MAKING THE CASE FOR NON-PAIN SYMPTOM MANAGEMENT

Mary Lynn McPherson
Consultant Pharmacist
mlm@pharmsmart.org

LEARNING OBJECTIVES

1. Identify the most like causes of target symptoms in a hospice population (e.g., constipation, nausea and vomiting, anxiety, depression and delirium).
2. Given a simulated patient with one of the target symptoms, describe the elements of an assessment and determination of pathogenesis
3. Given a simulated patient with one of the target symptoms, recommend an appropriate treatment regimen based on assessment data.
4. Describe use of the communication technique SBAR (situation, background, assessment, recommendation.

- **Constipation**
- Nausea/vomiting
- Anxiety
- Depression
- Delirium

HOSPICE PRAYER

Happy is the patient in the PM, who has a BM in the AM

CASE 1

- Ms. Pots is a 57-year-old woman recently diagnosed with stage 3 colon cancer.
- She is status post tumor resection and is discharged with an order for oxycodone 5 mg/acetaminophen 325 mg, 1-2 tablets every 4 hours as needed for pain.
- Although her pain is currently well controlled, Ms. Pots tells the community-based palliative care nurse that she is constipated (no BM x 4 days) despite straining and associated abdominal pain.

DEFINITION OF CONSTIPATION

A change, when initiating opioid therapy, from baseline bowel habits, defecation patterns, and what individuals would consider as abnormal that is characterized by any of the following:

- Reduced frequency of spontaneous (in contrast to induced) bowel movements
- Development or worsening of straining to pass bowel movements
- A sense of incomplete rectal evacuation
- Harder stool consistency

Gaertner J, et al. *J Clin Gastroenterol.* 2015.

CAUSES OF CONSTIPATION IN PALLIATIVE CARE

- Immobility
- Reduced food and fluid intake
- Cancer-Related
- Hypercalcemia and other chemical imbalances
- Concurrent diseases
- Pain on defecation (anal fissure)
- Social issues (reduced mobility, lack of privacy, commode/bed pan)
- Medication-related
  - Opioids
  - Anticholinergics (TCA's)
  - Antipsychotic agents
  - 5HT3 antagonists
  - Diuretics, antihypertensives
  - Antiparkinsonism drugs
  - Iron, calcium supplements
  - Antacids, chemotherapy

OPIOID-INDUCED CONSTIPATION

- Opioid agonism at receptors
  - Inhibition of peristalsis via inhibition of acetylcholine release
  - Increase in non-propulsive contractions of smooth muscle in gut via inhibition of nitric oxide release from inhibitory motor neurons
  - Delayed gastric emptying and increase gastrointestinal transit time
  - Inhibition of ion and fluid secretion
  - Occurs within 5-25 minutes of opioid use
- Tolerance does NOT develop

Dorn S, et al. *Am J Gastroenterol Suppl.* 2014. Holzer P. *Am J Gastroenterol Suppl*. 2014.

ASSESSMENT

- Review the patient's medical history and presence of any disease affecting bowel functioning
- Assess fluid and food intake, including amounts and types of fluids and foods
- Assess hydration status: skin turgor, urinary output
- Ask about medications
- Evaluate activity level and ability to use a toilet or bedside commode
- What does the patient mean by "constipation?"
- Last time bowels moved
- Describe normal bowel habits
- Any blood or mucus noted with recent stool(s)?
- Concurrent symptoms (bloated, abdominal pressure)
- Pain when moving bowels? Nausea?
- Efforts taken to relieve constipation

NON-PHARMACOLOGIC OPTIONS

- Increase fluid intake and dietary fiber
- Increase physical activity (within patient's capabilities)
- Privacy and comfort during defecation
- Positioning on the toilet to relax the puborectalis muscle (knees higher than hips, leaning forward with elbows on knees, straightened spine)
- Manual removed (if the constipation is severe and refractory to other therapies)

- Squattypotty.com

PHARMACOLOGIC OPTIONS

Laxative	Usual Adult Dose	Onset of Action	Side Effects
Bulk-Forming Laxatives			
Psyllium	Up to 1 tablespoon (~3.5 grams fiber) three times daily	12-72 hours	Impaction above strictures, fluid overload, gas and bloating
Methylcellulose	Up to 1 tablespoon (~2 grams fiber) or 4 caplets (500 mg fiber/caplet) three times daily	12-72 hours	
Polycarbophil	2-4 tabs (500 mg per tab) per day	24-48 hours	
Wheat dextrin	1-3 caplets (1 grams fiber/caplet) or 2 tsp (1.5 gram fiber/tsp) up to 3 times per day	24-48 hours	

PHARMACOLOGIC OPTIONS

Laxative	Usual Adult Dose	Onset of Action	Side Effects
Surfactants (softeners)			
Docusate sodium	100 mg two times per day	24-72 hours	Well tolerated. Use lower dose if administered with another laxative. Contact dermatitis reported.
Docusate calcium	240 mg once daily	24-72 hours	
Stimulant Laxatives			
Bisacodyl	10-30 mg as enteric coated tabs 1 time a day	6-10 hours	Gastric irritation
Bisacodyl	10 mg pr 1 time a day	15-60 minutes	Rectal irritation
Senna	2-4 tabs (8.6 mg sennosides/tab) or 1-2 tabs (15 mg sennosides/tab) as a single dose or divided twice daily	6-12 hours	Melanosis coli

