Oncologic Emergencies

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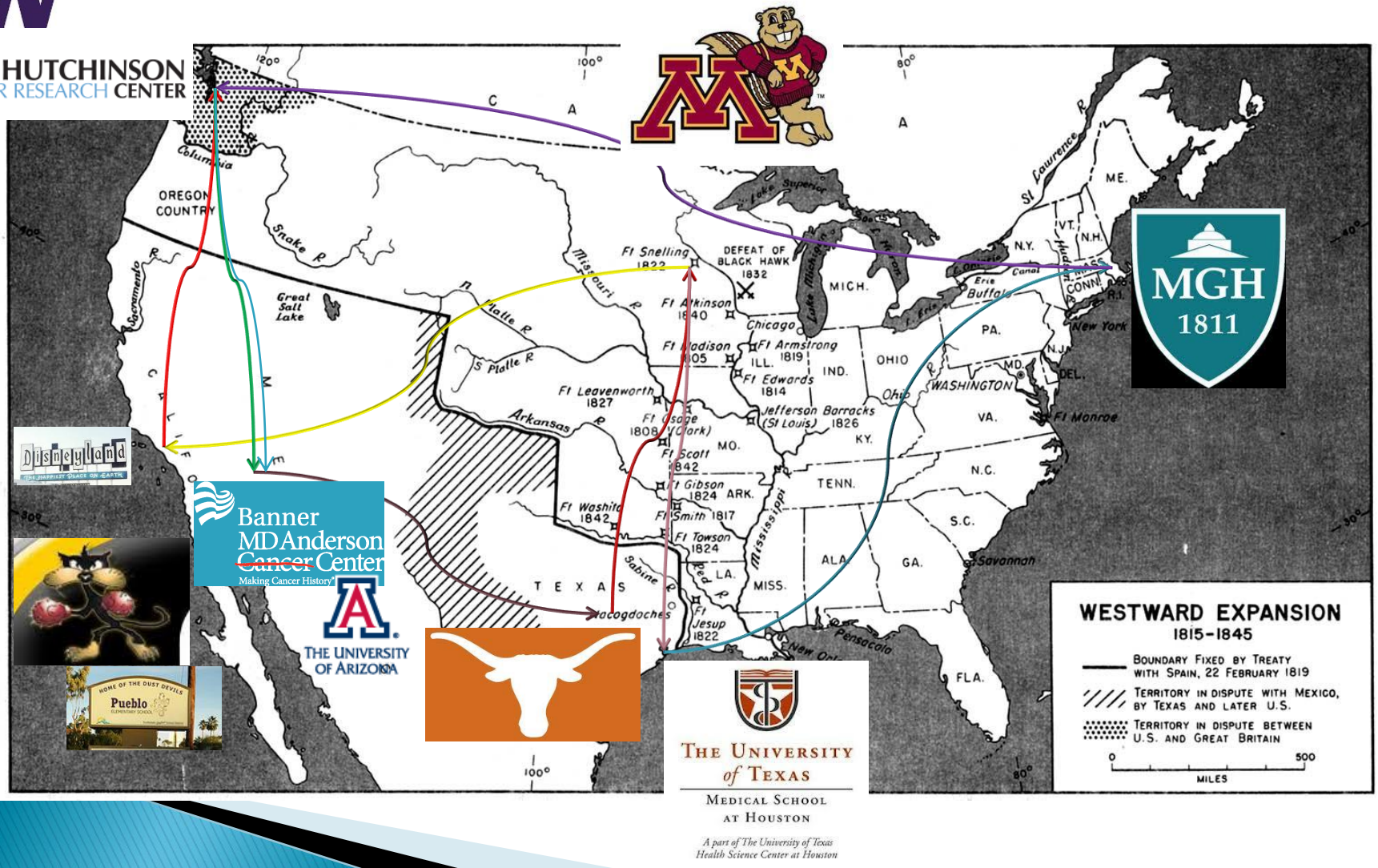
Where are you from?



Objectives

- Provide an overview of the diagnosis and management of common oncologic emergencies
- Help determine which situations are truly emergent
- Discuss the most common cancer types contributing to each presentation
- Help lower your pulse rate whenever you encounter these patients

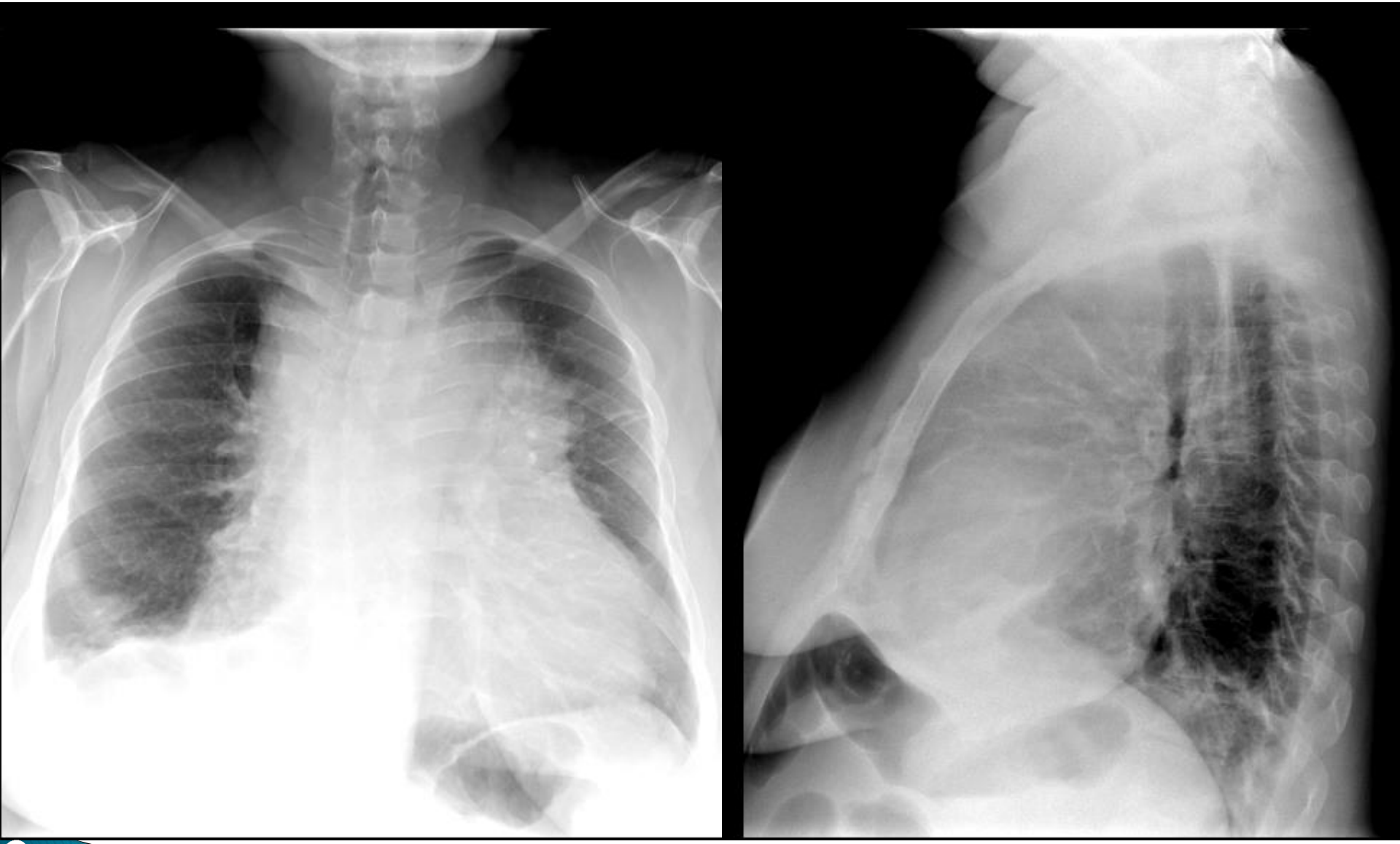
Oncologic Emergencies

- Is the situation truly emergent?
- Is the problem related to malignancy?
- Is the tumor sensitive to chemotherapy, radiation?
- Is further evaluation necessary?
- What are the wishes of the patient and family?
  - https://depts.washington.edu/toolbox/dnr.html

Case 1

- You are called to the ED at the VA to evaluate a 64yo woman with dyspnea, weight loss, and fevers for two weeks

- Exam: BP 100/60, HR 110, RR 20
  - 2cm R axillary adenopathy, bilateral cervical adenopathy. No papilledema
  - Decreased breath sounds over left lung base, no stridor
  - No organomegaly
  - ALT 150, AST 23, LDH 620, Alk Phos 250, Uric Acid 6.5
  - CBC 3.5>12<95 ANC 2000



