Palliative Care Emergencies

Great Lakes Palliative Care Conference

Katherine Recka, MD, Sarah Nickoloff, MD, and Samantha Wojnowiak, APNP

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knowledge changing life

MEDICAL COLLEGE OF WISCONSIN

Who’s in the Audience?

Objectives

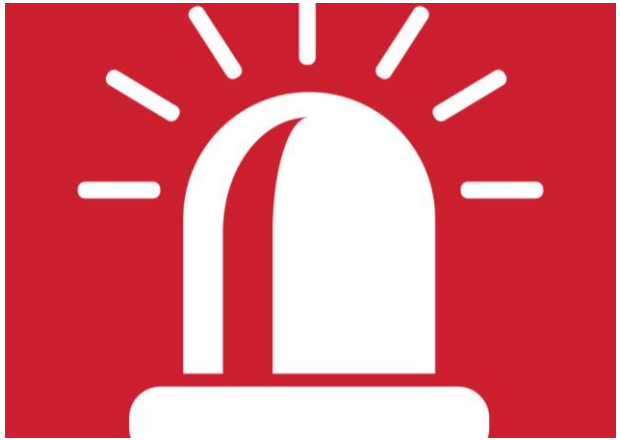
- Define emergencies
- Understand principles of response
- Learn how to recognize and treat specific Palliative Care emergencies

What is a Palliative Care emergency?

- A sudden, urgent, usually unexpected situation or condition during which the life and/or quality of life of a patient with an incurable disease is threatened.
- Requires immediate action and seeing it through.
- Can it be prevented?

What do you consider to be a Palliative Care Emergency?

Palliative Care Emergencies



- Bleeding
- Superior vena cava syndrome
- Seizures
- Spinal Cord Compression
- Pain Crisis
- Hyperalgesia/opioid toxicity
- Acute dyspnea
- Agitation
- Intractable cough
- Choking
- Stridor
- Hypercalcemia
- Obstructive nephropathy
- Fracture
- Tamponade
- Acute bowel obstruction

Principles of Emergency Response

- Mitigation: risk assessment to identify critical needs
- Preparedness: establish and maintain crisis action plan
- Response: implement crisis action plan
- Recovery: return to “normal”

Principles of Palliative Emergency Response

- Mitigation
  - Assess patient and family
    - Clinical status/disease process
    - Psychosocial needs
  - Anticipate possible emergencies
- Preparedness
  - Plan for potential emergencies
  - Educate patient and family about possible emergencies
    - How to identify
    - How to get help
    - What can and will be done to respond and treat the underlying cause

Principles of Palliative Emergency Response

- Response
  - Clear communication with patient and family
  - Remain calm
  - Determine cause of emergency
  - Enact treatment/plans for emergency
  - Ask for help if needed
- Recovery
  - Support patient
  - Support family
  - Care for yourself

Resources in Emergencies

- Palliative
  - Inpatient
  - Outpatient
- Hospice
  - Routine Home Care
  - Inpatient Respite Care
  - General Inpatient Care
  - Continuous Home Care

Palliative Resources

- Inpatient
  - Efficient
  - $$$
  - Ethics: what SHOULD we do vs what can we do
- Outpatient
  - Inefficient
  - Ineffective?

Hospice Resources: Home

- Routine Home Care
- Continuous Home Care
  - Crisis care requiring continuous nursing (**>50% RN or LPN**) to achieve symptom relief
  - Minimum/aggregate 8 hr during 24hr period
  - Begins and ends at midnight
  - Can be supplemented with hospice aides

Limits to Continuous Home Care

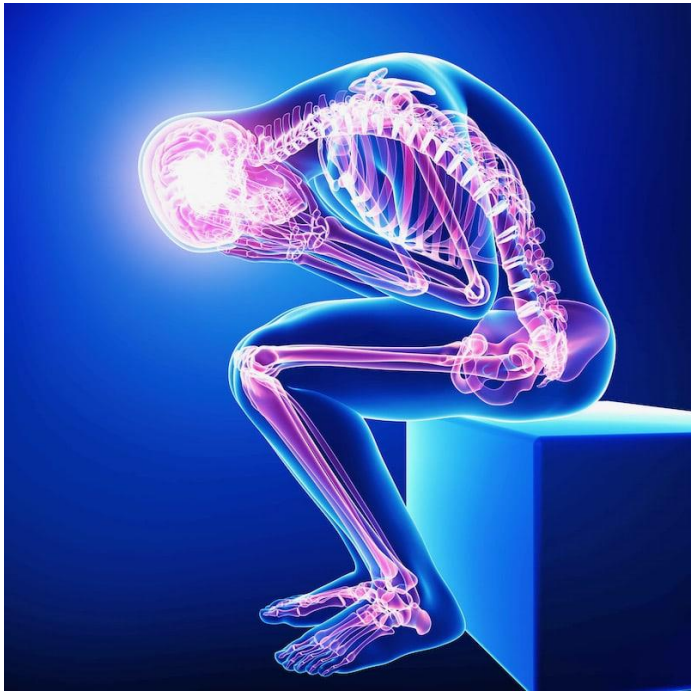
- Mainly related to nursing requirement
- Nursing is a core hospice service, so there are strict rules about contracting with RNs and LPNs solely for CHC
- More complex rules since COVID covered by CMS Extraordinary Circumstance
- Confusing time tracking: need to meet 8 hours, >50% by RN or LPN, from MN to MN
- **Bottom line: defer to hospice compliance officer/dept**

Hospice resources: GIP vs Respite

- Respite
  - Contracted hospital, hospice IPU, or LTC
  - Once per cert period
  - Up to 5 days consecutively
- General Inpatient: GIP
  - Pain or symptom management that **CANNOT** be provided in any other setting
  - Must have registered nursing available 24hr a day

Emergencies: Symptoms

Pain Crisis



Pain Crisis: Definition

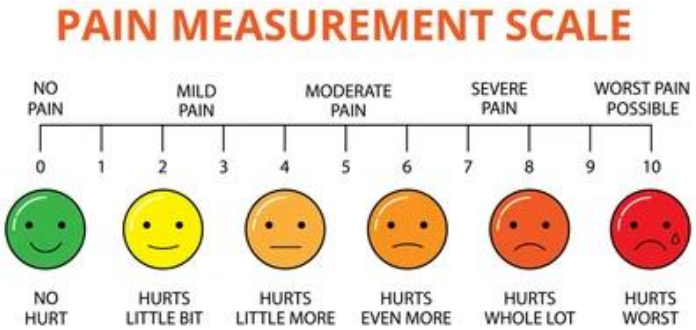
- Severe, uncontrolled pain
- Causing patient, family, or both severe distress
- May be acute onset or may have progressed gradually to intolerable pain
- Different from “breakthrough pain”
- Requires immediate intervention

Pain Crisis

- Most often due to cancer
  - Rupture or hemorrhage of HCC
  - Pathologic fractures from bone metastases
  - Obstruction or perforation of hollow viscus
- Other causes
  - Sickle cell
  - Infections
    - Herpes zoster
  - Thrombotic events (may also be related to cancer)
    - DVT
    - SVC obstruction

Pain Crisis: Assessment

- Exam, labs, imaging
- Cancer history
  - Extent of disease
  - Recent treatments
  - Recent interventions
- Pain characteristics
  - When it started
  - Location/distribution (e.g., well localized vs diffuse)
  - Intensity (0-10 scale, VAS, etc.)
  - Quality (burning, stabbing, sharp, cramping, etc.)
  - Aggravating/alleviating factors
  - Analgesic history (pharmacologic AND non-pharmacologic)



What Type of Pain?

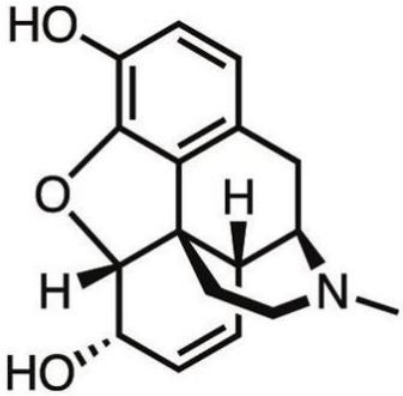
- Somatic
  - Aching, deep, dull, gnawing
  - Well localized (patients can often point to the area)
  - Example: bony mets
- Visceral
  - Cramping, squeezing, pressure
  - Referred (ACS, gallstone), colicky (obstruction), diffuse (peritonitis)
- Neuropathic
  - Burning, shooting, stabbing, tingling, hyperalgesia
  - Radicular (zoster, sciatica), stocking/glove (DM or chemotherapy neuropathy)

Pain Crisis: Management

- Rapid titration of short-acting opioids
  - +/- adjuvant therapies or co-analgesics
- Frequent, ongoing assessments
  - Pain, distress, side effects
- Manage both physical pain and psychosocial distress
- Consultation with other services
  - Interventional Pain, Acute Pain Medicine, Anesthesia, IR, MH, etc.
- Requires hospital admission in most cases

Pain Crisis: Opioids

- Opioid selection
  - Based on analgesic history, pain severity, type of pain
  - Consider medical comorbidities (e.g., avoid morphine in patient with renal failure)
- Route
  - Oral, IV, subcutaneous, transdermal, transmucosal, rectal
  - Epidural or intrathecal with anesthesia/acute pain service consultation
- Escalation and rotation
- Adverse effects
  - Nausea, vomiting, sedation, delirium, respiratory depression—tolerance may develop
  - Constipation—tolerance does not develop