PHARMACOLOGIC OPTIONS

Laxative	Usual Adult Dose	Onset of Action	Side Effects
Osmotic Agents			
Polyethylene glycol	8.5 to 34 grams in 240 ml (8 oz) liquids	1-4 days	Nausea, bloating, cramping
Lactulose	10-20 grams (15-30 ml) qod (up to bid)	24-48 hours	Abdominal bloating, flatulence
Sorbitol	30 grams (120 mg of 25% solution) once daily	24-48 hours	Abdominal bloating, flatulence
Glycerin	One pr (2-3 grams) for 15 minutes once daily	15-60 minutes	Rectal irritation
Magnesium citrate	200 ml (11.6 grams) once per day	0.5-3 hours	Watery stools and urgency. Caution with renal insufficiency.
Magnesium hydroxide	5-15 ml as needed up to 4 times daily	0.5-6 hours	
Magnesium sulfate	1-2 tsp (5-10 grams) in 240 ml water once daily	0.5-3 hours	

PHARMACOLOGIC OPTIONS

Laxative	Usual Adult Dose	Onset of Action	Side Effects
Enemas			
Docusate	283 mg docusate sodium, PEG and glycerin		
Sodium phosphate	7 g dibasic and 19 g monobasic sodium phosphate Adults – 118 ml; Children 2-12 years – 59 ml		
Bisacodyl	10 mg per 30 ml		
Mineral oil	Adults and children ≥ 12 years – 118 ml; Children 2-12 years – 59 ml		
Enemeez (Plus), others	Docusate, PEG, glycerin, benzocaine		
Other	Warm water/soap suds, other		

PHARMACOLOGIC OPTIONS

Laxative	Usual Adult Dose	Onset of Action	Side Effects
Other			
Lubiprostone	24 micrograms 2 times per day	24-48 hours	Nausea, diarrhea
Linaclotide	145 micrograms once daily	12-24 hours	Diarrhea, bloating

Lubiprostone – chloride channel activator (draws fluid into the bowel, increases motility)
Lubiprostone does not work well for methadone-induced constipation

Linaclotide – guanylate cyclase-C agonist; stimulates secretion of chloride and bicarbonate into the intestine

PAMORA's (peripherally acting mu opioid receptor antagonists)

PAMORA	Mechanism	Dose	Cost
Methylnaltrexone (Relistor)	Quaternary amine; cannot cross BBB	PO – 450 mg po QD SQ – 8-12 mg QOD prn	PO – $1630/month SQ - $1800/month
Naloxegol (Movantik)	Polyethylene glycose derivative of naloxone; PEG moiety reduces BBB permeability	PO – 25 mg QAM on an empty stomach	PO - $300/month
Naldemedine (Symproic)	Derivative of naltrexone to which a side chain has been added; increases MW and polarity, reduces ability to cross BBB	PO – 0.2 mg once daily with or without food	PO - $300/month

Laxative	Dose	NNT	Cost/month	Cost/responder
Lubiprostone (Amitiza)	24 mcg bid	13	$360	$4,680
Linaclotide (Linzess)	145 mcg qd	9	$380	$3,420
Methylnaltrexone (Relistor), SQ	12 mg QOD	2.5	$1800	$4,500
Methylnaltrexone (Relistor), oral	450 mg po qd	2.5	$1630	$4,075
Naloxegol (Movantik)	25 mg po qd	8	$300	$2,400
Naldemedine (Symproic)	0.2 mg po qd	7	$330	$2,310

CASE 1

- Ms. Pots is a 57-year-old woman recently diagnosed with stage 3 colon cancer. Status-post tumor resection.
- Complaining of no BM x 4 days, despite taking 4 docusate 100 mg tablets per day. What now?

A. Increase docusate to 6 tablets per day

B. DC docusate and start senna, two tablets per day

C. DC docusate and start naloxegol 25 mg by mouth per day

D. Add daily Fleet's enema to regimen

- Constipation
- **Nausea/vomiting**
- Anxiety
- Depression
- Delirium

CASE 2

- 69-year-old female with a past medical history of hypertension, diabetes, stage IV ovarian cancer (mets to abdominal wall), and recent hospitalization for UTI who presents with worsening abdominal pain and nausea/vomiting x 5 days.
- Per patient, she had been very constipated and after taking a “cocktail of laxatives,” developed diarrhea and subsequent dehydration which prompted her to seek medical attention.
- CT abdomen/pelvis revealed disease progression, no evidence of bowel obstruction.
- Palliative care consulted to assist with pain and nausea.

CASE 2

- Home medications
  - Amlodipine 10 mg po daily
  - Docusate 100 mg po BID
  - Ibuprofen 800 mg po TID PRN (takes 2-3 times per day on average)
  - Metformin 1000 mg po BID
  - Multivitamin 1 tab po daily
  - Ondansetron 4 mg po q8h PRN nausea/vomiting
  - Oxycodone 5mg po q4h PRN moderate pain (takes ~1 time per day on average)
  - Oxycodone 10 mg po q4h PRN severe pain (takes ~5 times per day on average)

THE BASICS

- **What is nausea?**
  - The unpleasant sensation of feeling the need to vomit, which may be accompanied by abdominal discomfort, sweating, or tachycardia.
  - Can be acute, anticipatory, delayed, or chronic.
- **What is vomiting?**
  - The process of ejection of gastric contents through the mouth as a result of prolonged contraction of the diaphragm and abdominal muscles.
  - **Retching** is defined as the spasmodic movements of the esophagus and gastric muscles, without vomiting.