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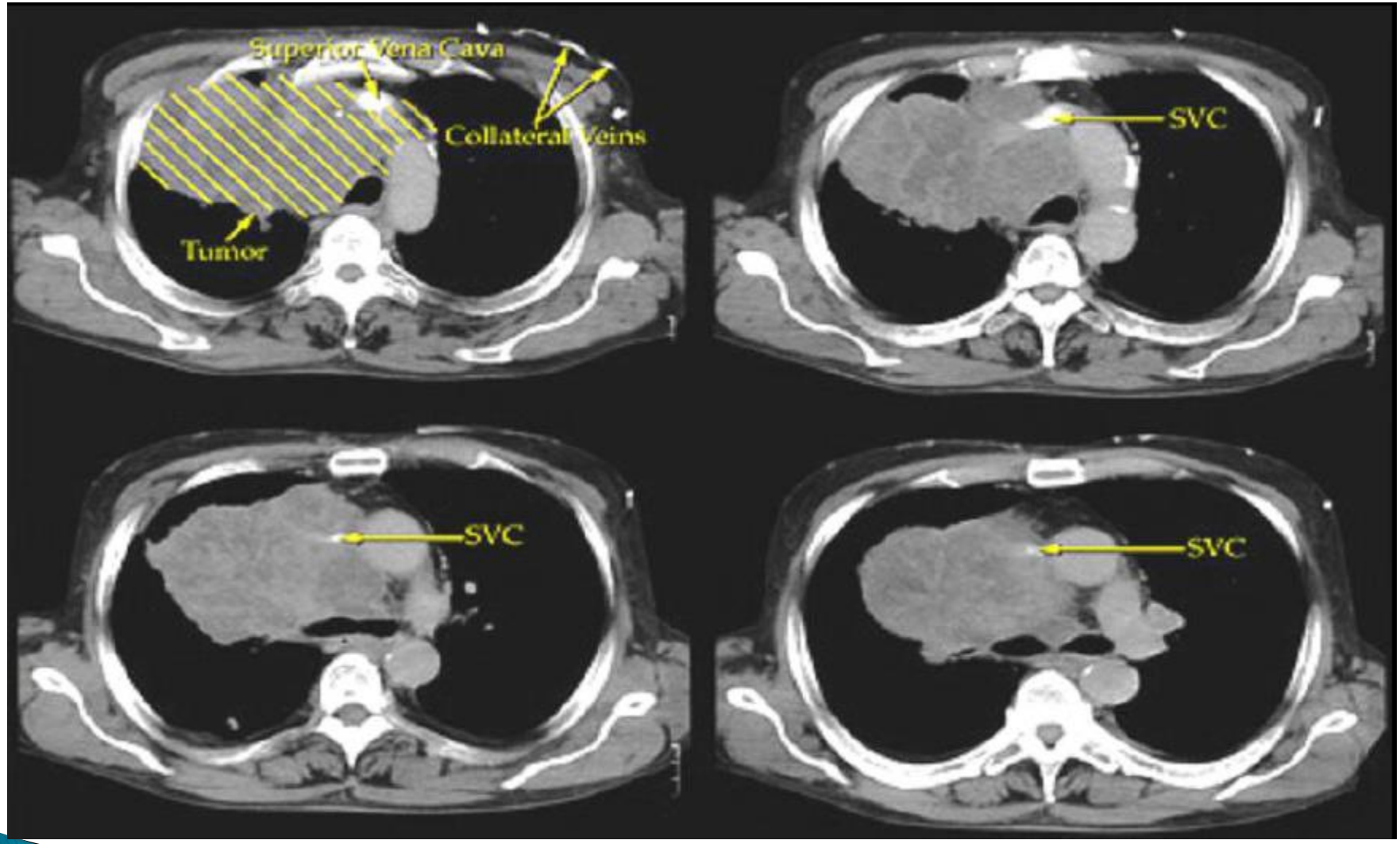
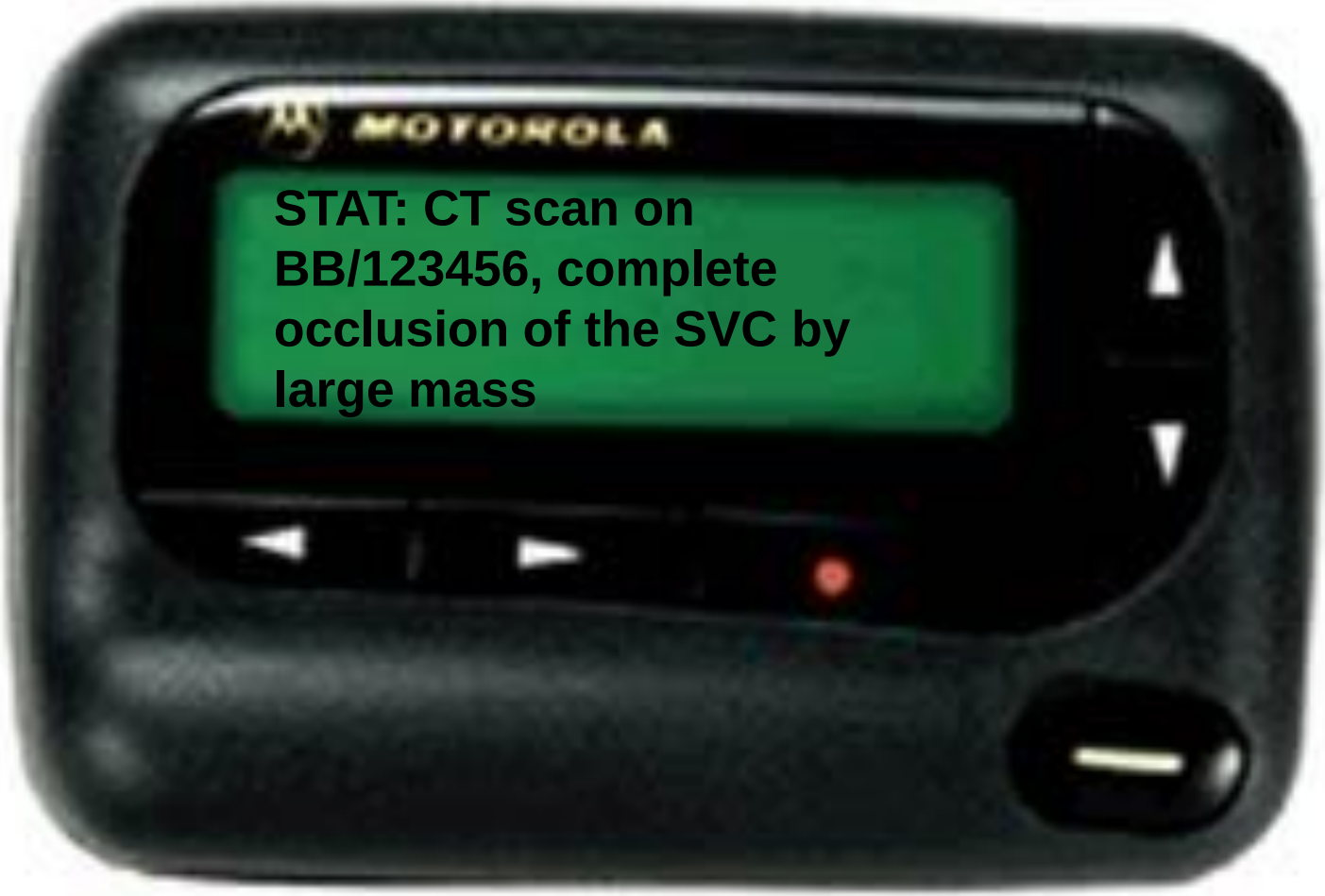

Superior Vena Cava
Collateral Veins
Tumor
SVC
SVC
SVC

What do you recommend?



SVC Syndrome

You recommend tissue biopsy but the attending surgeon calls you directly to say that the risk of surgery is too high in SVC syndrome patients. You say:

A) “Okay, sorry to bother you”

B) “There are data to support minimal to no increased risk with surgical biopsy in SVC syndrome”

C) “Ok, let’s just radiate to 50Gy in 25 fractions”

D) “Ok, but when the patient relapses, will you put in a stent without a tissue diagnosis?”

Biopsy in SVC Syndrome

Table 1. Surgical Procedure Performed

2 of the 4 were AF 5 of 13 were Abx

Type of Procedure	No. of Procedures*	Perioperative Complications	Intraoperative Complications	Postoperative Respiratory Complications	Significance
Cervical mediastinoscopy	32	4	1	3	NS
Medial sternotomy and resection	29	3	0	3	NS
Anterior mediastinotomy	20	4	1	3	NS
Thoracotomy and resection	12	1	1	0	NS
Thoracoscopy	8	2	1	1	NS
Cervical mediastinal exploration	6	2	0	2	NS
Extrathoracic lymph node biopsy	5	0	0	0	NS
Others	3	1	0	1	NS
Total	115	17	4	13	NS

* Some patients had more than one surgical procedure.

NS = not significant.

