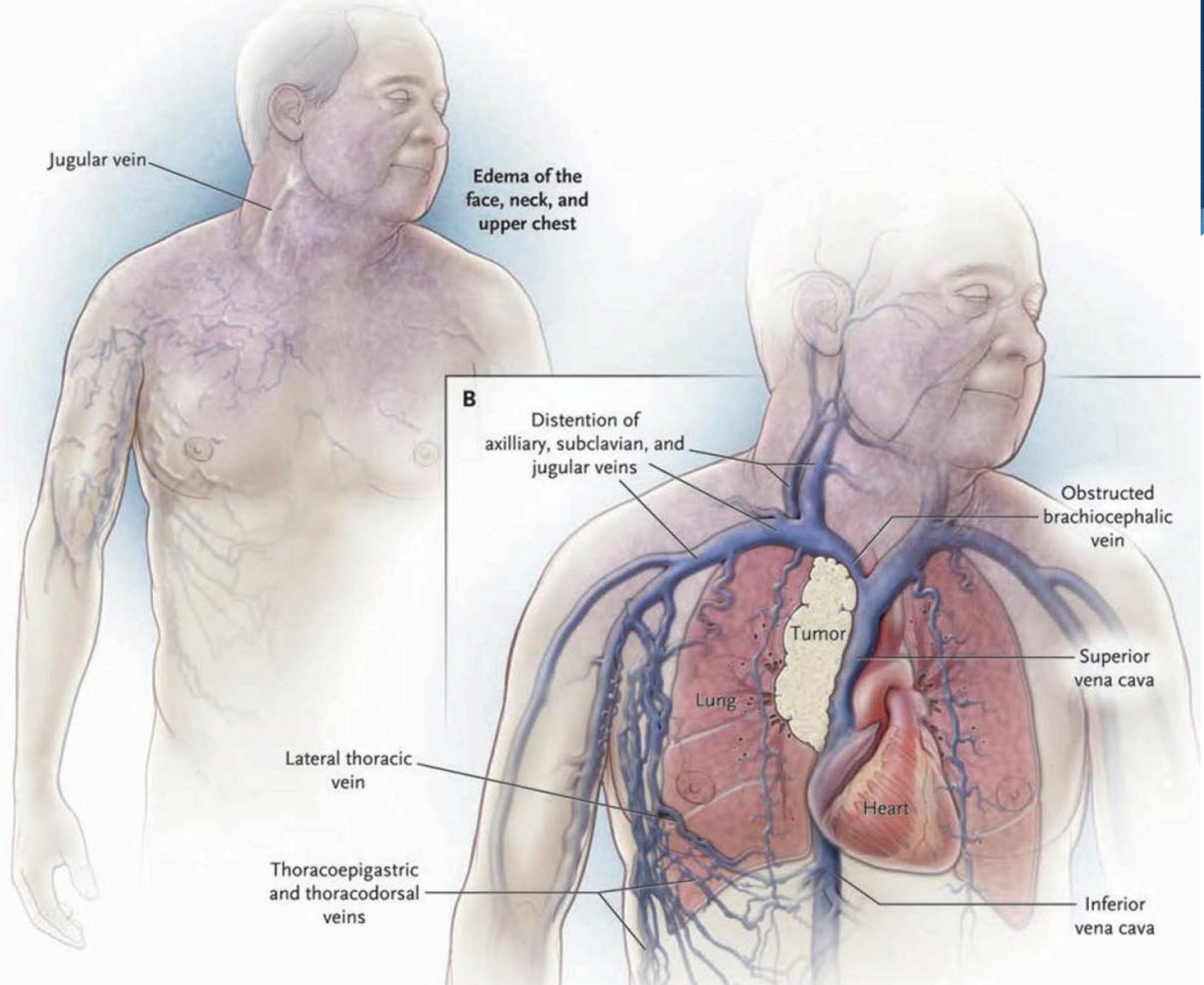
# Spinal cord compression

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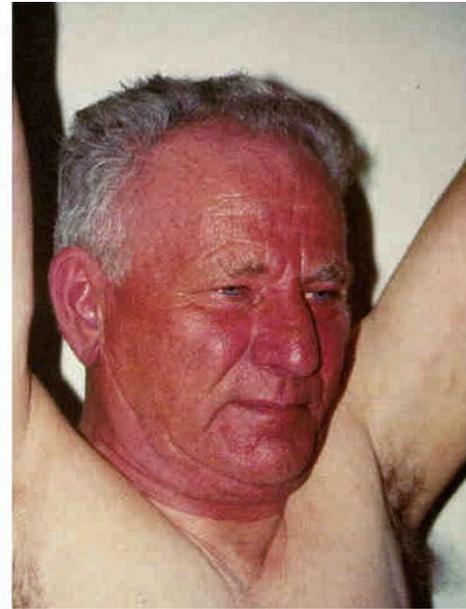
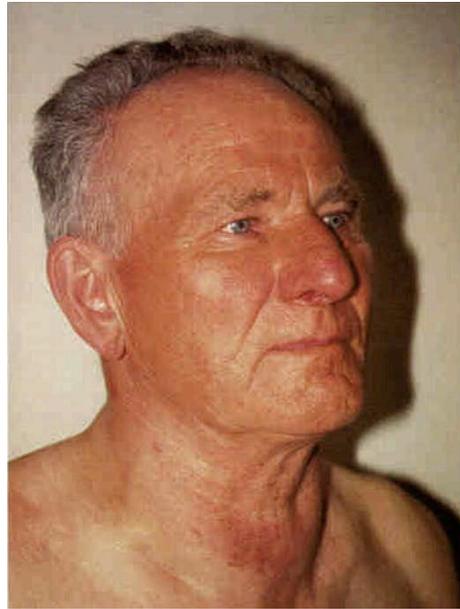
- A. Motor changes
- B. Sensory changes
- C. Back pain
- D. Bowel/bladder dysfunction

# SVC syndrome

- ◆ Definition: A constellation of signs and symptoms resulting from obstructed venous return through the superior vena cava.
  - ◆ The SVC is a thin walled collapsible vessel
  - ◆ The severity of symptoms depends on the time course of obstruction and the formation of collaterals.



# Pemberton's Sign



# SVC syndrome

## ◆ Symptoms

- ◆ Dyspnea 63%
- ◆ Fullness of head/facial swelling 50%
- ◆ Cough 24%
- ◆ Arm swelling 18%
- ◆ Chest pain 15%
- ◆ Dysphagia 9%

## ◆ Signs

- ◆ Distention of neck veins 66%
- ◆ Distention of chest wall veins 54%
- ◆ Facial edema 46%
- ◆ Plethora 19%
- ◆ Cyanosis 19%

# SVC syndrome

- ◆ Other signs/symptoms
  - ◆ Horner's syndrome (sympathetic chain)
  - ◆ Hoarse voice (recurrent laryngeal nerve)
  - ◆ Brachial plexopathy
  - ◆ Spinal cord compression

# SVC syndrome

## ◆ Causes:

### ◆ Malignant (60-86%)

- ◆ Lung cancer and lymphoma by far the most common

### ◆ Benign

- ◆ Intravascular catheter thrombosis
- ◆ Pacemaker wire thrombosis
- ◆ Sarcoid
- ◆ Aortic aneurysm
- ◆ Retrosternal goiter
- ◆ Fibrosing mediastinitis
- ◆ Benign tumors
- ◆ Infections (TB mediastinitis)

# SVC syndrome

- ◆ Investigations

- ◆ CXR - only 16% will have a normal CXR

- ◆ CT chest

- ◆ Biopsy if previously undiagnosed: obtain pathology

# SVC syndrome

- ◆ Management
  - ◆ ABCs first - airway compromise can occur