PREVALENCE AND COMPLICATIONS

- Up to 71% of palliative care patients will develop nausea and vomiting
  - 40% will experience these symptoms in the last six weeks of life
- ~20-30% of patients with advanced cancer experience nausea
  - 70% report nausea in the last week of life
- Up to 33% of patients with ESRD experience nausea and vomiting

Complications:

- Dehydration
- Metabolic disturbances
- Poor oral intake ➡ malnutrition
- Aspiration
- Esophageal tears

CAUSES OF NAUSEA AND VOMITING

Above the neck

- Masses
- Meningeal irritation
- Migraine/other headaches
- Movement

Below the neck

- Motility
- Mucositis
- Mechanical obstruction
- Myocardial infarction
- Maternity

Systemic

- Mentation
- Medication
- Microbes
- Metabolic

MEDICATION-RELATED CAUSES NAUSEA AND VOMITING

- Chemotherapy
  - Highly-emetogenic agents include AC combination, carboplatin AUC ≥ 4, cisplatin, cyclophosphamide > 1,500 mg/m^2, doxorubicin ≥ 60 mg/m^2
- Analgesics
  - Opioids, NSAIDs
- Antiarrhythmics
  - Digoxin, quinidine
- Antibiotics
- Oral contraceptives
- Metformin
- Antiparkinsonians
  - Bromocriptine, L-DOPA
- Anticonvulsants
  - Phenytoin, carbamazepine
- Antihypertensives
- Theophylline
- Anesthetic agents

For full list of emetogenic potential of antineoplastic agents, visit: NCCN Clinical Practice Guidelines in Oncology: Antiemesis

TOTAL NAUSEA

- Nausea is typically managed using a biomedical approach and emphasizes medication management.
- Similar to total pain, total nausea involves physical, emotional, social, and existential components.
- Best approached from a transdisciplinary perspective.
- Utilizes multiple complementary interventions to address suffering.

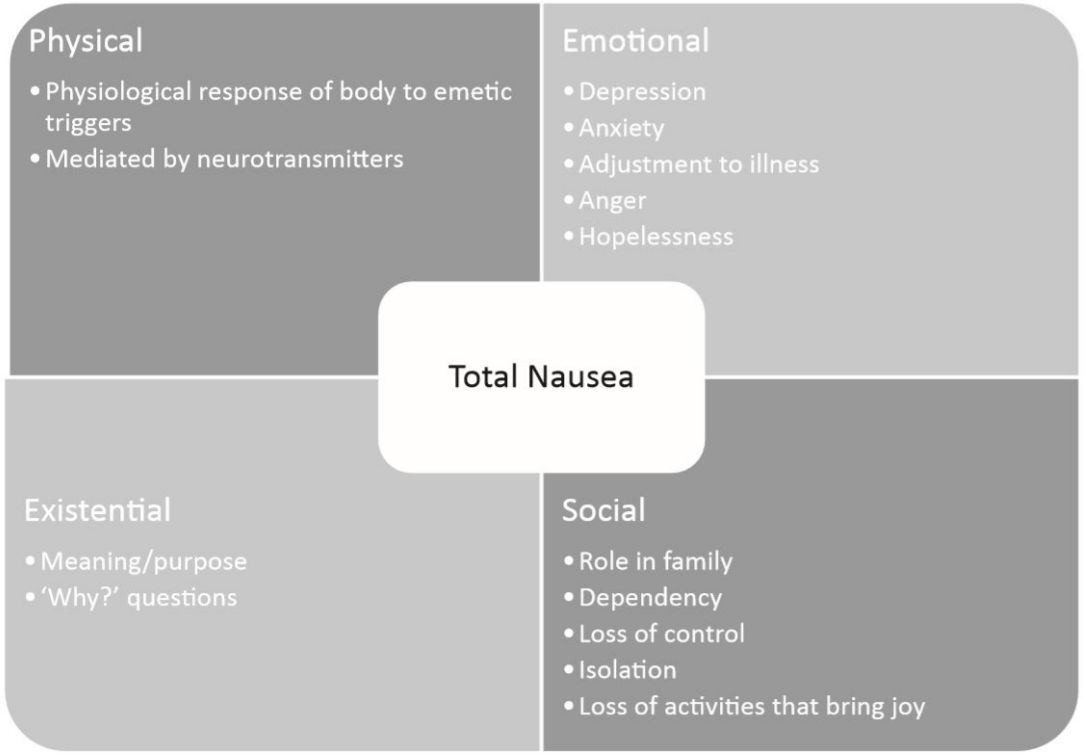


Fig. 1. "Total nausea" domains.

THE TWO MAIN QUESTIONS

- What is the likely mechanism?
- What receptors are likely to be involved?
  - Could be more than one mechanism

MANAGEMENT OF NAUSEA AND VOMITING

Non-Pharmacologic

- Relaxation techniques
- Acupressure, acupuncture
- Avoidance of strong odors, foods, or other known triggers
- Promoting good oral care
- Offer clear liquids, educate patients to sip liquids slowly (don't gulp)
- Eat small, frequent meals that patient desires
  - Cold and bland foods often better tolerated
  - Avoid greasy, fried, or spicy foods

Pharmacologic

- Dopamine antagonists
- Histamine antagonists
- Serotonin Antagonists
- Substance P (NK1) Antagonists
- Acetylcholine Antagonists
- Benzodiazepines
- Corticosteroids
- Cannabinoids
- Other