Bechard *Anesthesia* 2004

Intraoperative complications
(1) inability to ventilate or peak pressure >40 cm H2O
(2) severe pulmonary shunt (pulse oximetry <95% at FIO2 of 100%)
(3) hemodynamic instability (systolic BP <70 mmHg for 5 min or pulse rate <40 or >120 beats/min) necessitating treatment

Postoperative respiratory complications
occurring within 10 days after surgery and necessitating treatment
(1) Reintubation
(2) Noninvasive mechanical ventilation
(3) Bronchoscopy
(4) Inhalation therapy (racemic epinephrine, helium–oxygen mixture)
(5) Antibiotics

Dx: 31% lymphoma, 15% thymoma, 14% mets

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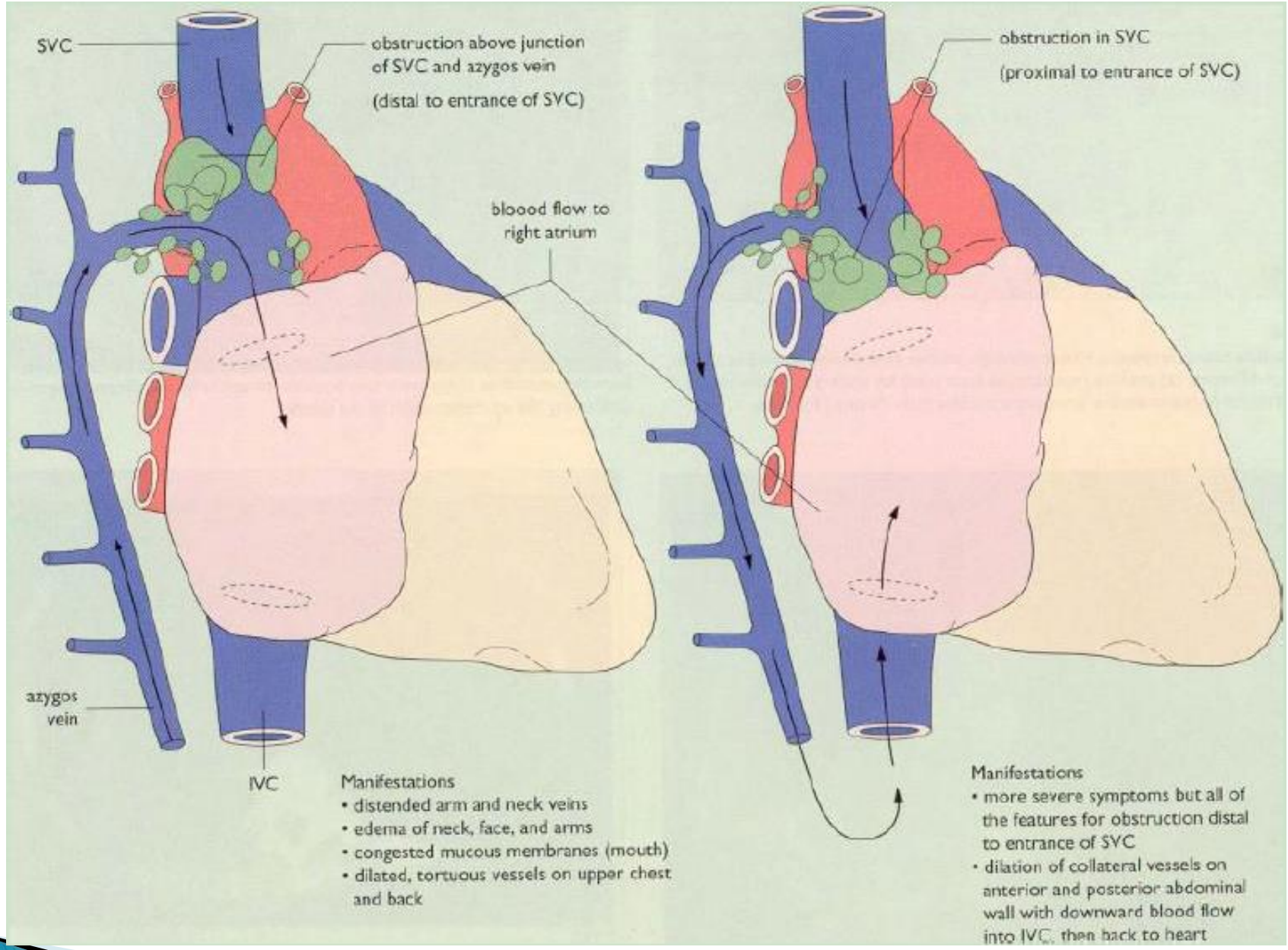

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SVC Syndrome

- Physiology
  - Partial or complete obstruction of the SVC and collaterals

- Manifestations
  - Dyspnea, dysphagia, cough, stridor, papilledema, edema of upper torso/face, plethora, dilated venous collaterals (sometimes none of these)
  - Rare: hoarseness, syncope, HA, chest pain

SVC Syndrome

- Etiology
  - Malignant in 85-95% of cases
  - Benign
    - CVC/thrombus, pacemaker, infection (TB, histo)

Histology	% of cases	Total (%)
Lung carcinoma		79
Small cell	34	
Squamous cell	21	
Adenocarcinoma	14	
Large cell/other	11	
Lymphoma		14
Non-Hodgkin's lymphoma	13	
Hodgkin's lymphoma	1	
Other malignancy		6
Adenocarcinoma		
Kaposi's sarcoma		
Seminoma		
Granulocytic sarcoma		
Leiomyosarcoma		

SVC Syndrome

- Immediate interventions:
  - Upright position (improve drainage), oxygen prn
  - Benefit of diuresis is questionable
  - Obtain necessary imaging
  - **Biopsy**
    - (FNA usually inadequate for lymphoma diagnosis)

  - Is this an emergency?

SVC Syndrome

- Tracheal obstruction or cerebral edema are the only true emergencies
- **Tissue diagnosis** is most important
  - (sputum cytology, bronchoscopy, node biopsy, trans-thoracic needle biopsy, mediastinoscopy, VATS, etc)
  - Low risk even with general anesthesia
- Treatment
  - Chemotherapy for sensitive tumors, corticosteroids after biopsy while awaiting tissue diagnosis
  - Radiation for other tumors
  - Surgery or stent in selected cases

SVC Syndrome

- Biopsy (IR or Surgery)
- Most aren't truly emergent
- Steroids while waiting for pathology (Onc)

Stone. Blood 2012. 119(10)

Case 2

- A 62yo man presents with fatigue, headaches, blurry vision, and epistaxis. He has generalized lymphadenopathy and a palpable spleen tip. Fundoscopic exam with enlarged retinal veins.

- CBC 6.5>7.4<155
- Cr 1.4 Ca 9.1
- T Prot 8.4 Alb 2.2
- Head CT negative

- What do you suspect?
- A. Cerebral sinus thrombosis
- B. Endocarditis
- C. Hyperviscosity syndrome
- D. Leukostasis

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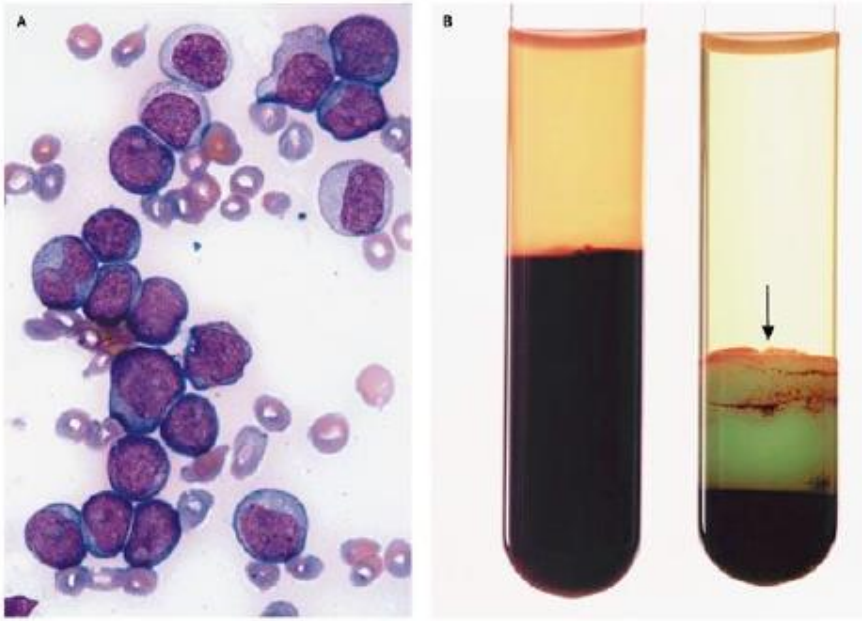
Hyperviscosity

- Increase in serum viscosity (above 4 cp) can cause sludging/microvascular insufficiency
  - Most commonly neurologic, pulmonary symptoms
- Waldenstrom Macroglobulinemia is common cause due to IgM secretion (10-30% pts)
  - 80% IgM intravascular; therefore can remove with plasmapheresis.
  - After reducing viscosity, then treat disease
    - chemotherapy and targeted agents for the lymphoplasmacytic lymphoma (LPL)