Pain Crisis: Opioid Escalation

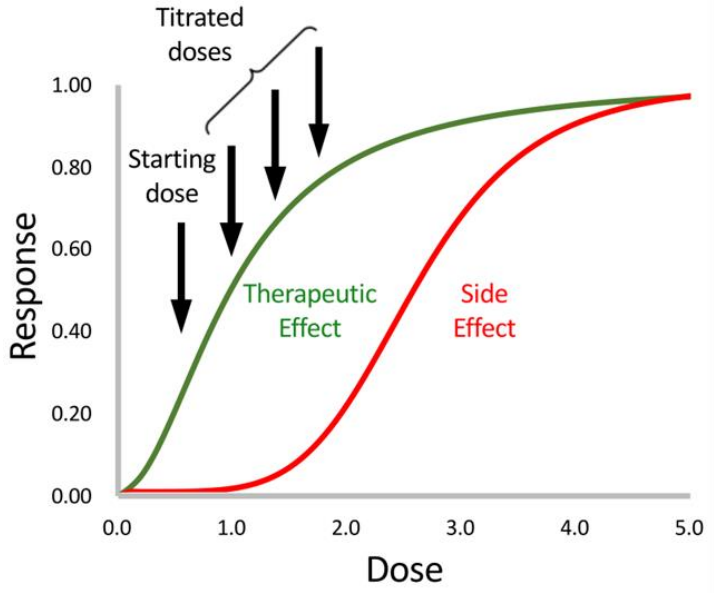
- Rapid titration of short-acting opioids
- Initial short-acting dose:
  - Currently taking opioids: 10-20% of prior 24h opioid dose
  - Not taking opioids: start with lowest dose of appropriate opioid
  - Consider initiation of co-analgesics
  - Acetaminophen
  - NSAIDs (musculoskeletal pain, inflammation)
  - Anticonvulsants (neuropathic pain)
  - Tricyclic antidepressants, SNRI's (neuropathic pain)
  - Muscle relaxants (muscle spasm)
  - Corticosteroids (inflammation, nerve compression)

Pain Crisis: Opioid Escalation

- Dose escalate based on starting dose and severity of pain
  - Mild pain: increase by 25%
  - Moderate pain: increase by 25-50%
  - Severe pain: increase by 50-100%
- Dose escalation timing
  - IV: every 30-60 min
  - Short-acting oral: every 1-2 hours
  - Long-acting oral: every 24 hours
  - Transdermal: every 3 days

Pain Crisis: Opioid Rotation

Consider if adverse effects or inadequate relief from current opioid



Oxycodone

- Well tolerated, effective, semisynthetic opioid
- Undergoes first pass metabolism in liver to oxymorphone (active metabolite)
  - CYP3A and CYP2D6
- Patients with heterozygous cytochromes may be partial metabolizers
- May result in inadequate pain control due to lower concentrations of oxymorphone
- Consider rotation early on if ineffective

Pain Crisis: Opioid Rotation Steps

- Stop current opioid
- Calculate total dose of current opioid used in previous 24h
  - Scheduled and PRN
- Calculate dose of new opioid using dose conversion table
- Calculate for incomplete cross tolerance
  - Decrease dose of new opioid by 25-50%
- Calculate breakthrough dose
  - 10-20% of new dose Q1h PRN

Opioid Dose Conversion Table

Opioid	Oral Dose (PO)	Parenteral Dose (IV/SC)	Conversion Factor: Parenteral to Oral Opioid	Conversion Factor: Oral Opioid to Oral Morphine
Morphine	30 mg	12 mg	2.5	1
Oxycodone	20 mg	N/A	N/A	1.5
Hydrocodone	30 mg	N/A	N/A	1
Oxymorphone	10 mg	1 mg	10	3
Hydromorphone	7.5 mg	3 mg	2.5	4
Fentanyl [1]	N/A	120 mcg	N/A	Should be managed by clinicians experienced in pain management
Methadone and buprenorphine should only be initiated and managed by clinicians experienced in pain management. Consider consult to pain specialists if needed.				

Fentanyl

- 80-100 times more potent than morphine
- Transdermal formulation has a long half-life (17h)
  - Not recommended for use in opioid naïve patients
  - Use only in patients with stable opioid requirements (cannot titrate rapidly)
  - Wait at least 24h to evaluate maximum analgesic effect
  - Titrate no more frequently than every 3 days
- In general:
  - 1mg IV morphine or 2.5mg PO morphine = 10 mcg IV fentanyl
  - 10mg IV morphine or 25mg PO morphine = 12mcg transdermal fentanyl

Methadone

- Can be very effective in patients whose pain is uncontrolled with other opioids
  - NMDA receptor antagonist
  - Inhibits uptake of serotonin and norepinephrine
- Half-life is highly variable
  - 17 to 50 hours (up to 190 hours in rare cases!)
- Equianalgesic ratio dose depends on patient's degree of tolerance to prior opioid
  - Can vary over 10-fold from patient to patient
- Use with caution and only in consultation with palliative or pain specialist

Pain Crisis: Sedation

- Temporary therapy (Respite Sedation)
  - While other pain relief measures are being explored
- Destination therapy (Palliative Sedation)
  - Is it acceptable to be sedated if that is the only way to achieve adequate pain control?
  - Dying patients only
  - Patient is experiencing unendurable suffering that is not amenable to any standard palliative treatment measures

Principle of Double Effect

- Applied to situations in which it is impossible to avoid all harmful actions
  - Helps clinicians, patients, families decide whether a potentially harmful action is ethically indicated to achieve a desired outcome

Principle of Double Effect

- Four basic components
  - Nature of the act must be good or morally neutral
    - Not prohibited or intrinsically wrong
  - Intent of the provider must be good
    - Good effect must be intended and therefore bad effect may be tolerated or permitted
  - Distinction must be made between means and effect, and ***death must not be the means to the good effect***
    - Good effect must be produced directly by the action, not by the bad effect
  - Good effect must exceed or balance the bad effect

Opioid-Induced Neurotoxicity

Opioid-Induced Neurotoxicity (OIN): Definition

- Underdiagnosed yet distressing and potentially deadly syndrome in patients receiving opioids
- Consists of a constellation of neuropsychiatric symptoms:
  - Delirium
  - Drowsiness
  - Hallucinations
  - Myoclonus
  - Hyperalgesia
  - Allodynia
  - Seizures

OIN: How Often is it Happening?

- Lim, et al., 2018
  - 390 inpatient palliative care patients
  - Assessed for symptoms of OIN
  - 15% of patients developed OIN
  - Most common symptom was delirium (47%)
  - High MEDD significantly associated with OIN
  - OIN was not significantly associated with shorter overall survival

OIN: Clinical Case

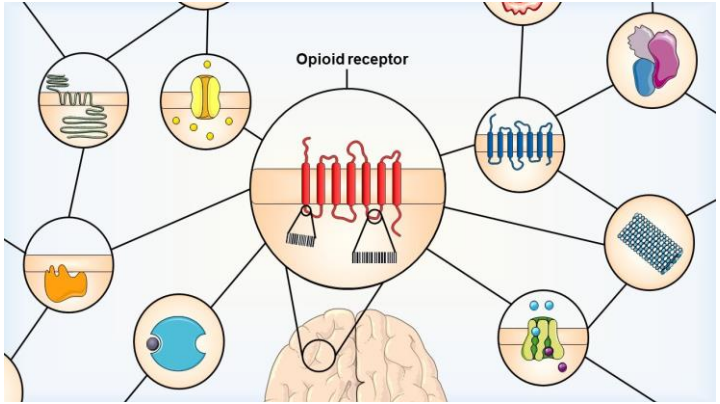
- 57 yo M with prostate cancer presented with low back and R femur pain
- Hydromorphone PCA initiated
  - Bolus 0.4mg
  - 10 min lockout
  - No basal rate
- Home methadone dose (150mg po bid) continued
- MRI revealed diffuse bony metastases and pathologic R femoral neck fracture
- He underwent radiation to spine and R THA
- Pain improved

OIN: Clinical Case

- POD 6: pt reported increasing pain “all over”
- Hydromorphone PCA had been titrated over 48h to 20mg bolus, 10 min lockout, 9mg/hr basal
- Pain continued to worsen (hyperalgesia)
- Patient developed additional symptoms
  - Delirium
  - Visual hallucinations
  - Allodynia
  - Myoclonus (16 beats/minute) in bilateral arms

OIN: Causes

- Likely multifactorial
  - Excess opioid metabolites
    - 3-glucuronide metabolites (no analgesic effect, accumulate rapidly)
  - Endocytosis of opioid receptors
  - Stimulation of NMDA receptors
- Opioids with active metabolites most common culprits
  - Morphine, codeine, meperidine, oxycodone, hydrocodone
- Fentanyl and methadone less likely to cause OIN
  - No active metabolites
  - Methadone is partial NMDA receptor antagonist



OIN: Risk Factors

- Physiologic
  - Dehydration, renal failure, infections
- Treatment-related
  - Concurrent psychoactive meds, long-standing or high dose opioid use, medications that increase plasma concentration of opioids, rapid opioid dose escalation
- Comorbidities
  - Advanced age, baseline cognitive impairment, substance abuse, chronic pain, MH conditions

OIN: Evaluation

- Labs
- Physical exam
  - Presence of OIN symptoms
- Medication review
- Thorough review of opioid type, dosages, and dose changes
  - At least 2 opioid dose escalations

OIN: Treatment

- If pain controlled, reduce opioid dose by 50-75%
- If pain uncontrolled, rotate to structurally dissimilar opioid at 25-50% MEDD
- Treat exacerbating factors
  - IV hydration
- Initiate benzodiazepines to raise seizure threshold
- Consider low-dose ketamine as adjuvant to reduce opioid dose
  - IV infusion 0.5mg/kg over 40 min
- Naloxone DOES NOT treat OIN and should not be used
  - May provoke a pain crisis or seizure

OIN Clinical Case

- Labs unremarkable
- Medications and opioid doses and escalation reviewed
- PCA stopped for 90 minutes
- Restarted at 50% prior bolus dose (10mg) and no basal
- Methadone continued at home dose
- Lorazepam 1mg q4h scheduled x48h
- Pain improved and symptoms resolved within 48h