MECHANISM OF NAUSEA/RECEPTORS INVOLVED

Cause	Receptor(s)	Useful Medications	Examples
V – Vestibular	Cholinergic, histaminic	Anticholinergic, Antihistaminic	Scopolamine, promethazine
O – Obstruction of bowel by constipation	Cholinergic, histaminic, likely 5HT3	Those that stimulate the myenteric plexus	Senna products
M – DysMotility of upper gut	Cholinergic, histaminic, 5HT3, 5HT4	Prokinetics which stimulate 5HT4 receptors	Metoclopramide
I – Infection, inflammation	Cholinergic, histaminic, 5HT3, Neurokinin 1	Anticholinergic, 5HT3 Antagonists, Neurokinin 1 Antagonists	Promethazine, prochlorperazine
T – Toxins that stimulate CTZ in brain	Dopamine 2, 5HT3	Antidopaminergic, 5HT3 Antagonists	Prochlorperazine, haloperidol, ondansetron

CASE 2

- 69-year-old female with a past medical history of hypertension, diabetes, stage IV ovarian cancer (mets to abdominal wall), and recent hospitalization for UTI who presents with worsening abdominal pain and nausea/vomiting x5 days.
- Per patient, she had been very constipated and after taking a “cocktail of laxatives,” developed diarrhea and subsequent dehydration which prompted her to seek medical attention.
- CT abdomen/pelvis revealed disease progression, no evidence of bowel obstruction. Palliative care consulted.
- Amlodipine, docusate, MVI, ibuprofen, metformin, ondansetron, oxycodone.

- Constipation
- Nausea/vomiting
- **Anxiety**
- Depression
- Delirium

CASE 3

- Mary Ellen is a 68-year-old admitted to hospice with end-stage lung cancer.
- Her physical symptoms are managed, but she tells the admission nurse “I’m simply terrified. I’ve done some things I’m not proud of in my life, and I believe I’m going to go to hell when I die. I don’t want to spend eternity paying for my sins.”
- Mary Ellen was raised as a strict Catholic, and she tells you she is constantly nervous and on edge, she simply cannot stop worrying about this, she can’t relax at all, and she is frankly terrified.

ANXIETY

- A state of apprehension and fear resulting from the perception of a current or future threat to oneself
- The term is used to describe a symptom and a variety of psychiatric disorders in which anxiety is a salient symptom
- Prevalence
  - 25% cancer patients (3% GAD)
  - 50% of CHF and COPD patients (10% GAD)

Stoklosa J, et al. Fast Facts #186. Anxiety in Palliative Care

COMMON CAUSES OF ANXIETY IN PALLIATIVE CARE

- Situational
  - Recent diagnosis of serious illness
  - Impending surgery or chemotherapy
  - Impending diagnostic imaging
  - Perceived risk for getting bad news
  - Fear of death
- Symptom-related
  - Pain
  - Dyspnea
  - Palpitations
  - Nausea
- Metabolic disturbances
  - Hypercalcemia
  - Hypoglycemia
  - Carcinoid syndrome
  - Pulmonary embolus
  - Paraneoplastic syndrome

Akechi T, Uchitomi Y. Depression/anxiety. In: Bruera E. Textbook of Palliative Medicine and Supportive Care.

COMMON CAUSES OF ANXIETY IN PALLIATIVE CARE

- Drug-associated
  - Akathisia due to antipsychotics or antiemetics (dopamine-2 antag)
  - Steroids
  - Bronchodilators
  - Psychostimulants
  - Thyroid replacement
  - Allergic reaction
  - Substances or withdrawal from substances
- Psychiatric disorders
  - Delirium
  - Depressive disorders
  - Panic disorders
  - Posttraumatic stress disorder
  - Phobias
  - Generalized anxiety disorder

Akechi T, Uchitomi Y. Depression/anxiety. In: Bruera E. Textbook of Palliative Medicine and Supportive Care.

GENERALIZED ANXIETY DISORDER

- Feeling nervous, anxious, or on edge
- Not being able to stop or control worrying
  - 0 – not at all
  - 1 – several days
  - 2 – more than half the days
  - 3 – nearly every day
- GAD $\geq$ 3

- Worrying too much about different things
- Having trouble relaxing
- Being so restless that it is hard to sit still
- Becoming easily annoyed or irritable
- Feeling afraid, as if something awful might happen
- GAD $\geq$ 9

Ebell MH. Am Fam Phys 2008;78(4):501-502.

https://www.hiv.uw.edu/page/mental-health-screening/gad-2

Generalized Anxiety Disorder 2-item (GAD-2)

Share

The Generalized Anxiety Disorder 2-item (GAD-2) is a very brief and easy to perform initial screening tool for generalized anxiety disorder.[1]

Over the **last 2 weeks**, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	+1	+2	+3
2. Not being able to stop or control worrying	0	+1	+2	+3

GAD-2 score obtained by adding score for each question (total points)

Interpretation:

A score of 3 points is the preferred cut-off for identifying possible cases and in which further diagnostic evaluation for generalized anxiety disorder is warranted. Using a cut-off of 3 the GAD-2 has a sensitivity of 86% and specificity of 83% for diagnosis generalized anxiety disorder.

Scores of 5, 10 & 15 are the cut-offs for mild, moderate and severe anxiety.