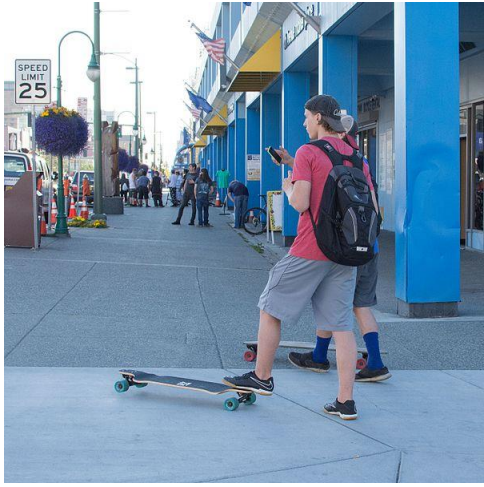
Leukostasis

- Can also cause hyperviscosity-like symptoms
  - Myeloid blast count >50k (AML)
  - Lymphoid blast count >400k (ALL)
  - Rare in CML, CLL, Leukemoid reaction
  - RBC transfusion increases viscosity, so delay until after cytoreduction if not urgent need
  - Treat with leukapheresis
  - Or just start chemotherapy

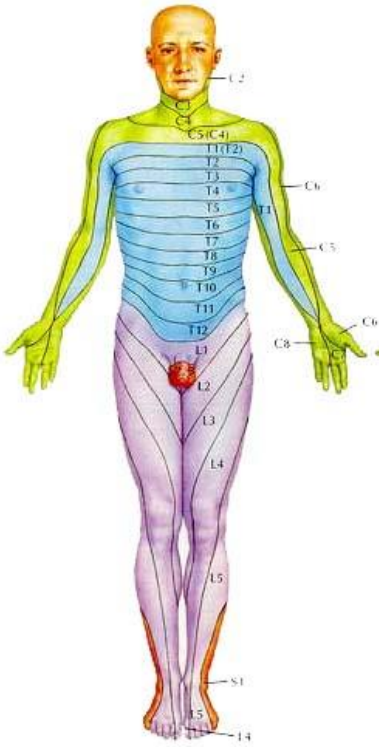


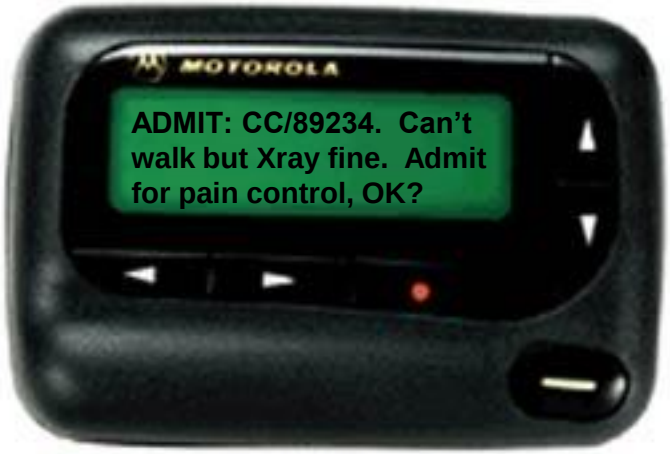
Mauro MJ NEJM 2003. 349:767

Case 3



- 22yo male presents to the ER with weight loss, back pain, dyspnea, fatigue, and difficulty walking. In fact he ran into a wall three times while playing posting to snapchat.
- Exam: BP 110/72, HR 100, RR 18
  - Orthostatic
  - Back tender to palpation
  - Decreased sensation in a band starting at T5, LE weakness with 3/5 in BLE
  - Phone seems inseparable from his R hand, with 6+/5 grip strength noted
- Chest xray and Thoracic spine xray negative





- The ED physician calls to send him up to the floor, where your team is busy admitting 4 new arrivals. You say:
- A) "Sure, as long as you put in some holding orders"
- B) "How about an MRI?"
- C) "How about starting dexamethasone, then getting an MRI?"
- D) "I'm capped, save him for the night float"

- MRI entire spine (cord compression protocol)
- Consider PSA, breast exam, CXR, SPEP as indicated if no prior diagnosis

Epidural cord compression

- Compression of spinal cord by tumor extending from vertebral body or through foramina.
- Location
  - Thoracic (70%) > lumbar > cervical spine
- Manifestations
  - Pain (95%), weakness, sensory changes, bowel/bladder dysfunction

Cord Compression

- Malignant in >90% of cases
  - Benign causes include trauma, DJD, osteoporosis and fracture, spinal stenosis, abscess
- Diagnosis
  - MRI
    - If cord compression is suspected, image the ENTIRE spine
    - >50% patients with multi-level involvement

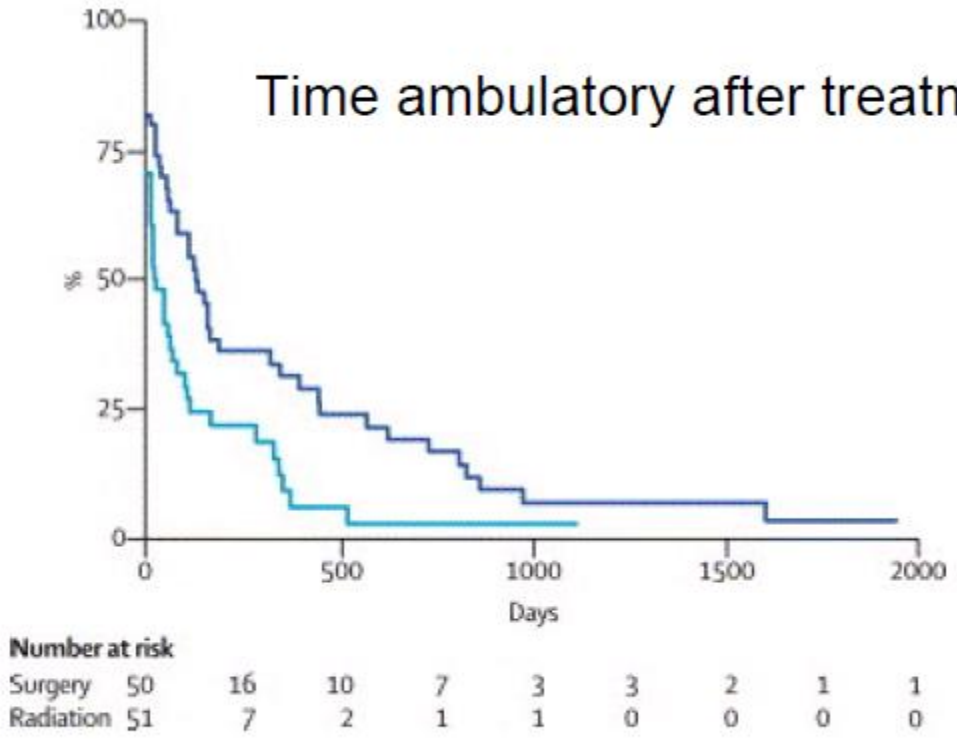
Histology	% of cases
Lung	18
Breast	13
Unknown primary	11
Lymphoma	10
Myeloma	8
Sarcoma	8
Prostate	6
Gastrointestinal tract	4
Renal	5
Other	17
Total Number of Cases	896

Cord Compression

- Treatment
  - Dexamethasone 10mg (some use 100mg) IV x 1 then 4mg IV q6hrs. Taper once compression resolved/XRT completed
  - Surgery then XRT vs Radiation alone
    - (Patchell et al. Lancet 2005. 366:643)
      - Primary endpoint, ability to walk
      - N=101
      - Had to be symptomatic (pain included)
      - Could not have been paraplegic for >48hrs
      - Tumor in one single area (could be multiple contiguous vertebrae)
      - Excluded 'very radiosensitive tumors'
        - Lymphoma, myeloma, leukemia

Back on their feet

- Surgery median 122 days
- Radiation median 13 days



Other Outcomes

- Patients who entered treatment unable to walk
  - Surgery/radiation: 62% were ambulatory after treatment
  - Radiation alone: 19% ambulatory

	Radiation group (n=51) median	Surgery group (n=50) median	Relative risk*	95% CI*	P*	Significant predictors**
Maintenance of continence	17 days	156 days	0·47	0·25–0·87	0·016	Surgery RR=0·51 (0·29–0·90) Baseline Frankel Score RR=0·56 (0·3–0·73)
Maintenance of ASIA score	72 days	566 days	0·28	0·13–0·61	0·001	Surgery RR=0·30 (0·14–0·62) Stable Spine RR=0·43 (0·22–0·83) Cervical Spinal Level RR=0·49 (0·26–0·90) Baseline Frankel Score RR=0·65 (0·46–0·91)
Maintenance of Frankel score	72 days	566 days	0·24	0·11–0·54	0·0006	Surgery RR=0·26 (0·12–0·54) Stable Spine RR=0·39 (0·20–0·75) Cervical Spinal Level RR=0·53 (0·74–0·98) Baseline Frankel Score RR=0·62 (0·44–0·88)
Survival time	100 days	126 days	0·60	0·38–0·96	0·033	Surgery RR=0·60 (0·40–0·92) Breast Primary Tumour RR=0·29 (0·13–0·62) Lower Thoracic Spinal Level RR=0·65 (0·43–0·99)

*Based on a Cox model with all covariates included. **Based on a Cox model with only significant predictors included (stepwise selection).