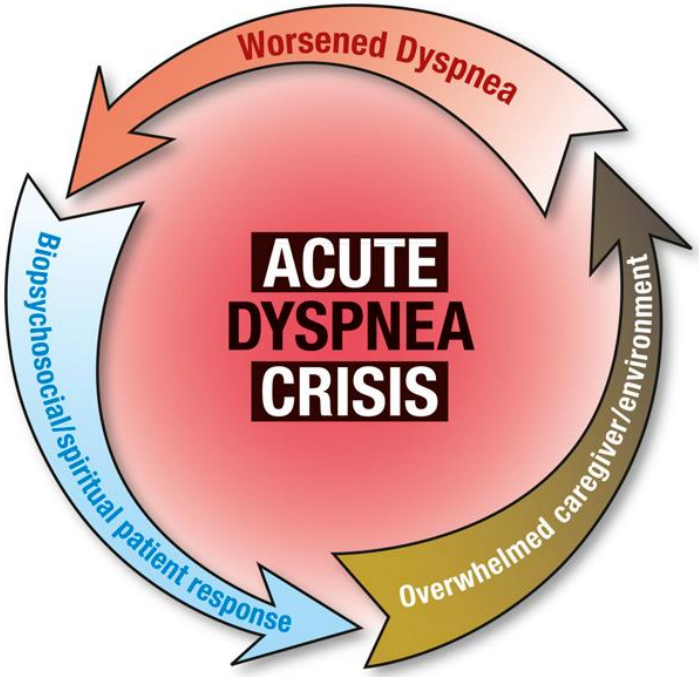
Dyspnea Crisis

Dyspnea Crisis: Definition

- Sudden, sustained and severe breathing discomfort at rest
- Occurs in patients with advanced, life-limiting illness
  - Intubation and mechanical ventilation often not in line with goals/preferences
- Unresponsive to immediate treatment efforts
- Overwhelms patient and caregivers' ability to achieve symptom relief

Dyspnea Crisis

- Commonly occurs in the home or care facility
  - Patient with acute worsening of dyspnea and heightened psychosocial response
  - Unprepared or overwhelmed caregivers
  - Advanced medical resources are not available



Dyspnea: Prevalence in Advanced Disease

Population	Prevalence of dyspnea (%)	References
Cancer (mixed)	10 to 70	Solano 2006[1]
AIDS	11 to 62	Solano 2006[1]
Lung cancer (primary or metastatic)	62 to 95	Currow 2010[2]
Heart disease	60 to 88	Solano 2006[1]
COPD	90 to 95	Solano 2006[1]
Renal disease	11 to 62	Solano 2006[1]
Stroke	37	Addington-Hall 1995[3]
ALS	47 to 50	O'Brien 1992[4], Hicks 1993[5]
Dementia	70	Lloyd-Williams 1996[6]
No cardiorespiratory disease (ie, no primary or secondary lung malignancy, cardiac failure, or respiratory disease)	45 to 81	Currow 2010[2]

AIDS: acquired immunodeficiency syndrome; COPD: chronic obstructive pulmonary disease; ALS: amyotrophic lateral sclerosis.

UpToDate, Inc., 2022

Dyspnea Crisis Clinical Case

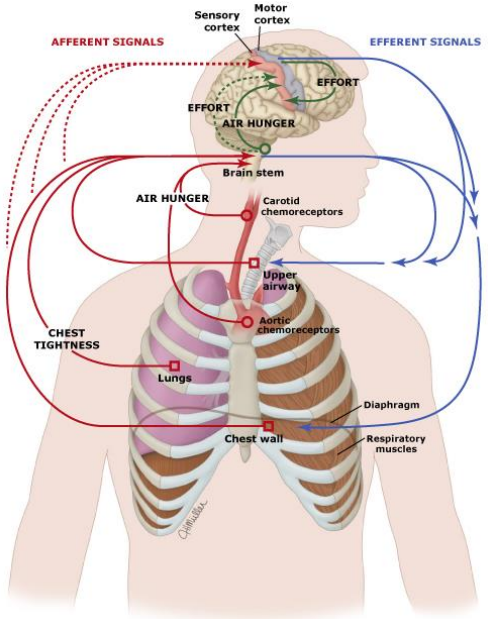
- 73 yo M with h/o advanced COPD, atypical MAC, PE, multiple vascular issues, admitted from home with worsening dyspnea
- Found to have spontaneous L pneumothorax
  - Pigtail catheter place, removed 2d later after ptx resolved
- Symptoms improved, but did not return to baseline
  - Unable to ambulate or perform ADLs without desaturation and worsening dyspnea
- Palliative consulted on HD #14 for goals of care and symptom management
- Goals remained life-prolonging after initial visit

Dyspnea Crisis Clinical Case

- HD #19, Palliative at bedside and pt developed acute worsening of dyspnea
- 02 saturation in low 80s on 8L 02
  - Improved to low 90s on 16L
- Life prolonging goals >> labs, imaging, EKG
- Imaging showed large mucus plugs bilaterally
- Chest PT, nebulizers and Vapotherm initiated (40 LPM, 65% FiO2)
- Symptoms improved somewhat
  - Patient and family wished to continue treatments for 24h to evaluate effectiveness

Dyspnea Crisis: Assessment Goals

- Understand intensity and impact of symptoms
  - History, descriptors, impact on activity level
  - Anxiety, fear, panic
- Diagnose potentially reversible contributing factors
  - Airway obstruction
  - Bronchoconstriction
  - Pneumonia
  - Heart failure
  - Pleural effusion
  - Pneumothorax
  - Pulmonary embolism
- Evaluate and monitor response to interventions



Dyspnea Crisis: Management

- Treat underlying disease or etiology, if aligns with goals/values
- Reposition
  - Elevate head of bed, sit upright, “tripod” position
- Oxygen
  - May provide some relief in hypoxemic patients, unlikely to help if not hypoxemic
  - Increasing air movement with a fan or open window often as effective as oxygen
- Opioids
  - Drug of choice
- Anxiolytics
  - Benzodiazepines helpful if anxiety present and contributing

Dyspnea Crisis in Dying Patients

- Noninvasive positive pressure ventilation
  - Limited data on efficacy
  - May reduce work of breathing
  - May help maintain wakefulness (reduce need for opioids, improve hypercapnia)
  - Prolong life for short-term goals (e.g., allow time for family to arrive to say goodbye)
- Palliative sedation
  - Similar approach as pain crisis
  - Only for severe distress that cannot be relieved with standard measures
- Don’t forget to stop parenteral fluids

Dyspnea Crisis: Opioids

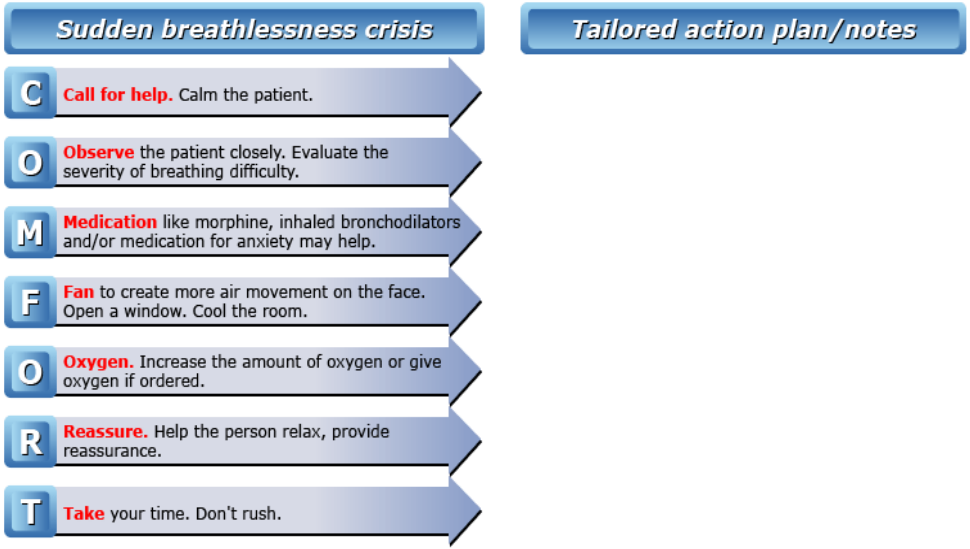
- Parenteral route is fastest and most effective in crisis
- Doses needed to achieve control of dyspnea crisis are often lower than pain crisis
- Opioid naïve:
  - Start with lowest dose and titrate up
  - Dose escalate every 30-60 minutes for IV, 1-2 hours for oral
- Inpatient setting:
  - Consider continuous infusion or PCA once opioid requirement established
- Nebulized morphine
  - No evidence to support use over IV morphine

Dyspnea Crisis Clinical Case

- HD #20, pt's symptoms continuing to worsen despite maximum supportive therapy
- Patient and family decide to transition to comfort
- Morphine initiated at 2mg IV q1h prn, lorazepam 1mg IV q4h prn
- Morphine drip started at 2mg/hr after 3 consecutive hours of 2mg/hr dosing
  - 2mg IV q1h prn continued
- Pt died about 8 hours after drip initiated
  - Drip at 6mg/hr at time of death
  - He was comfortable

Dyspnea Crisis: Anticipatory Guidance

- Prepare the patient and family
- Provide education about symptoms and interventions
- Develop an action plan
  - May change as disease progresses or goals change