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Total Score ___ = Add Columns ___ + ___ + ___

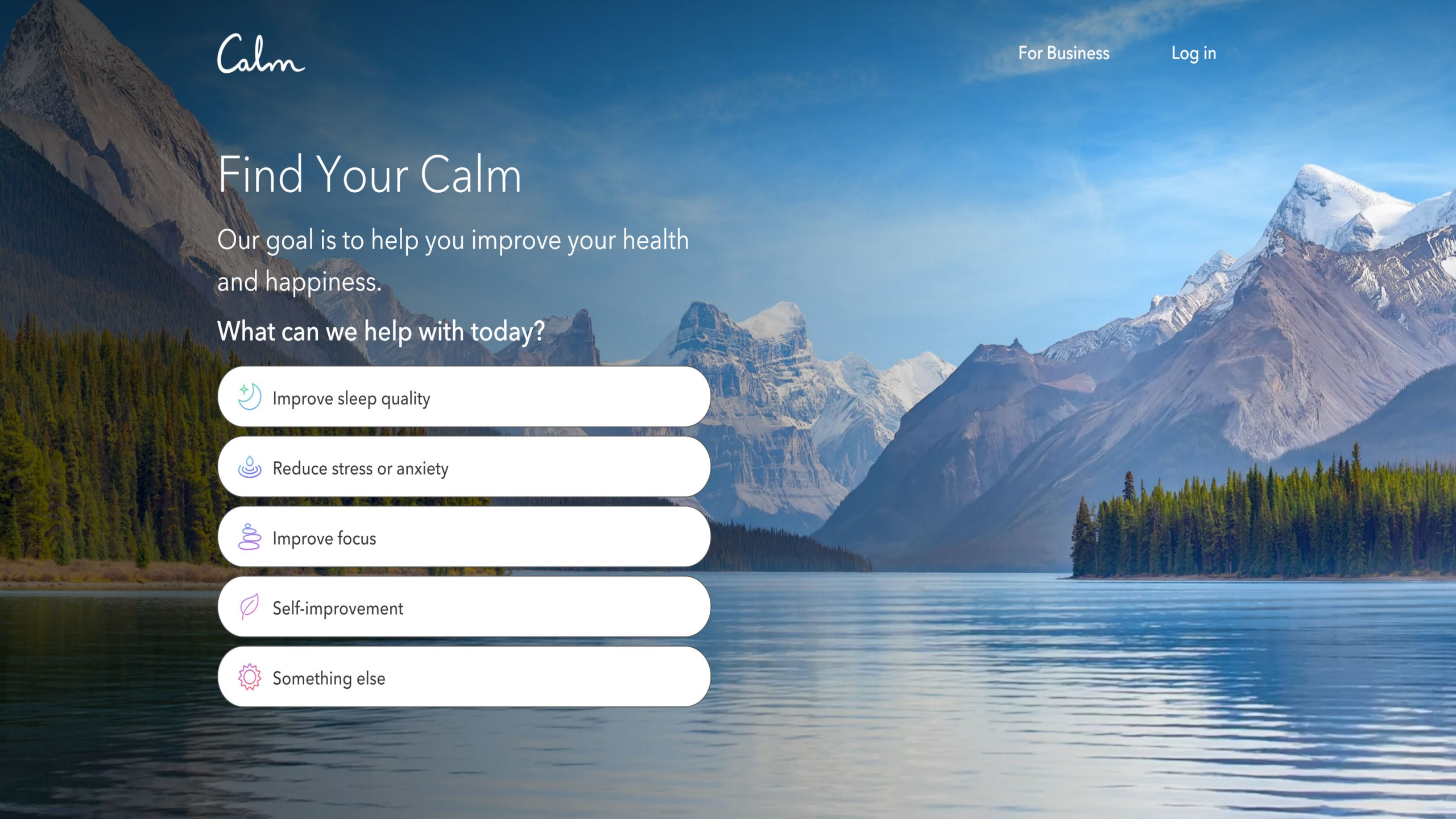
If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

NON-PHARMACOLOGIC MANAGEMENT OF ANXIETY

- Exercise
- Meditation
- Relaxation therapy, breathing
- Psychosocial/spiritual support
- Guided imagery
  - *"Position yourself as comfortably as you can, shifting your weight so that you're allowing your body to be fully supported by your chair/couch/bed…Take a deep, full cleansing breath…inhaling as fully as you can…breathing deep into the belly if you can…and breathing all the way out…Imagine a place where you feel safe and peaceful and easy…a place either make-believe or real…"*
  - http://academyforguidedimagery.com

Cooper K, Stollings S. Fast Facts and Concepts #211, Guided Imagery for Anxiety


Calm
For Business
Log in
Find Your Calm
Our goal is to help you improve your health and happiness.
What can we help with today?
Improve sleep quality
Reduce stress or anxiety
Improve focus
Self-improvement
Something else

This Genius Anxiety Hack Can Help You Calm Down In Seconds

All you need is an ice cube and a few seconds for yourself.

A Grounding Exercise

https://www.doctoroz.com/ice-cube-anxiety-hack

PHARMACOLOGIC MANAGEMENT OF ANXIETY

- Benzodiazepines
  - Alprazolam
  - Diazepam
  - Lorazepam
  - Clonazepam
  - Midazolam
- Antidepressant agents
  - SSRI and newer antidepressants
  - Tricyclic antidepressants
- Neuroleptic agents
  - Haloperidol
  - Atypical antipsychotics
- Other drug therapies
  - Buspirone
  - Beta blockers (for autonomic symptom relief)
  - Sedative hypnotics (for relief of insomnia)
  - Antihistamines

Akechi T, Uchitomi Y. Depression/anxiety. In: Bruera E. Textbook of Palliative Medicine and Supportive Care.

CASE 3

- Mary Ellen is a 68-year-old admitted to hospice with end-stage lung cancer.
- Her physical symptoms are managed, but she tells the admission nurse “I’m simply terrified. I’ve done some things I’m not proud of in my life, and I believe I’m going to go to hell when I die. I don’t want to spend eternity paying for my sins.”
- Mary Ellen was raised as a strict Catholic, and she tells you she is constantly nervous and on edge, she simply cannot stop worrying about this, she can’t relax at all, and she is frankly terrified.
- Scores 12 on the GAD. What should we do?