Patchell, Lancet 2005

Modified Tokuhashi Score

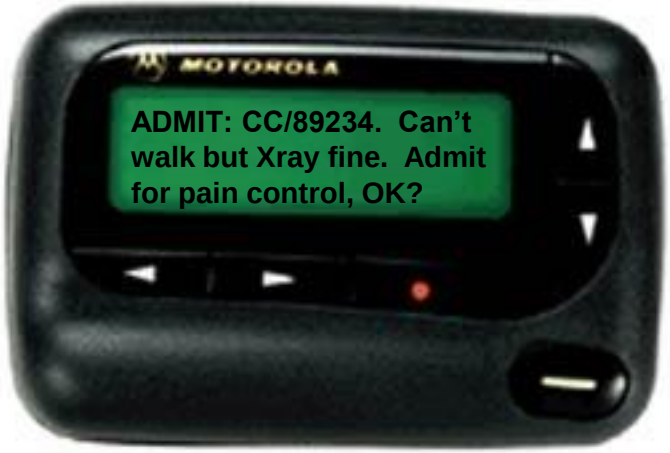
Ann R Coll Surg Engl 2012; **94**: 28–33 and *Spine* 1990. **15**:1110-1113

Original study suggested aggressive interventions for score ≥9 and less invasive if ≤5.

Feature	Score 0	Score 1	Score 2
Performance status	KPS 10–40%)	KPS 50–70%	KPS 80–100%
# Extraspinal bone mets	≥3	1–2	0
# vertebral body mets	≥3	1–2	0
Visceral Mets	Unresectable	Resectable	None
Primary Tumor	Lung/ Stomach	Kidney/liver/ uterine	Thyroid, prostate, breast, rectal
Spinal cord palsy	Complete	Incomplete	None

Cord Compression

- Empiric steroids as soon as suspicious
- Diagnose with MRI (even if pain alone with no neuro symptoms and suspicious)
- Decompression (Neurosurgery/Ortho, RadOnc)
  - Surgery better than radiation alone in selected patients



Case 4

- 24yo woman with stage IV Burkitt Lymphoma is admitted for urgent treatment with R-hyper-CVAD
- Exam: BP 120/70, HR 90, RR 26
- Hepatosplenomegaly
- Cr 2.4 (baseline 0.7), CO2 14, Uric acid 20, Potassium 6.4, Ionized Ca 1.9, Phosphate 9.0

- What is the first step in management?
- A. Emergent hemodialysis
- B. IV fluids
- C. Calcium gluconate
- D. Rasburicase

Tumor Lysis Syndrome

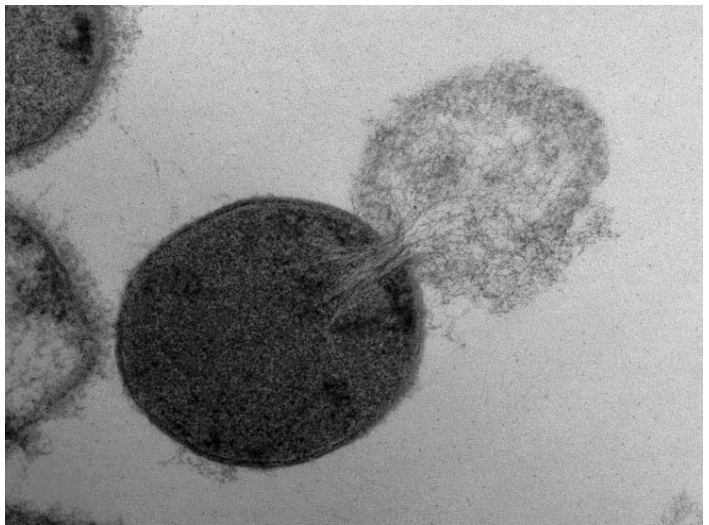
- Metabolic derangements associated with tumor necrosis (spontaneous or due to chemo)
  - Release of cellular purines, phosphate, potassium
- Hyperuricemia with acidemia induces crystal formation and obstructive uropathy
- Etiology: Lymphoma, Leukemia, Small cell lung,
- High risk features: tumor >10 cm, LDH > 2x ULN, leukemic cells > 25k/uL, pre-existing renal failure.

(*JCO* 2008;26:2767)

TLS Diagnosis

- **Cairo-Bishop laboratory definition**
  - At least <u>two</u> of the following:
    - Uric acid > 6.5-8 mg/dL or >25% above baseline
    - K > 6 mEq/L or > 25% above baseline
    - Phos > 6.5mg/dL or > 25% above baseline
    - Ca < 7mg/dL or < 25% below baseline
- **Clinical tumor lysis**: lab tumor lysis plus
  - Cr 50% above baseline
  - Arrhythmia (hyperK, hypoCa)
  - Seizure (from hypocalcemia)

Image: Daniel Nelson, UMD

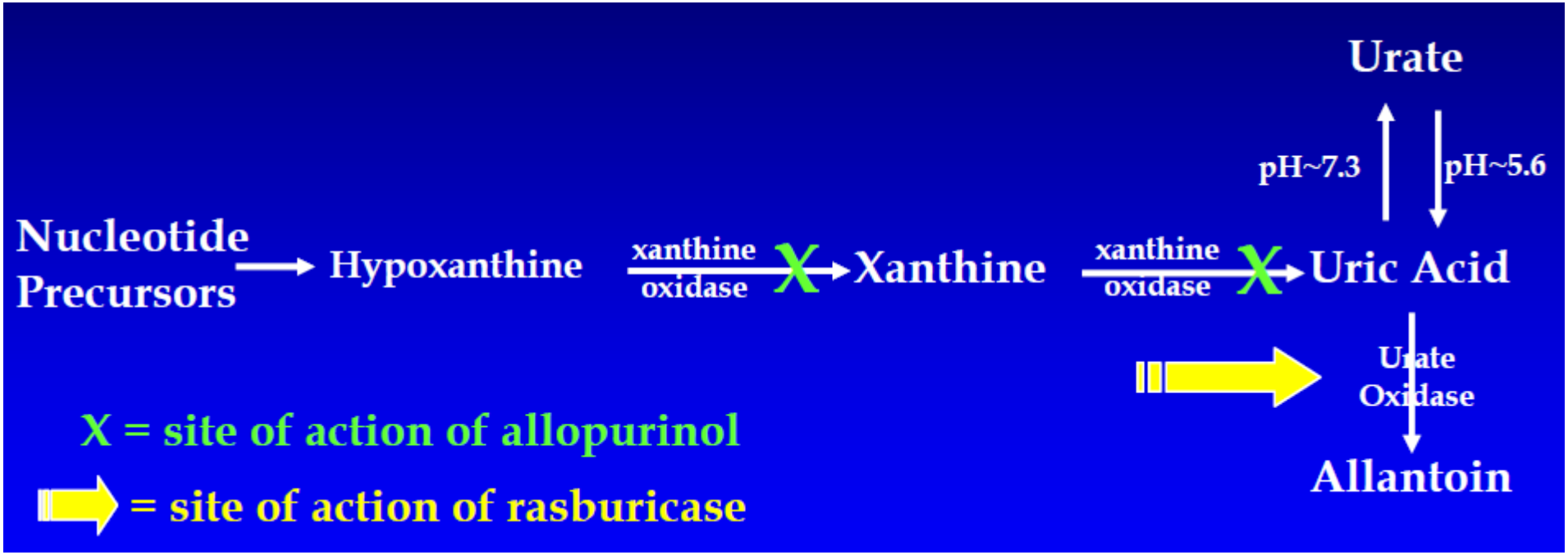


TLS prevention and Treatment

- **Prophylaxis**
  - Hydration: 0.9% NS (No potassium in IVF). Goal UOP 80-100 mL/hr
  - Allopurinol: allopurinol 300mg PO daily

- **Treatment** (as above plus:)
- Electrolyte abnormalities:
  - Use caution prior to repleting for hypocalcemia
    - (Ca x PO4 >60 increases risk of precipitation)
  - Severe cases may require hemodialysis.
  - Loop diuretics can assist with uric acid excretion when patient no longer hypovolemic.
- *May **alkalinize** the urine with goal urine pH of 7 if uric acid is >8mg/dL and phosphate is not >6.5mg/dL.
  - (alkalinization makes uric acid more soluble – but phosphate less soluble, so may trigger precipitation esp when Ca x PO4 is >60mg/dL. With rasburicase available, alkalinization is **rarely** indicated)

TLS Treatment



- – **Rasburicase**: (recombinant urate oxidase enzyme) for selected high-risk patients (uric acid >10), treat with 3-6mg IV x 1
  - may repeat after 8 hours in rare cases, esp if uric acid remains >8.5mg/dL
  - Caution: agent can cause hemolysis in G6PD deficient patients.
- Check level 6 hours after dose: **Note well**: Uric acid samples taken after administration of rasburicase must be collected in chilled heparin tubes, kept in ice, and run within 4 hours of collection as the enzyme will continue to be active within the tube and cause spuriously low results (Use *RASBURICASE* uric acid level order).