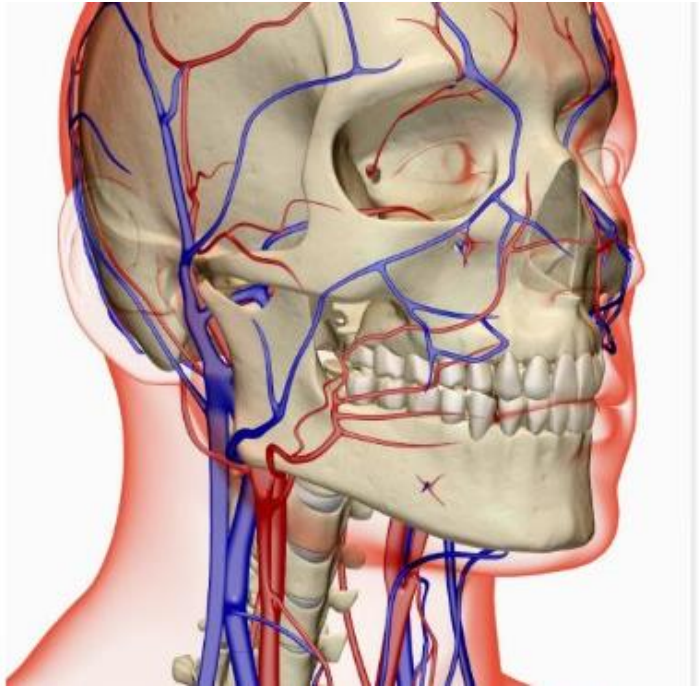
American Thoracic Society, 2015

Emergencies: Heme and Onc

Palliative emergencies-Heme

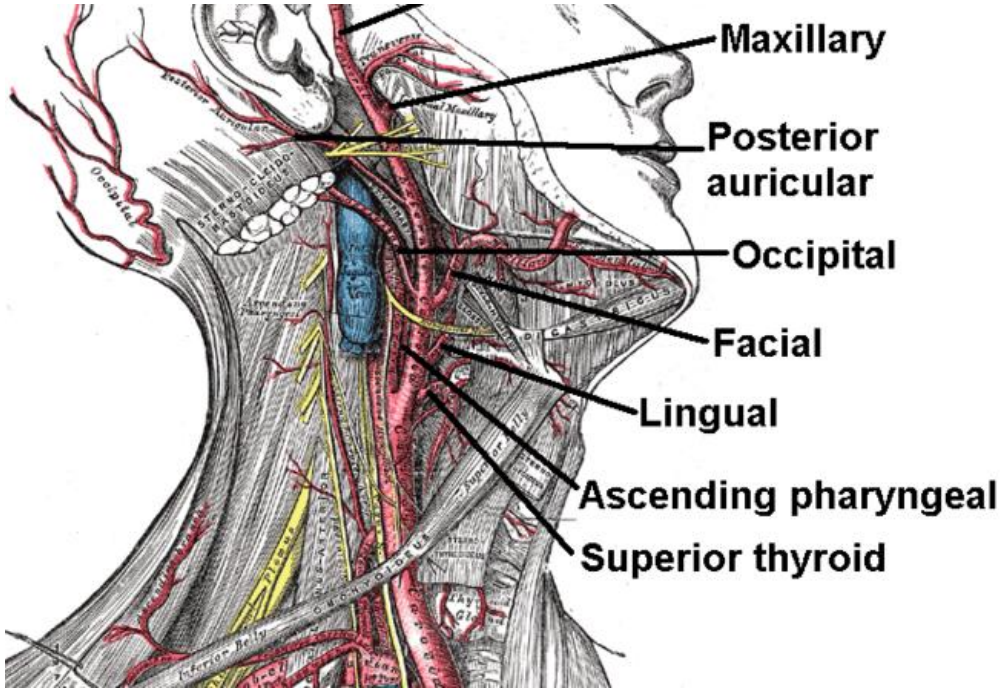
- Uncontrolled bleeding
- SVC
- Hypercalcemia

Palliative Emergencies-Bleeding Case 1



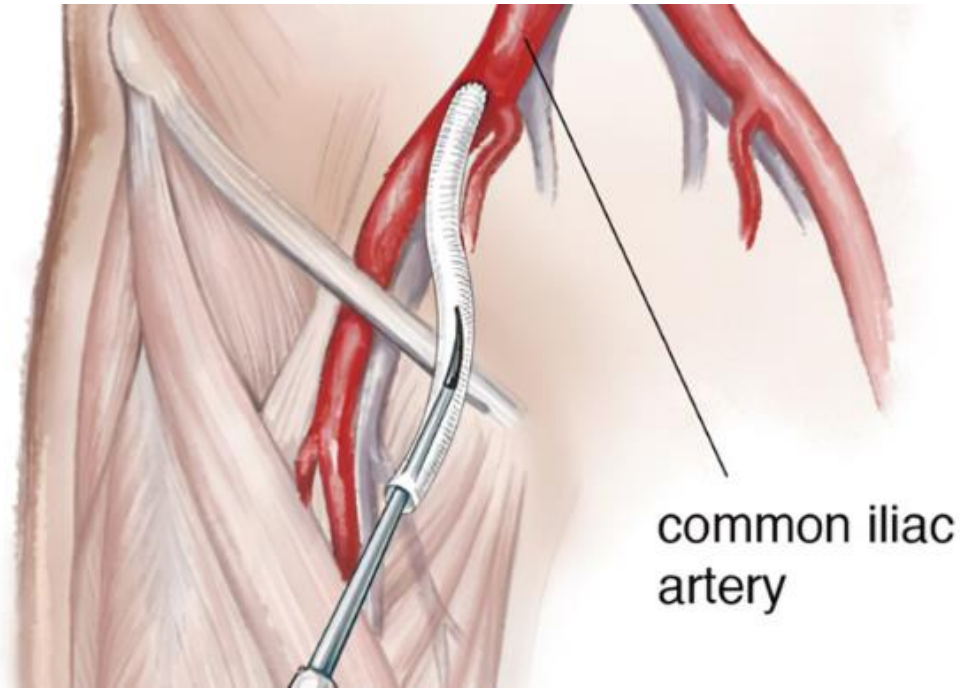
- Mr. M1: 68 yo with >30y h/o H&N ca
- Currently on a study drug
- Admitted after a fall, intractable pain, dx with osteo
- Sudden onset large volume oral bleeding vs epistaxis
- **What do you do?!**

Case 1- Mr. M1



- Oral packing by ENT with oxymetazoline soaked gauze
- Neurointerventional: angio with embolization of left pharyngeal a and R lingual a
- 3 days later found in a large pool of blood with no HR or BP

Bleeding-Case 2-Mr. M2



- 85 yo with severe PVD, admitted to our IPU with b/l gangrene
- Found to have left inguinal wound
- Per Vascular-L fem endarterectomy graft was exposed and infected
- **What to do?**

Case 2-Mr. M2

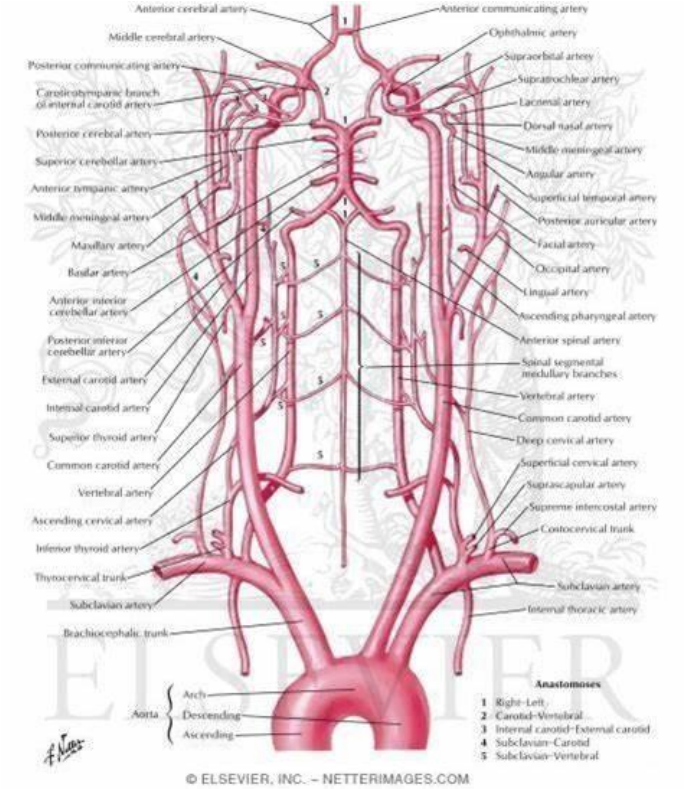
- Vascular recs…dark towels

Generalized Bleeding

- Heme malignancies
- Major bleeding in up to 30% patients with advanced hematologic malignancies
- Higher in thrombocytopenia <20, acute blast crisis or AML
- Other causes of thrombocytopenia
  - Drugs
    - Anticoagulation/antiplt
    - Chemo
    - OTCs
    - supplements
  - Immune
  - Liver disease
  - ID

Local bleeding=solid tumor

- Wounds
- Hemoptysis
- H&N
  - Epistaxis
  - carotid
- Gynecological
- GU
- GI
- Retroperitoneal



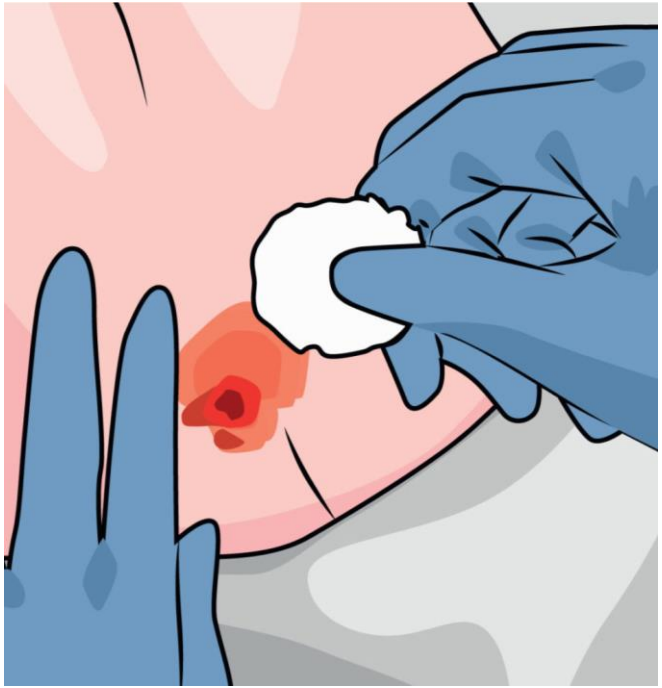
In general

- Review goals and resources
- If you can reach it
  - Apply pressure
  - Topicals
  - GI mucous membranes-sucralfate, octreotide
- Consider systemic medications
  - Reverse underlying cause, Vit K, stop anticoag
  - Tranexamic or aminocaproic acid
- Consider local control with IR vs RT interventions
- Blood products

Localized bleeding wounds

- Most common in breast, head and neck and skin cancer
- Can have significant social, spiritual, existential burden
- Use in combination
  - Dressings/topicals
  - Adequate pain management
  - Systemic Medications