CASE 3

- Hospice care is provided by a team for a reason!
  - Psychosocial / spiritual support to the rescue!
  - Priest or spiritual advisor
- Guided imagery, relaxation
- Depending on Mary Ellen's prognosis consider an SSRI, with a prn benzodiazepine

- Constipation
- Nausea/vomiting
- Anxiety
- **Depression**
- Delirium

CASE 4

- Roland Dalyrumple is a 48-year-old man diagnosed with amyotrophic lateral sclerosis (ALS).
- He is seen in the ALS clinic, and palliative care clinic.
- Roland is EXTREMELY discouraged over this diagnosis because he understands that his prognosis is 2-5 years.
- Roland is married and has three children at home under the age of 18.
- He is worried about the fate of his family when he dies. He is the primary money maker in the family, and his wife has limited marketable skills.

Is Roland Depressed, Anxious, or Just Discouraged?

- 1 in 4 palliative care patients have depression, especially when they have metastatic cancer.
- Primary symptoms are weight loss, anhedonia, loss of energy, fatigue, insomnia.
- Single question test:
  - “Are you depressed?”
  - “Are you feeling down, depressed or hopeless most of the time over the last 2 weeks?”
  - “Please grade your mood during the past week by assigning it a score from 0 to 100, with a score of 100 representing your usual relaxed mood. A score of 60 is considered a passing grade.”

Arnold R. Fast Facts and Concepts 146.

Is Roland Depressed, Anxious, or Just Discouraged?

- Two question test:
  - “Have you found that little brings you pleasure or joy over the last two weeks?”
  - “Have you often been bothered by having a lack of interest or pleasure in doing things?”
- Longer tests available

Arnold R. Fast Facts and Concepts 146.

Common Barriers to Assessment of Depression in Patients With Cancer

- Overlap of physical symptoms of depression and symptoms of cancer or its treatment
  - Clinician's under-recognition of hopelessness, feelings of worthlessness, or suicidal ideation
  - Clinician's uncertainty about how to interpret screening instrument cut-offs
  - Lack of clinician's routine discussion with patients and family about low mood, not like pain assessment
  - Limited understanding by cancer professionals regarding which patients are most at risk
  - Time constraints in busy oncology settings

Akechi T, Uchitomi Y. Depression/anxiety. In: Bruera E. Textbook of Palliative Medicine and Supportive Care.

Common Barriers to Assessment of Depression in Patients With Cancer

- Overlap of physical symptoms of depression and symptoms of cancer or its treatment
  - Cost constraints limiting access to professionals with behavioral health training
  - Few mental health programs and specialists connecting with oncology
  - Poor continuity of care over the trajectory of illness
  - Stigma concerning mental illness or weakness perceived by the patient/family
  - Patient/family fear that revealing depression will lead to undertreatment of the cancer

Akechi T, Uchitomi Y. Depression/anxiety. In: Bruera E. Textbook of Palliative Medicine and Supportive Care.

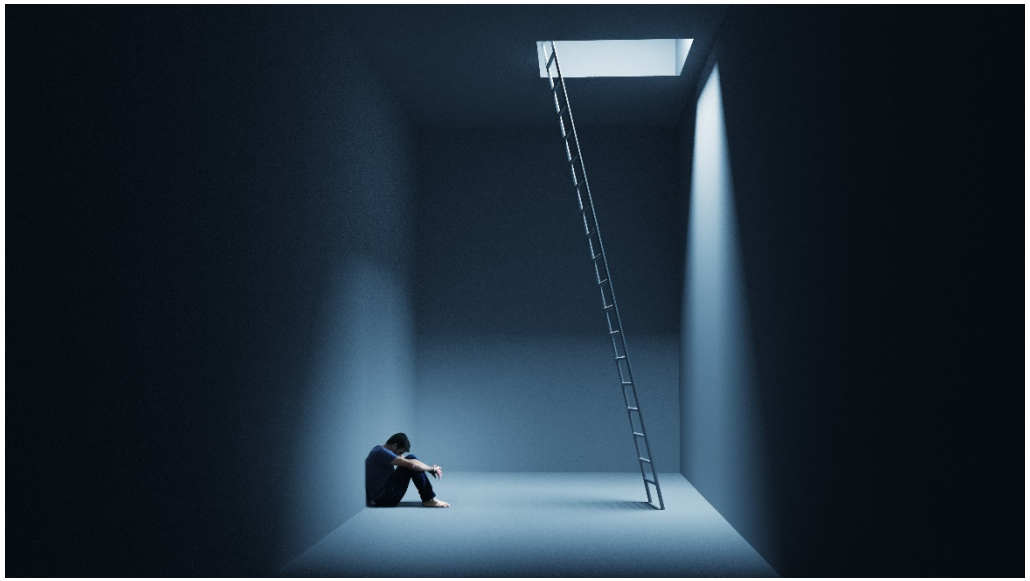
Risk Factors for Depression in Cancer

- Social and environmental factors
  - Recent losses (e.g., spouse, family, friends, animals)
  - Financial stressors
  - Poor social support
  - Sexual and/or physical abuse
  - Childhood trauma or parental loss
- Psychiatric factors
  - Family and own history of depressive disorder
  - History of substance abuse
- Cancer-related factors
  - Advanced stage of disease
  - Poor performance status
  - Poor pain control
- Cancer treatment factors
  - Corticosteroids
  - Interferon alfa, interleukin-2
  - Amphotericin-B
  - Procarbazine, L-asparaginase
  - Paclitaxel

Akechi T, Uchitomi Y. Depression/anxiety. In: Bruera E. Textbook of Palliative Medicine and Supportive Care.