Case Continued

- Patient was managed aggressively with control of her electrolyte abnormalities and her Cr improved without dialysis

- She completed 8 cycles of hyper-CVAD, entered remission, and was cured

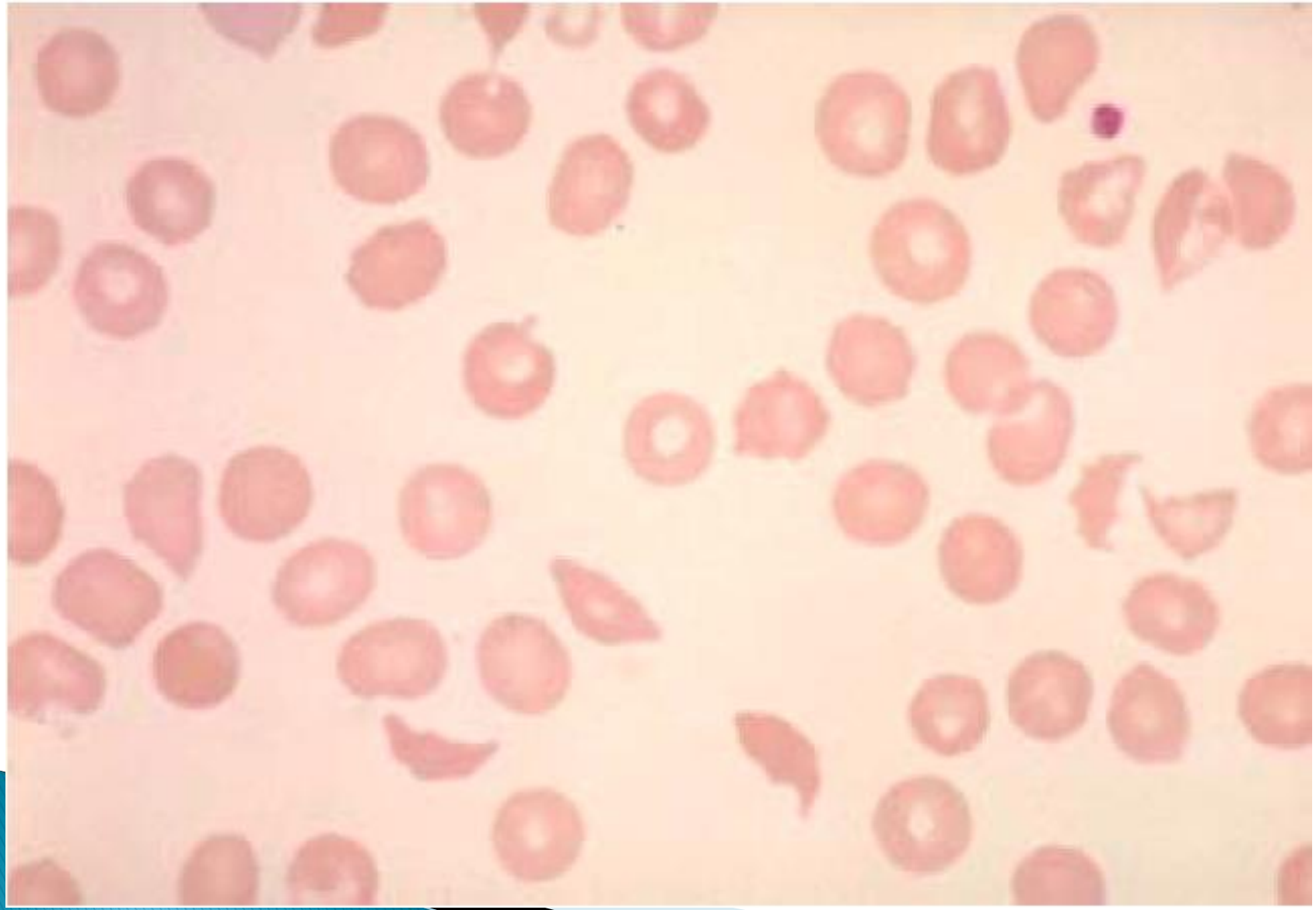
Case 5

- 36yo woman with no PMHx presents with RUQ abdominal pain, nausea/vomiting, and jaundice.
- No bleeding or bruising, no fevers

- · CBC 10.5>7 <12
- · INR 1.2, PTT 30
- · LDH 1,059
- · Cr 1.7, TBili 4.8
- · Albumin 3.6

- Abdominal ultrasound reveals pericholecystic fluid and mild gallbladder wall thickening
- She is planned for cholecystectomy

Peripheral Smear

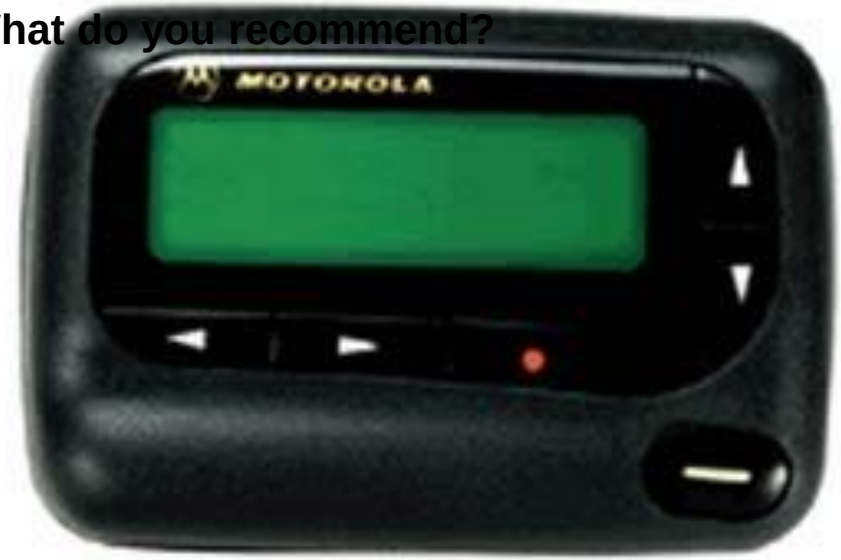


Next Steps?

- What is the next step in management?

A. Urgent Plasma exchange
B. Urgent Hemodialysis
C. Transfuse platelets for cholecystectomy
D. Treat for hepatic crisis with sickle cell disease

What do you recommend?