  - ◆ Supportive measures
    - ◆ Head of bed elevated
    - ◆ Steroids
    - ◆ Diuretics
  - ◆ Definitive therapy
    - ◆ RT+/-chemo
    - ◆ Endovascular stenting

# SVC syndrome

- ◆ Steroids:
  - ◆ Greatest benefit in lymphomas
  - ◆ Dexamethasone 4mg q6h
- ◆ Diuretics
  - ◆ For symptomatic benefit; not commonly used
- ◆ Radiation:
  - ◆ Relatively fast acting
  - ◆ Highly effective
    - ◆ Complete resolution of symptoms in 56%, partial resolution in another 40%
  - ◆ Well tolerated
    - ◆ Dysphagia most common side effect (24%)
  - ◆ Recurrences common

# SVC syndrome

- ◆ Endovascular stenting
  - ◆ Immediate relief of symptoms
  - ◆ Highly effective >90% relief of symptoms
  - ◆ Long lasting - 90% of those who had relief of symptoms did so until their death
  - ◆ Complication rate ranges from 0-50%
    - ◆ bleeding, stent thrombosis, occlusion, PE
    - ◆ Beware in highly chemo/radiation sensitive tumours- stent can migrate

# SVC syndrome

- ◆ General approach

- ◆ Stable vs unstable

- ◆ If unstable likely need airway protection and steroids.

- ◆ Stenting preferred if available

- ◆ Known pathologic diagnosis

- ◆ Steroids +/- RT or stent

- ◆ If diagnosis is unknown, pursue diagnosis first before any therapy if patient is not severely symptomatic to avoid obscuring pathology

# SVC Question

- ◆ 36 year old female comes in with increased facial edema, shortness of breath, and stridor. CT demonstrates SVC syndrome. What would be your first intervention after ABCs?
- ◆ A. Radiation
- ◆ B. Obtain Biopsy
- ◆ C. Steroids
- ◆ D. Chemotherapy

# SVC Question

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# SVC syndrome

◆ Questions?