Pharmacologic Management of Depression

- Determine patient's prognosis
  - Most traditional antidepressants take ≥ 4 weeks to become effective
  - If < 4 weeks – consider a psychostimulant such as methylphenidate or dextroamphetamine (acts in 1-2 days; rule out CV disease/delirium)
- Consider co-morbid conditions
  - Insomnia, neuropathic pain, poor appetite
  - Past response to antidepressants?
  - Consider drug interactions



Rosenberg L, Thoomas JD. Fast Facts and Concepts #309.

Pharmacologic Management of Depression

- SSRIs
  - Start at a low dose and titrate to the minimum effective dose
  - AE – QTc prolongation, sexual dysfunction, headaches, nausea and diarrhea
  - Fluoxetine is associated with emotional activation and may worsen anxiety
  - Paroxetine can be sedating and lead to withdrawal phenomena with missed doses
  - Best choices – sertraline, citalopram, escitalopram
    - Fewer AE, not activating or sedating
  - Sertraline also available in a concentrated liquid formulation

Rosenberg L, Thoomas JD. Fast Facts and Concepts #309.

Pharmacologic Management of Depression

- SNRIs
  - Useful for concurrent depression and neuropathic pain, vasomotor instability and anxiety-predominant depression
  - Venlafaxine effective for treatment of hot flushes
  - Venlafaxine and duloxetine beneficial for chemo-induced neuropathy
  - Venlafaxine 37.5 mg to start; 75-225 effective dose
  - Duloxetine 30 mg to start; 60 mg (to 120 mg) effective dose
- TCAs – cost effective, but significant toxicities
  - Anticholinergic effects (delirium), prolong QTc, dangerous in overdose
  - Start low (10-25 mg); rarely need > 50-75 mg a day
- Other – mirtazapine (insomnia, poor appetite, nausea, neuropathy)

Rosenberg L, Thoomas JD. Fast Facts and Concepts #309.

Case 4

- Roland Dalyrumple is a 48-year-old man diagnosed with amyotrophic lateral sclerosis (ALS).
- Roland now screens positive for depression. His prognosis is 2-3 weeks. Which antidepressant would you recommend?
  A. Sertraline 25 mg po qd to start; titrate
  B. Methylphenidate 2.5 mg with breakfast, 2.5 mg with lunch; titrate
  C. Nortriptyline 25 mg at bedtime; titrate
  D. Mirtazapine 15 mg at bedtime; titrate

- Constipation
- Nausea/vomiting
- Anxiety
- Depression
- **Delirium**

CASE 5

JR is a 72-year-old man admitted to hospice with a diagnosis of end-stage Alzheimer's disease.

JR has been "pleasantly confused" for several months, but over the past couple of weeks things have taken a turn for the worse.

JR is now becoming combative and seems very frightened.

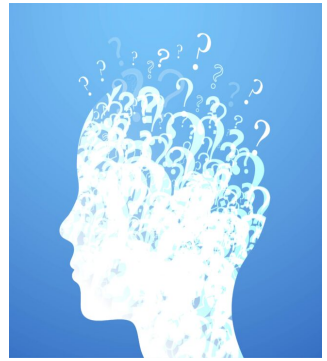
His sleep-wake cycle is reversed, and this behavior comes and goes (worse from about 5 pm on)

His 71-year-old wife is having a hard time caring for him

What should we do?

CLINICAL FEATURES OF DELIRIUM

- Disturbance in the level of alertness (consciousness)
- Attentional disturbances, disorientation, disorganized thought process
- Rapidly fluctuating clinical course and abrupt onset of symptoms
- Disorientation, disorganized though process
- Cognitive disturbances (memory impairment, executive dysfunction, apraxia, agnosia, visuospatial dysfunction, language disturbances)
- Increased or decreased psychomotor activity
- Disturbance of the sleep-wake cycle; hallucinations/delusions
- Mood symptoms (depression, mood lability)
- Incoherent speech



Alici Y, Breitbart W. Delirium. In: Bruera E. Textbook of Palliative Medicine and Supportive Care.

CAUSES AND SCREENING TOOLS FOR DELIRIUM

- Direct CNS causes
  - Primary brain tumors
  - Metastatic spread to CNS
  - Seizures
- Indirect causes
  - Metabolic encephalopathy
  - Electrolyte imbalance
  - Treatment side effects
  - Infections
  - Nutritional deficiencies

- Memorial Delirium Assessment Scale
- Confusion Assessment Method
- Bedside Confusion Scale
  - Recite the months of the year backwards!