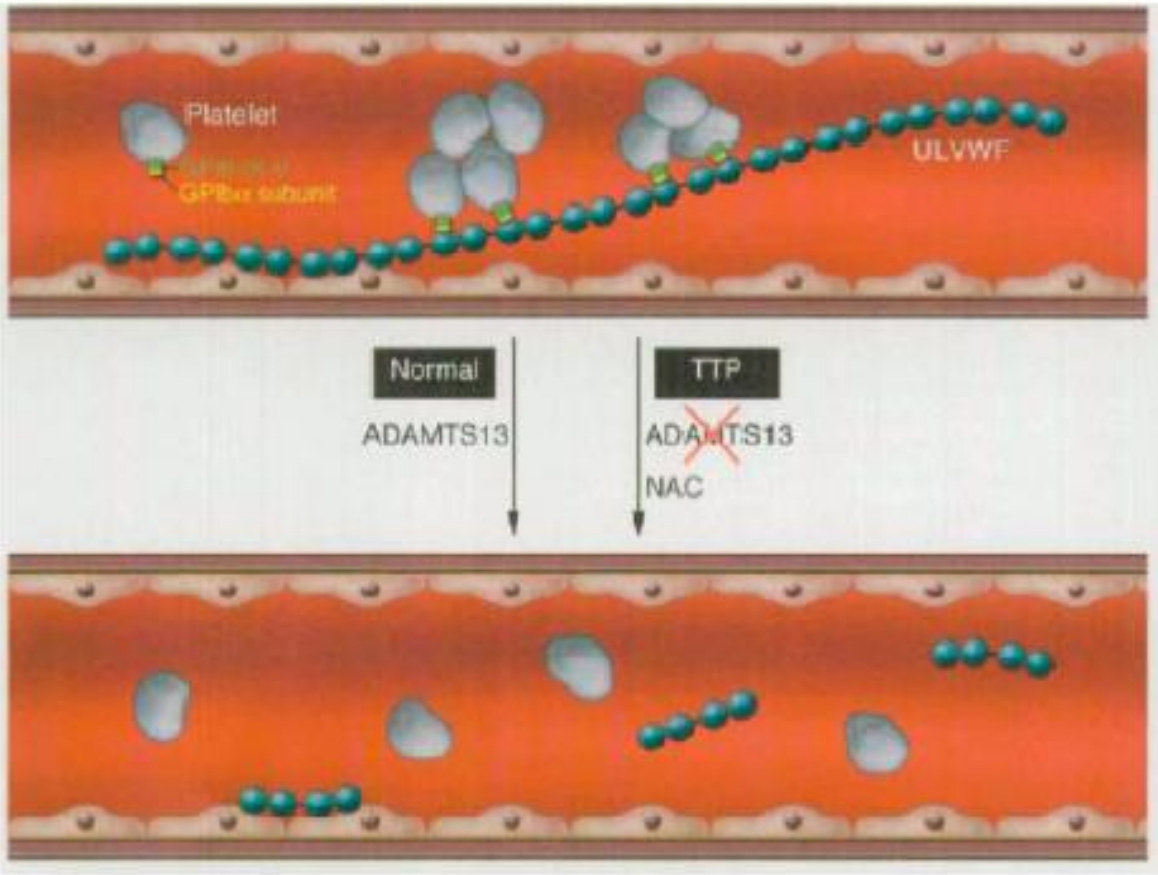


Thrombotic Thrombocytopenic Purpura (TTP)

- Thrombocytopenia and microangiopathic hemolytic anemia (MAHA) are only requirements to suspect diagnosis
- Treat with emergent plasma exchange (large bore pheresis line)
  - Replace the ultralarge vWF with normal spectrum of vWF
  - UL vWF is more adhesive than shorter vWF
  - Platelets bind to vWF
- Many cases are autoimmune (inhibitor against ADAMTS13) – steroids can be helpful
- Confirm diagnosis with ADAMTS13 activity level with reflex to inhibitor

TTP Physiology

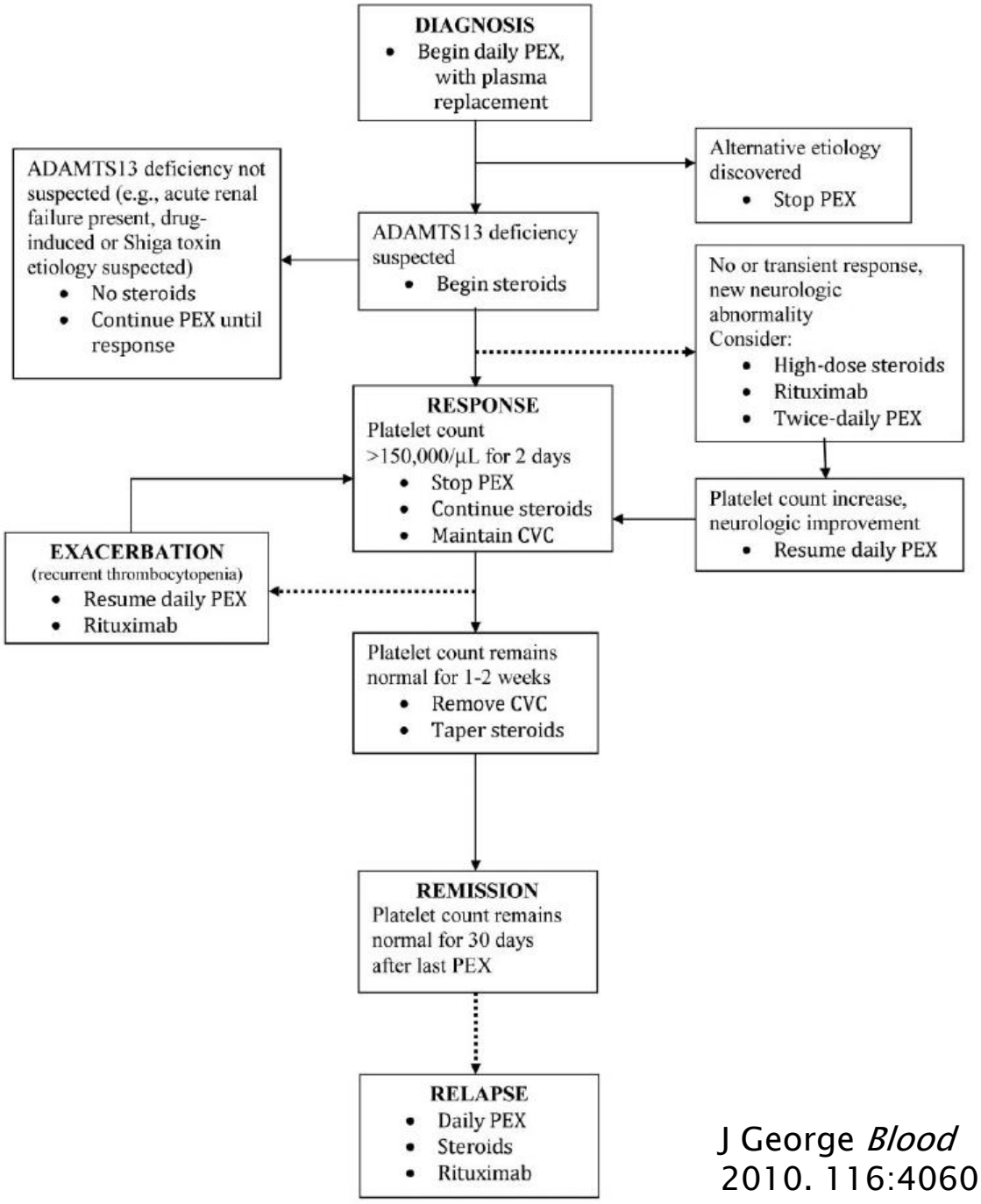
- Early plasma exchange decreases mortality from 90% to 15%



JCI 2011. 121:522.

Treatment

- Platelet transfusion?
  - Minimize
  - Likely ok if required to get line placed



J George *Blood* 2010. 116:4060

Questions

AEQUANIMITAS

Thou must be like a promontory of the sea, against which, though the waves beat continually, yet it both itself stands, and about it are those swelling waves stilled and quieted.

Marcus Aurelius.

I say: Fear not! Life still
Leaves human effort scope.
But, since life teems with ill,
Nurse no extravagant hope:
Because thou must not dream, thou need'st not then despair

Matthew Arnold, Empedocles on Etna.

["Aequanimitas," *Aequanimitas*, p. 3]

Sir William Osler, 1889

I

AEQUANIMITAS[1]

To many the frost of custom has made even these imposing annual ceremonies cold and lifeless. To you, at least of those present, they should have the solemnity of an ordinance—called as you are this day to a high dignity and to so weighty an office and charge. You have chosen your Genius, have passed beneath the Throne of Necessity, and with the voices of the fatal sisters still in your ears, will soon enter the plain of Forgetfulness and drink of the waters of its river. Ere you are driven all manner of ways, like the souls in the tale of Er the Pamphylian,[2] it is my duty to say a few words of encouragement and to bid you, in the name of the Faculty, God-speed on your journey.

I could have the heart to spare you, poor, careworn survivors of a hard struggle, so "lean and pale and leaden-eyed with study;" and my tender mercy constrains me to consider but two of the score of elements which may make or mar your lives—which may contribute to your success, or help you in the days of failure.

In the first place, in the physician or surgeon no quality takes rank with imperturbability, and I propose for a few minutes to direct your attention to this essential bodily virtue. Perhaps I may be able to give those of you, in

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- @MattUlricksonMD

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Case 6

- 85yo male with a history of multiple myeloma recently stopped therapy after entering a remission. His wife calls you while you are covering calls for the clinic.
  - Has a history of familial pemphigus
  - Worsening rib pain
  - Previously functional, his wife reports that he is more confused and lethargic