Bleeding wounds: dressings

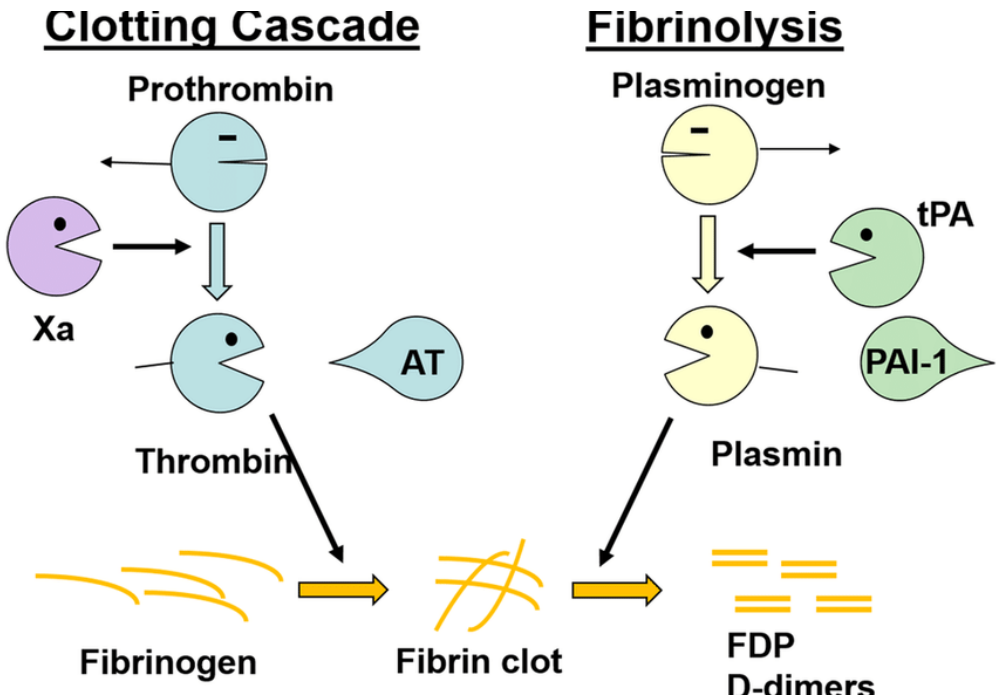


- Top layer: Minimize adherence
  - Protect skin
  - Soft silicone
  - Hydrogel
  - Petroleum jelly gauze
- Second layer: Absorptive/hemostatic
  - Calcium alginate
  - Sucralfate
  - Hydrocolloid

Bleeding: Topicals

- *in order of how realistic in may be to get them*
  - Oxymetazoline (AfrinTM)
  - Aminocaproic acid (AmicarTM)
  - Tranexamic acid-soaks or paste
  - Silver nitrate for smaller wounds
  - Sucralfate paste
  - Topical vasopressin *case reports in non variceal esophageal lesions
  - Thromboplastin powder
  - Mohs paste (ZnOh)
    - Pain is main side effect!

Bleeding: systemic medications



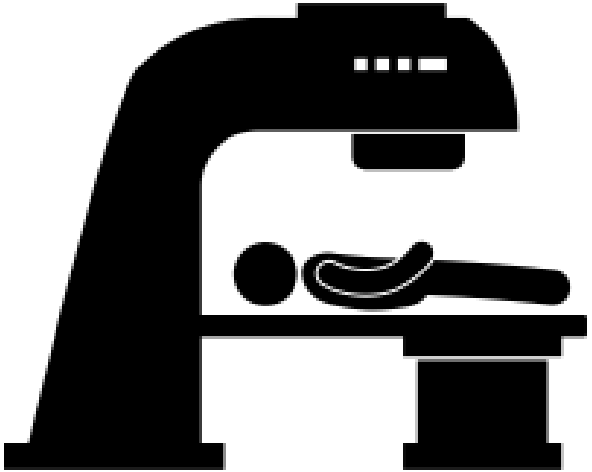
- Oral synthetic antifibrinolytic agents
  - Aminocaproic acid (Amicar)
  - Tranexamic acid
- Main side effects are GI: n/v
- Both come in IV and PO
- Empiric Vit K in liver dx

Bleeding: Blood products?

- More straightforward in palliative (?)
- Complicated on hospice

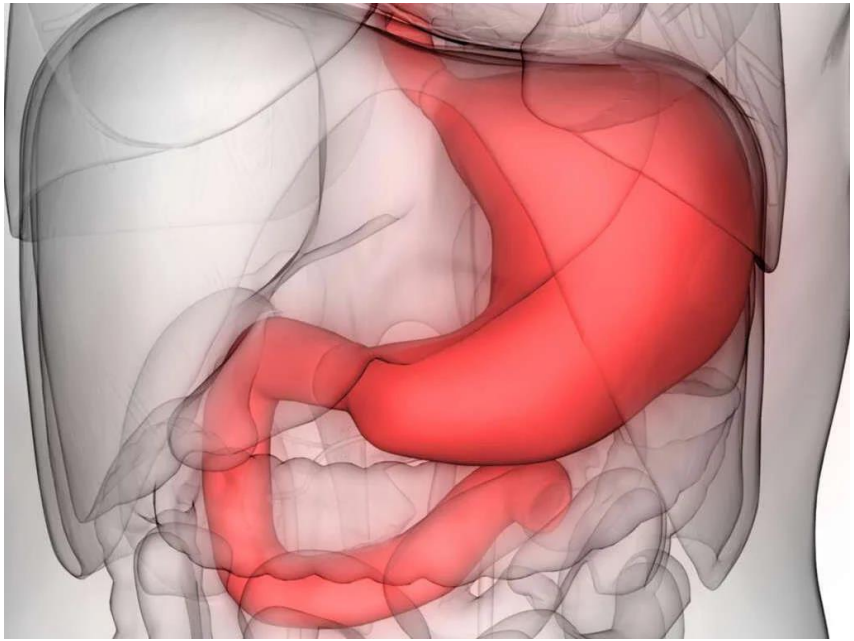
Localized bleeding next steps

- Endoscopy
- IR embolization
- RT

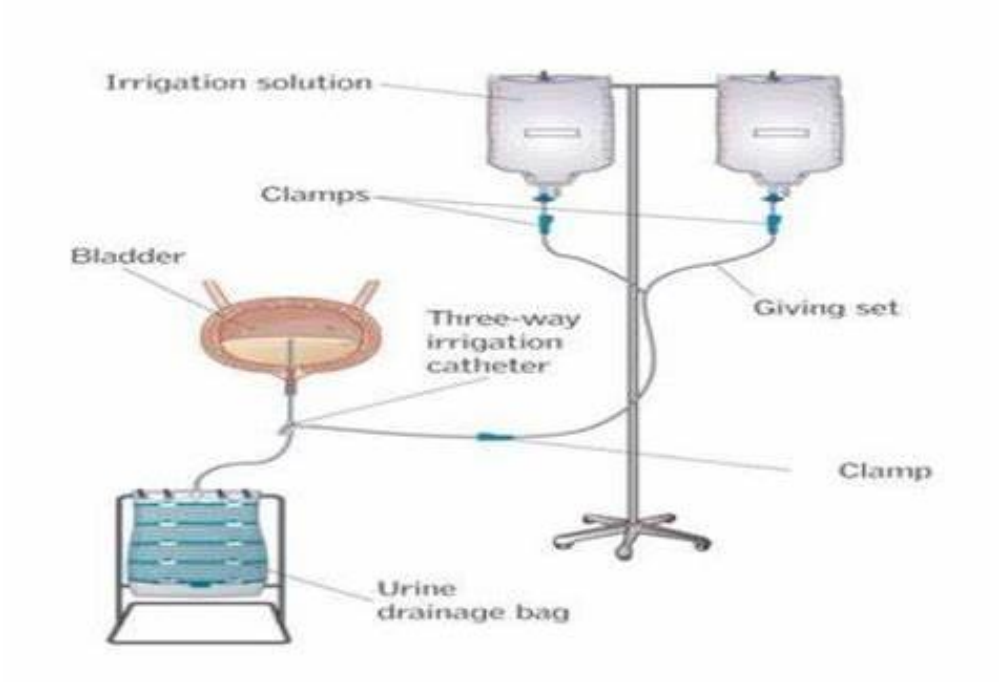


GI bleeds

- Low volume: consider systemic medications
  - Tranexamic acid orally
  - Octreotide sc
  - Sucralfate
  - Acid blockers
- Rectal bleeding
  - topicals
- Large volume: support



Urinary tract/GU bleeds



- Bladder irrigation with tranexamic acid
- Continuous bladder irrigation in urinary retention
- RT
- IR

Bleeds: non pharm basic principles

- Interdisciplinary!
- Minimize trauma
- Wound dressings
- Soft foods, gentle oral care
- Minimize emotional trauma
- Prepare
- Positioning
- Suction at bedside
- Dark sheets

Bleeding: support

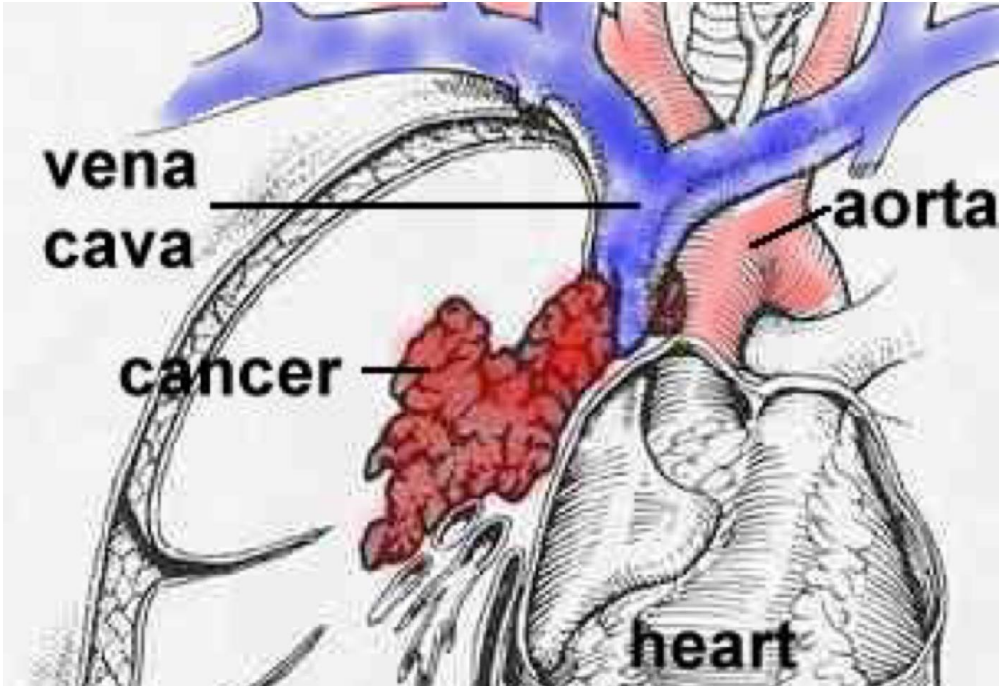
- Bleeding at end of life can be sudden
- Palliative sedation is an option if time and resources
- Need support for family and caregivers