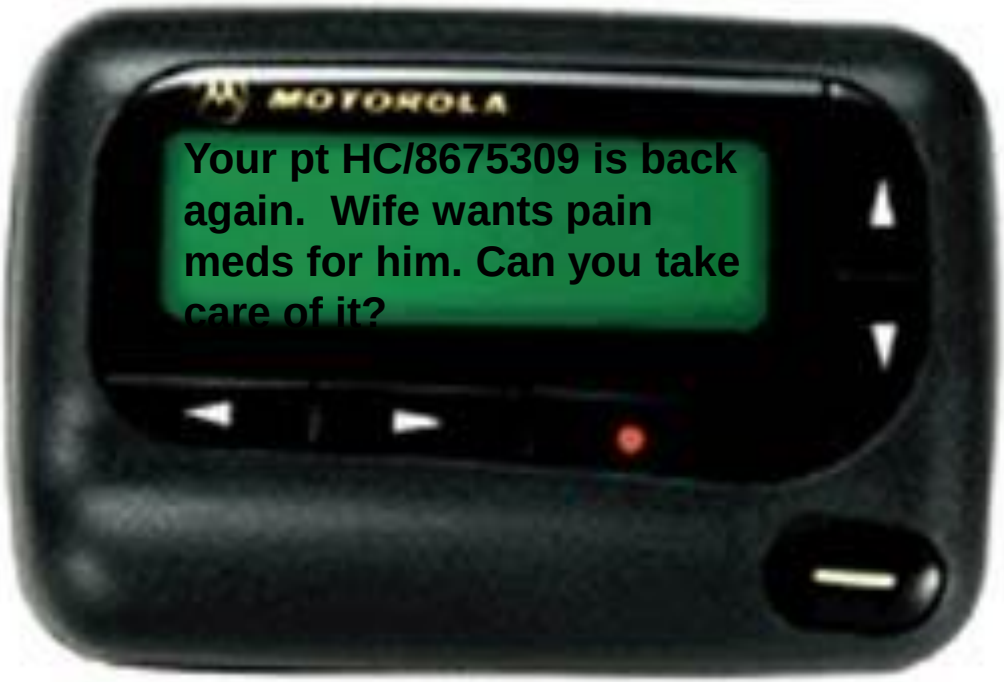
You advise him to present to ED for evaluation

- CBC: 11.1>32%<325 ANC 8000
- Lytes: Na 134, Cr 1.3, LFTs WNL
- CXR: Normal
- No sensory loss or other neurologic changes.
- Due to the negative evaluation, they send the patient home for outpatient management

- What else should they have checked?
- A. His insurance card
- B. A CT scan of the brain
- C. An ionized calcium
- D. A high sensitivity troponin

The next day

- Patient returns home from ED at 1am; the next afternoon he is brought back to the ED by EMS with worsening confusion and pain



The next day

- Patient returns home from ED at 1am; the next afternoon he is brought back to the ED by EMS with worsening confusion and pain

- Serum Calcium = 14.2 (Alb 3.2)

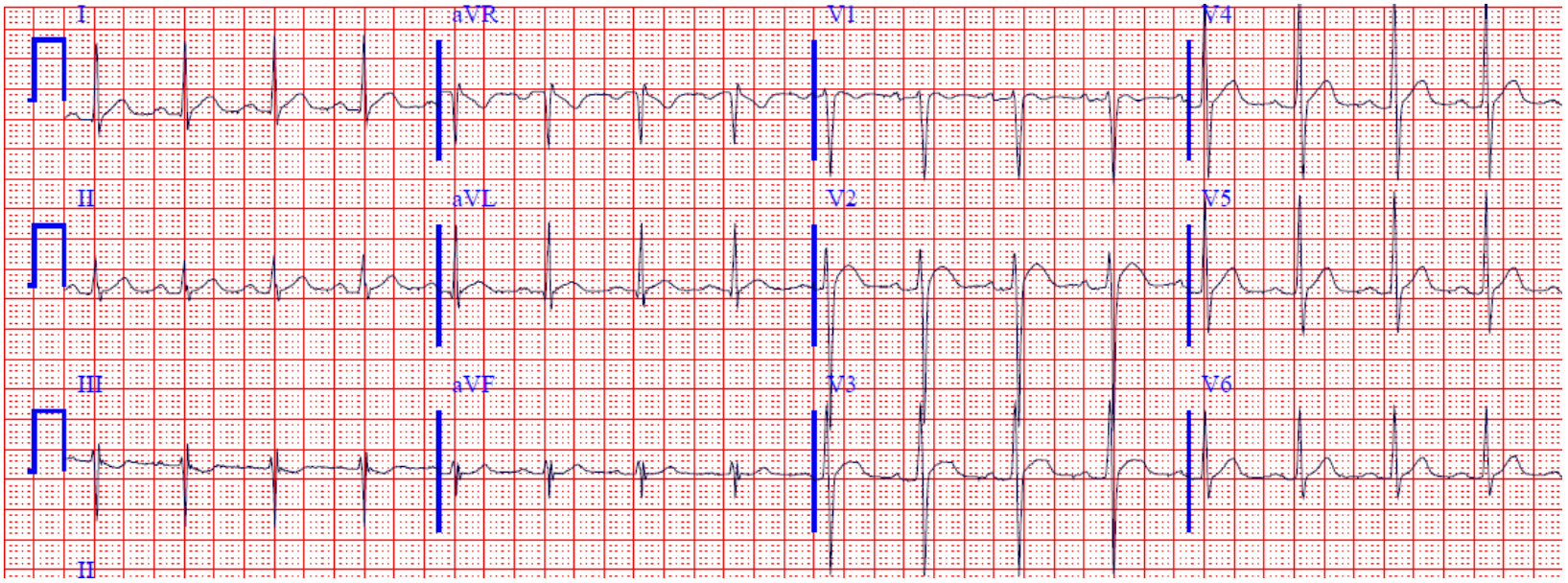
Hypercalcemia

- Occurs in 10-20% of patients with cancer
- Malignancy most common cause inpatient (hyperPTH most common in clinic)
  - NSCLC, Breast Ca, Myeloma
  - **15% of patients with hypercalcemia AND malignancy have a **separate** cause for the hypercalcemia
    - PTH, thiazide, milk-alkali, granuloma, hyperthyroid, etc
- Physiology
  - PTHrP
  - Increased 1,25 Vit D (lymphoma)
  - Increased bone breakdown (bony lesions)

Histology	% who develop hypercalcemia
Breast	19-30%
Lung	10-35%
Multiple myeloma	20-30%
Head and neck	5-24%
Renal	17%

Hypercalcemia

- Symptoms
  - Nausea, emesis, polyuria/ polydipsia, confusion/ somnolence, psychosis, pain, hyporeflexia, constipation, AKI, bradycardia, ECG changes
    - Prolonged PR, short QT, wide T



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Hypercalcemia

- Treatment
  - Treat underlying malignancy
  - Hydration (~3-7 liters in 24-36hrs)
  - Hydration (Goal UOP >75cc/hr)
  - Hydration
  - Diuretics (furosemide or other loop)
  - Bisphosphonate
  - Dialysis if necessary
  - Calcitonin can help slightly for a few days
    - NOT nasal; must be SQ

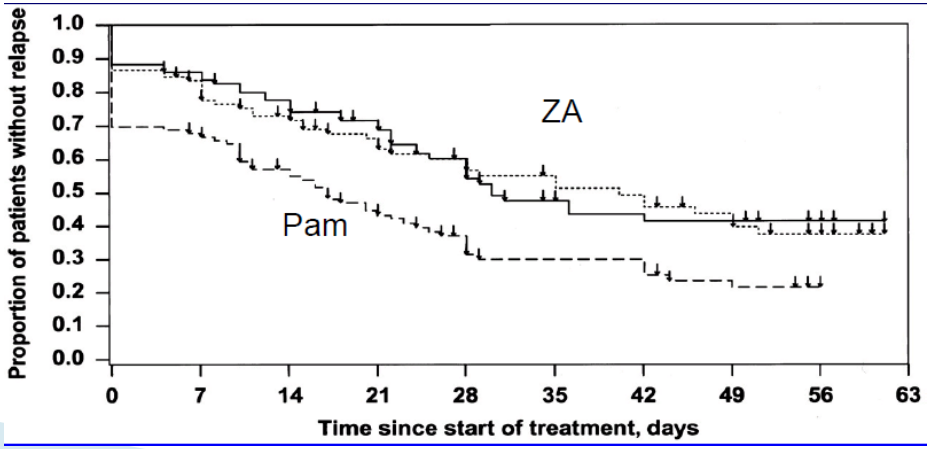
Algorithm for management of hypercalcemia

Calcium level	Symptoms	Therapy
<12 mg/dl (3.0 mM)	None	Observation, or hydration followed by observation
<12 mg/dl (3.0 mM)	Present	Hydration, Bisphosphonate
12-14 mg/dl (3.0-3.5)	Present	Hydration, Bisphosphonate
>14 (>3.5)	Present	Hydration, Bisphosphonate
>14 (3.5)	Severe	Hydration, loop diuretics, calcitonin, bisphosphonate Alternatives; plicamycin, gallium nitrate, prednisone phosphate, dialysis

Bisphosphonates

- With first infusion, can cause ‘acute phase’ symptoms: fever, nausea, pain
  - Usually does not recur with later infusions
- Zoledronic acid 4mg or Pamidronate 90mg
  - May cause hypocalcemia in vit D deficiency
  - Rarely osteonecrosis of the jaw
  - Onset of benefit in 24-48hrs
  - Duration of effect 30-40 days
  - If CrCl <30,
    use pamidronate

JCO 2001. 19:558



- Hydration
- Bisphosphonates if symptomatic
- Identify cause (History, PTH, PTHrp, 1,25 VitD)
- Consider furosemide, calcitonin, HD