Case 3: Mr. G

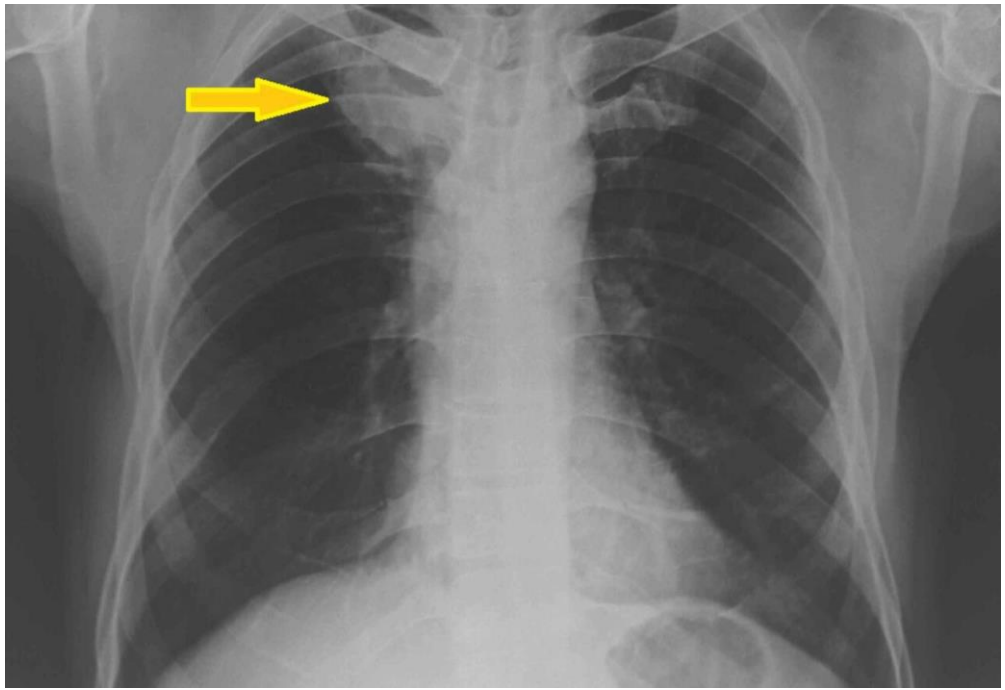
- Mr. S-77 yo with h/o H&N ca and HFpEF enrolled in hospice at time of diagnosis of his metastatic lung cancer
- Functional status is intact and minimal pain-still able to come into clinic
- Increased dyspnea on exertion with cough
- Exam seems normal-no signs of volume overload
- Face seems flushed when he raises his hands
- **What are you worried about?**

SVC

- Pemberton sign=facial plethora with bilateral arm elevation



- Extrinsic compression of SVC via tumor or lymph nodes
- Tumors may not allow collaterals to form
  - Slowly progressive SVC from sclerosis of veins
  - CVL
  - Pacemaker wires
  - Connective tissue dx-fibrosing mediastinitis



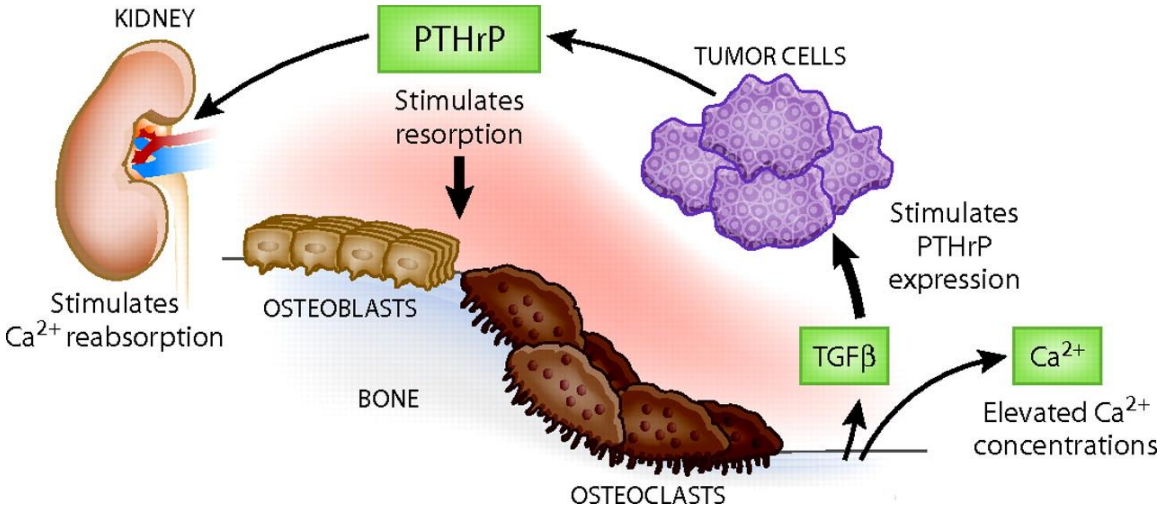
- Little consensus other than considering RT and/or stent
- Steroids may be helpful if RT causes swelling or if it's steroid responsive cancer like lymphoma

Case 4-Mr. S

- Mr. S-complex hx of severe COPD and cirrhosis seen in Palliative clinic
- Inpatient now for delirium
- Chart review: 20lb wt loss last 2 months
- CT consistent with new left pleural effusion and moderate constipation
- Labs: Na 132, Cr 2.7 (baseline wnl), Ca 10.8, albumin 1.8
- **Consult for pain and symptom management**

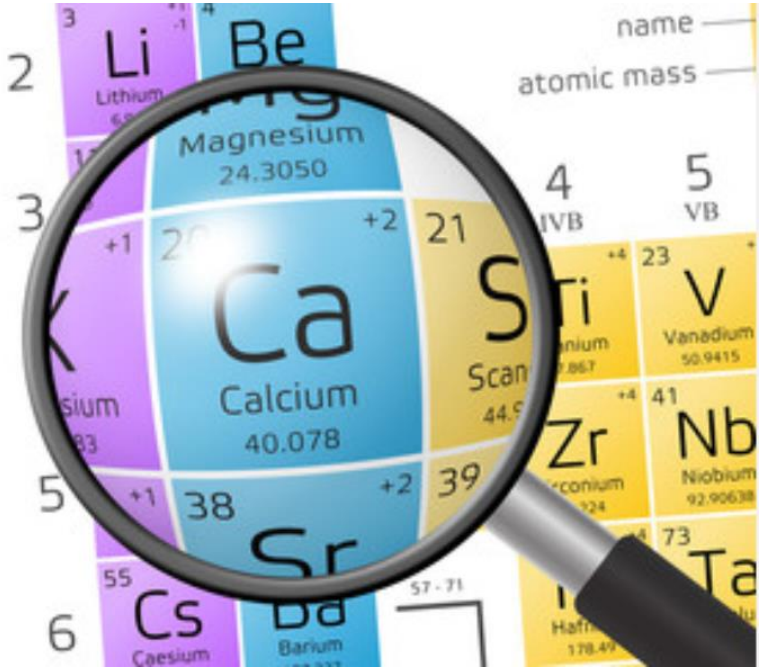
Hypercalcemia of Malignancy

- Stones=Kidney stones
- Bones
  - Pathological fx
  - Bone pain
- Groans
  - Malaise
  - Fatigue
- Thrones
  - Polyuria
  - Polydipsia
- Psychiatric overtones



Hypercalcemia of Malignancy

- Common
  - SCC
  - Renal
  - Bladder
  - Breast
  - Ovarian ca
  - MM
  - Lymphoma
- Poor overall prognosis
- Poor functional status



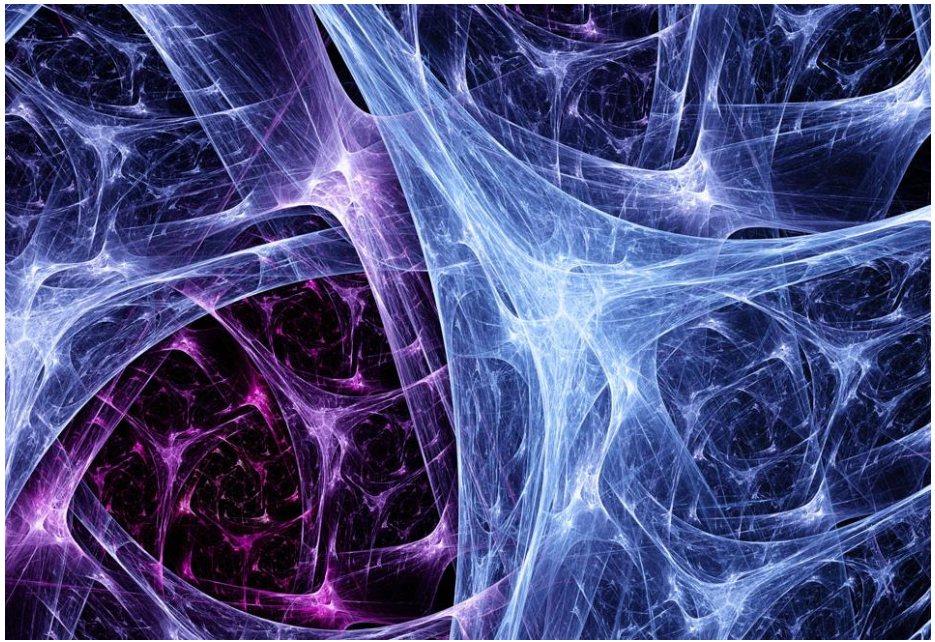
Hypercalcemia-consider treating

- Outpatient
  - Hydration
  - Stop diuretics, supplements, OTC
  - Anticipatory guidance
- Inpatient
  - Bisphosphonates
  - Calcitonin vs denosumab (XgevaTM, monoclonal ab)
  - HD

Emergencies: Neuro

Seizures and Spinal Cord Compression

Seizures



- Distressing for patients and families
  - Both in the moment and with fear of recurrence
- Caused by a structural and/or systemic insult to the brain
- Can occur in about 13% of cases in Palliative Care context.

Tradounsky, 2013

Prevalence

- 25-50% of Palliative patients who develop seizure activity have brain mets.
- Of those with primary brain tumors, 25-40% will present with convulsions at diagnosis. More develop seizures as their disease progresses.

- 70-100% of slow growing brain cancers (such as oligodendroglioma and low grade astrocytoma)
- 10-20% aggressive glioblastoma

Tradounsky, 2013

Causes of Seizure

Structural

- Primary Tumors
- Metastases
- Abscesses
- Reversible Posterior Leukoencephalopathy Syndrome
- Paraneoplastic Limb Encephalitis
- Hemorrhage
- Radiation Necrosis

Systemic

- Hypoxia
- Hypo/Hyperglycemia
- Hypo/Hypernatremia
- Hypo/Hypercalcemia
- Low magnesium level
- Uremia
- Hepatic failure
- Meds such as: Ondansetron, Antipsychotics, & Chemo agents
  - Proconvulsant effect or by lowering seizure threshold

Tradounsky, 2013

Clinical Case

- 78 yo F with L parietal GBM s/p GTR 9/2021
- Initially admitted to OSH with R gaze deviation and R sided/facial twitching.

Workup

- ALWAYS includes
  - Prompt history and physical
  - Review of meds
- Depending on patient/activated HCPOA's goals of care, MAY include:
  - Labs
  - Imaging
  - LP with CSF cytology
  - Infectious workup
  - EEG

Tradounsky, 2013

Keep Patient and Others Safe

- Place patient in prone or lateral position (preferably on flat surface) to avoid aspiration
- Move injurious objects out of the way
  - Remove eyeglasses
- Loosen tight clothing around patient's neck
- **DO NOT** restrain patient
- **DO NOT** put fingers or objects into patient's mouth

Bank and Bazil, 2019

Treatment

TABLE 3. RELEVANT INFORMATION ON COMMON BENZODIAZEPINES FOR REFERENCES[30–33]

Drug name	*Form*	*Dose*	*Action onset (minutes)*	*Peak effect (minutes)*	*Approximate cost (US)*
Clonazepam	ODT	0.125–1 mg tabs	20–40	60–240	$1.30/tab
Lorazepam[a]	Oral	0.5–1 mg tabs	20–30	120	$32–$42/tab
	Buccal	2 mg/mL syrup	20–30	120	$1.60/mL
	Sublingual[b]	0.5–1 mg tabs	60	60	N/A
	Intravenous/subcutaneous[c]	2 mg q3–5 minutes	15–30	60	$0.62–$4.06/mL
Diazepam	Rectal	2.5—20 mg gel	2–10	90	$300–450/dose
	Nasal	5–20 mg spray	<10	90	$330/pack
Midazolam	Nasal	5 mg spray	<10	30	$330/pack
	Buccal	2 mg/mL syrup	10–20	30–120	$0.70–$2.10/mL
	Intramuscular	10 mg once	5–15	15–60	$0.19–$3/mL
	Intravenous/subcutaneous[c]	1–5 mg q5–15 minutes	1–5	3–5	$0.19–$3/mL

[a]When used in an emergency for seizure abortion, 2 mg is a reasonable starting dose. Up to 0.1 mg/kg can be used in frequent dosing for status epilepticus.
[b]Not available in the United States.
[c]Off-label route, to be used when other routes are unavailable in a palliative setting.
ODT, oral disintegrating tablet.

Image and table from Sharma et al., 2021

Status Epilepticus

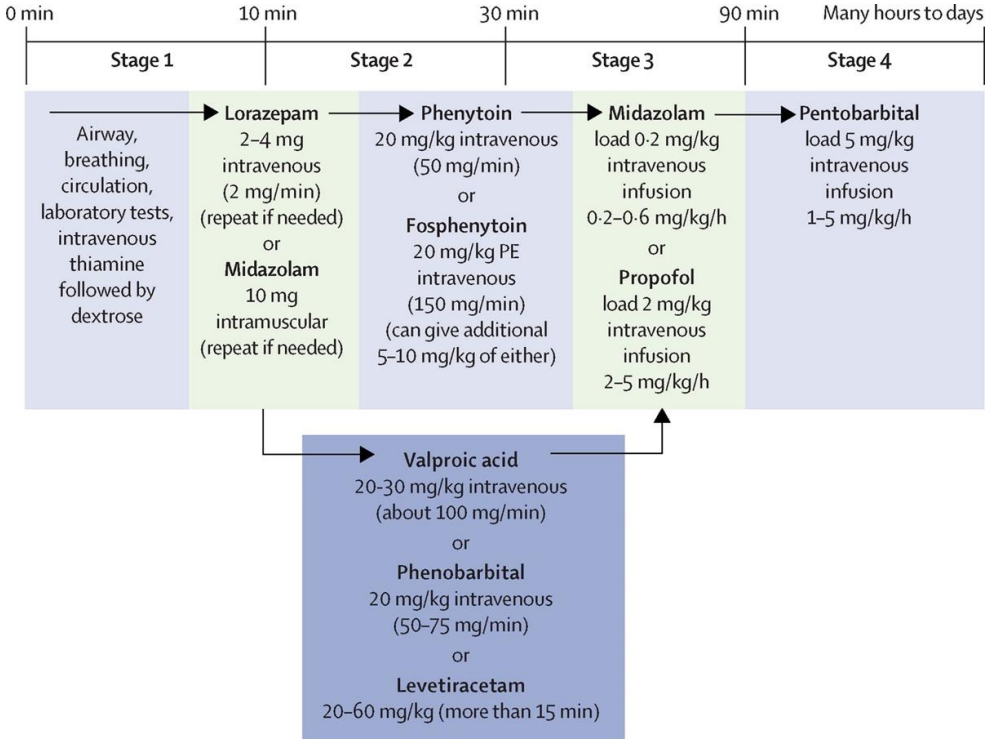


Image and algorithm from Betjemann, 2015

- Defined as:
  - Seizure activity (convulsive or nonconvulsive) for >30 min
  - OR 3 episodes without return of consciousness within 30 min
- HIGH mortality – 20%
- Complications: Acidosis, rhabdomyolysis, & cerebral damage
- Longer episode = greater neuronal injury
  - Pharmacoresistance more likely and anticonvulsants less effective.

Tradounsky, 2013

Clinical Case

- CTH negative for acute intracranial hemorrhage with otherwise expected results.
- Given 2 mg Ativan and loaded with Keppra and fosphenytoin at OSH ED. Transferred to our hospital for further care. Neurosurgery consulted.
- Continuous EEG then ordered – no sign of seizures. Discontinued.
- Keppra increased to 1000 mg BID.

Special Considerations

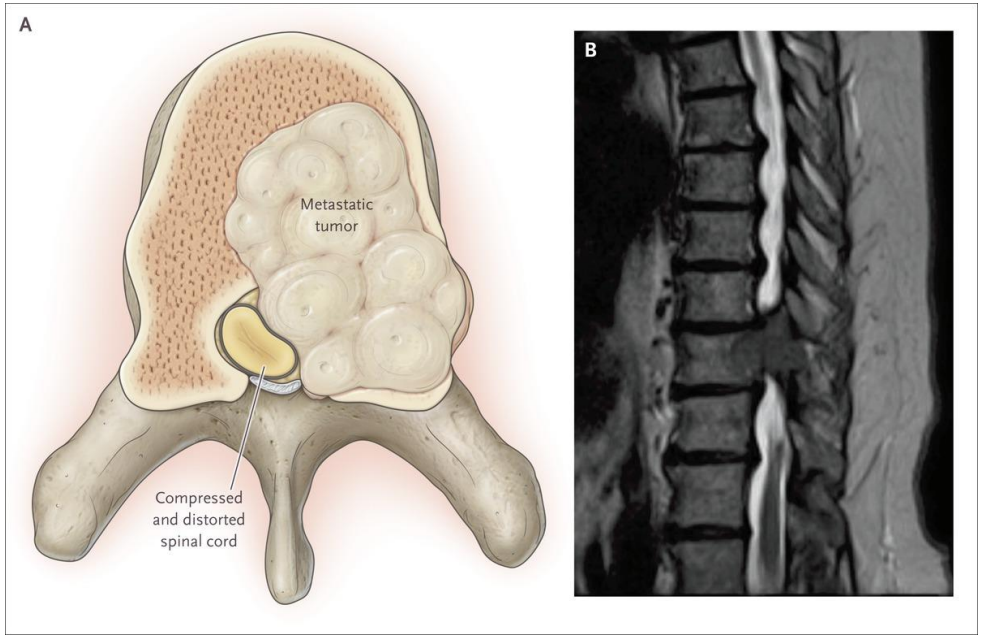
- Discomfort or agitation due to ongoing seizures with need for AEDs may warrant discussion with patient/family re: prioritizing comfort over level of alertness.
- Significant caregiver burden
  - Health psychologist
    - Sleep/Meditation Apps: Headspace, Insight Timer, Calm
  - Resources
    - Example: Imerman Angels Support Community
      - Imermanangels.org

Clinical Case

- Initially poorly interactive - likely post-ictal. Significant improvement in mental status the next day, but continued to have redirectable agitation + sundowning issues. Also with concern for dysphagia + aspiration PNA requiring tube feeding.
- Outpatient regimen had been Temozolomide and Avastin.
  - Episodes of agitation continued IP and wasn't at baseline. Palliative consult to discuss goals of care due to uncertainty re: whether she would recover back to baseline.
    - Caregiver burden (her husband) a concern for their children. Contemplating placement.
    - Would further treatment benefit her? What if seizures recur?
  - Ultimately she did improve, and pursuit of IPR was recommended. Planned to continue w/treatment.

Malignant Spinal Cord Compression

MSCC Definition



- Expanding tumor mass compressing thecal sac, spinal cord, and surrounding vascular structures.
- Compounded by collapse of the vertebral body secondary to lytic bone destruction.

Sodji et al., 2017

Risk Factors

No. risk factors	Occurrence, %
0	4
1	10
2	21
3	23
4	52
5	87

SCC, spinal cord compression.

Talcott et al., 1999

- Retrospective cohort study – MSCC in 258 patients with cancer.
  - Radiographic evidence of vertebral fracture
  - Bony metastasis diagnosed >1 year earlier
  - Increased deep tendon reflexes
  - Incapacity to ambulate
  - Age younger than 60 years

Sodji et al., 2017

Incidence: Estimated Average Lifetime Risks of MSCC in Various Primary Tumors

Primary tumor	Average lifetime risk, %
Prostate, breast, myeloma, kidney	6.2
Nasopharynx, melanoma, lung (SCLC, NSCLC)	2.5
Cervix, lymphoma, uterus	1.6
Head/neck, bladder, colorectal	1.0
Ovary, stomach, leukemia, pancreas	0.4

SCLC, small-cell lung cancer; NSCLC, non–small-cell lung cancer; SCC, spinal cord compression.

Loblaw et al., 2000

Clinical Case

- 64 yo M with metastatic prostate cancer, s/p chemotherapy with new onset BLE weakness.
  - Days prior, had been in his usual state of health – able to independently perform ADLs.
  - Started to notice slightly increased lower back pain over several weeks PTA, but didn't think anything of it.
  - Began to notice BLE weakness at home.

RED FLAGS?

Importance of Early Recognition and Treatment

- Resulting debility and serious impact on QOL if not treated early.
  - Pain
  - Paralysis
  - Sensory loss
- Early treatment is generally well tolerated.

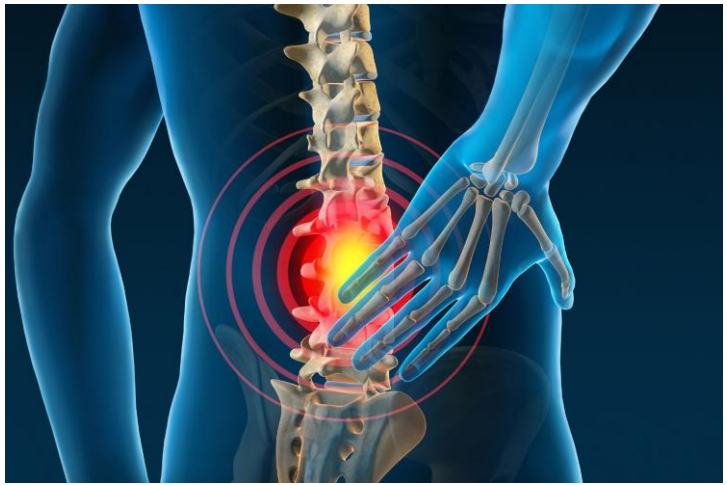
Lawton, et al., 2019

Be Vigilant!

- Malignant spinal cord compression should be strongly considered if patient presents with **new or worsening back pain** prior to development of sensory, motor, bowel, or bladder deficits.

Lawton, et al., 2019

Most Common Symptom: Back Pain



- Reported by 80-95% of patients with MSCC
- Early MSCC pain:
  - Constant
  - Aching
  - Worse at night
  - May be exacerbated by coughing, sneezing, Valsalva maneuvers, and lying flat

Lawton, et al., 2019

Location of MSCC and Possible Pain Descriptors

- Cervical
  - Midscapular pain
- Thoracic
  - Thoracic pain or band-like tightness across chest or upper abdomen
- Lumbosacral
  - Lumbosacral or hip pain
- Radicular burning pain or referred pain may indicate advanced MSCC

Lawton, et al., 2019

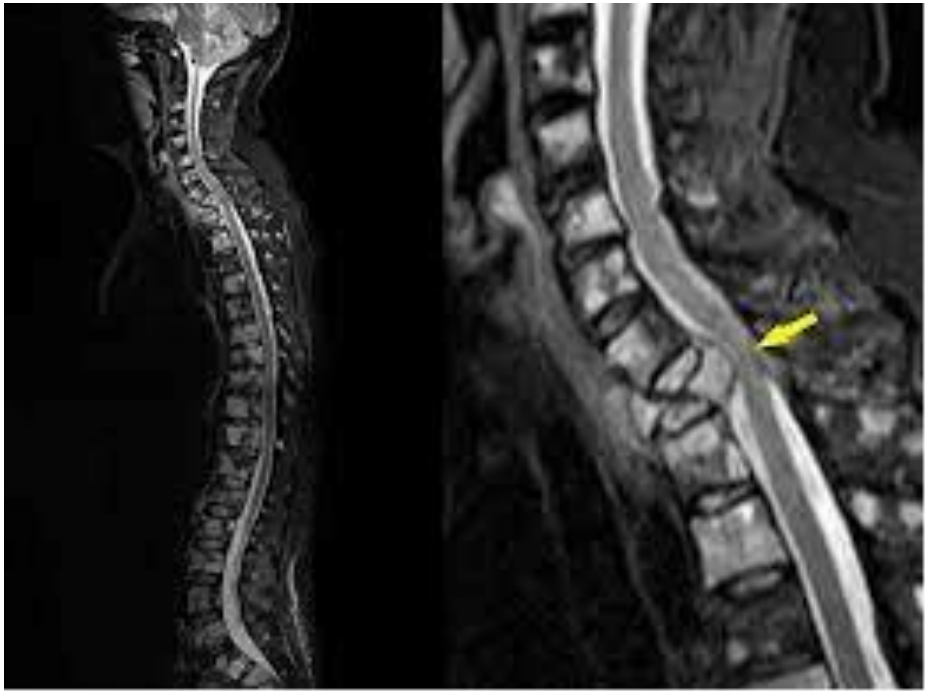
Other Symptoms

- Autonomic deficits (bowel/bladder dysfunction) and worsening motor weakness usually occur later.
  - Associated with worse outcomes following treatment.

Highlights the importance of early intervention

Lawton, et al., 2019

MRI STAT!



- MRI = gold standard for MSCC diagnosis
  - Necessitates imaging of **ENTIRE** spine
    - May have multiple levels of compression
    - Pain, neuro deficits may not correlate with level of spinal lesions on imaging

Lawton, et al., 2019

TABLE 1. Pain Management in Opioid-Naïve Patients With Metastatic Spinal Cord Compression

Drug	Initial Dose
Opioids	
Morphine*	
Immediate release	7.5-15 mg orally every 3 hours as needed or 2-4 mg intravenously every 2 hours as needed
Sustained release†	15 mg orally every 8-12 hours
Oxycodone*	
Immediate release	5-10 mg orally every 3 hours as needed
Sustained release†	10 mg orally every 8-12 hours
Hydromorphone*	
Immediate release	2-4 mg orally every 3 hours as needed or 0.4-0.8 mg intravenously every 2 hours as needed
Fentanyl*	
Sustained release†	12 μg/h transdermally every 72 hours
Neuropathic pain adjuvants	
Dexamethasone	10 mg orally or intravenous load, then 4-6 mg orally or intravenously every 6 hours
Gabapentin*	100 mg orally twice daily; 300 mg at bedtime
Pregabalin*	75 mg orally twice daily
Amitriptyline	10-25 mg orally at bedtime
Nortriptyline	10-25 mg orally at bedtime
Bone pain adjuvants	
Zoledronic acid‡	4 mg intravenously every 3-4 weeks
Pamidronate‡	90 mg intravenously every 3-4 weeks
Acetaminophen§	1,000 mg orally every 8 hours
Bowel regimen medications	
Senna	1-2 tablets twice daily
Polyethylene glycol	17 g one to two times daily
Bisacodyl suppository	Daily as needed

NOTE. From Abrahm[18] and Dworkin et al.[42]
*Decrease dose in renal (creatinine clearance < 50 mL/min) or hepatic impairment.
†Only use as an initial dose if the patient is already taking the equivalent of oral morphine.
‡Decrease dose or avoid in renal impairment (creatinine clearance < 50 mL/min).
§Limit to 2,000 mg/d in the setting of hepatic impairment.

Lawton, et al., 2019

Pain and Symptom Management

- Dexamethasone is the standard for glucocorticoid therapy.
  - Pain relief and preservation of neurologic function
  - Unknown what optimal dosing is
    - Many experts recommend 10mg IV followed by 4-6 mg IV q6h with taper over 2 weeks following RT completion.
- Opioids in addition to adjuvant pain meds
- Anticipate constipation
  - High risk given opioids, autonomic injury, and limited mobility
  - Bowel regimen may include:
    - Senna and miralax
    - Addition of suppository, enema, lactulose, or methylnaltrexone if severe
    - Some patients may require bowel program

Surgery and Radiotherapy

- Surgery (minimally invasive decompression vs more involved intervention (i.e. surgical decompression with instrumented fusion))
    - Whether to pursue before RT depends on factors such as spinal stability, presence of neurologic deficits, and prognosis.

» Important to discuss goals of care

- Radiotherapy
  - Need to consider dose, fractionation, whether to re-irradiate
  - Studies have supported short course of RT for patients with prognosis <6 months, longer course for longer prognosis.

Lawton, et al., 2019

Clinical Case

- MRI spine revealed multifocal thoracic, lumbar, sacral, and pelvic girdle metastases with epidural mass at T9-11 and T7
  - IV dexamethasone started: 8mg q8h
  - Palliative RT initiated – 2 fractions to thoracic spine
    - Was scheduled for total of 10 fractions, but transferred for Neurosurgery eval
    - Despite above treatment, BLE weakness continued to worsen while IP.
  - Neurosurgery consult: recommended emergent decompression laminectomy with plastic closure.
    - Decision made to pursue surgery: held off on completing radiation until post-surgical healing period had passed.
  - Opioids (oxycodone), dexamethasone, gabapentin, flexeril utilized for symptom management. Pain overall well controlled.
  - Significant concerns with constipation – aggressive bowel regimen + bowel program

Psychosocial Concerns

- Patients diagnosed with MSCC may be processing a lot of difficult emotions.
  - Concerns about being a burden.
  - Grieving the loss of the life they once had.
  - Fears over what may come in the future/prognosis.
- Advanced care planning discussions are important.
- Anxiety and depression assessment and management
  - Psychiatry and/or health psychology

Clinical Case

- Patient began to state to his medical team that his new quality of life was unacceptable to him. Given overall poor prognosis, expressed interest in forgoing any further treatment (such as RT) with pursuit of hospice support.
  - Palliative Consult: patient confirmed his above wishes
    - Expressed concerns with being a burden.
    - Significant financial concerns with facility placement.
  - Referral made to hospice agency.
    - Discharged home with hospice after family members received teaching from PT/OT re: safe transfers at home, hoyer use, etc., and from RNs re: bowel program.

Questions?

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