- Hypoactive vs. hyperactive delirium

Alici Y, Breitbart W. Delirium. In: Bruera E. Textbook of Palliative Medicine and Supportive Care

NON-PHARMACOLOGIC TREATMENT OF DELIRIUM

- Reducing polypharmacy
- Control of pain
- Sleep hygiene (minimize noise and interventions at bedtime)
- Monitor for dehydration and fluid-electrolyte disturbances
- Monitor nutrition, monitor for infection
- Monitor for sensory deficits, provide visual and hearing aids
- Encourage early mobilization
- Monitor bowel and bladder functioning
- Reorient the patient frequently/orientation board
- Encourage cognitively stimulating activities

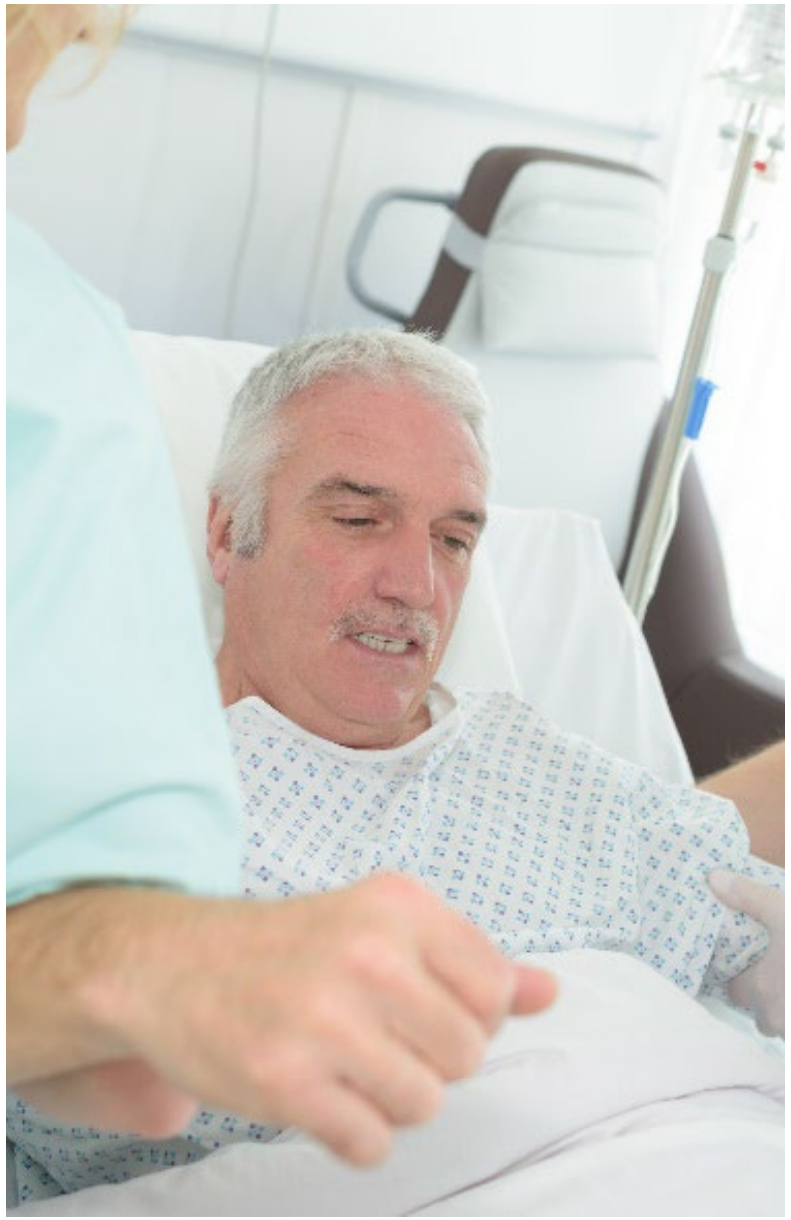
Alici Y, Breitbart W. Delirium. In: Bruera E. Textbook of Palliative Medicine and Supportive Care

PHARMACOLOGIC TREATMENT OF DELIRIUM

- 1st generation antipsychotic agents
  - Haloperidol, chlorpromazine
- 2nd generation antipsychotic agents
  - Olanzapine, quetiapine, risperidone, aripiprazole
- Benzodiazepines – can make delirium worse, and precipitate withdrawal syndromes
- Valproate (VPA) – 500-1500 mg PO/IV a day in 2-3 doses
- Melatonin receptor agonists (melatonin and ramelteon)
- Dexmedatomidine, clonidine, cholinesterase inhibitors

FDA has issued a black box warning about increased risk of death and stroke with antipsychotics in the treatment of dementia-related psychosis in the elderly

Quijada E, Bukowy E, Billings JA. Fast Facts and Concepts #60; Fernandez C, Correa I, Davis M. Fast Facts and Concepts # 397.



CASE 5

- JR is a 72-year-old man admitted to hospice with a diagnosis of end-stage Alzheimer's disease.
- JR is now becoming combative and seems very frightened.
- His sleep-wake cycle is reversed, and this behavior comes and goes (worse from about 5 pm on)
- Implement non-pharmacologic interventions
- Consider melatonin or ramelteon; consider valproic acid.

KEY TAKEAWAYS

- Patients with a serious or advanced illness experience many symptoms, including pain and non-pain symptoms.
- Poorly managed symptoms increase the burden on the patient, causing discomfort and suffering.
- Neuropsychiatric symptoms may be frightening for the patient AND the family.
- Consider non-pharmacologic interventions before, or concurrently with pharmacologic interventions.

MAKING THE CASE FOR NON-PAIN SYMPTOM MANAGEMENT

Mary Lynn McPherson
Consultant Pharmacist
mlm@pharmsmart.org

Well that’s a giant pain in the neck! Assessing and reporting on physical complaints!

Mary Lynn McPherson, PharmD

TJC Sentinel Events

- Communication failures are associated with untoward events
  - 65% of sentinel events
  - 90% root cause analyses
- National Patient Safety Goal 2E
  - Clear, concise and thorough communication of pertinent clinical information
  - Improved patient safety and clinical outcomes

Haig KM et al. Joint Commission Journal on Quality and Patient Safety 2006;32:167-175

Differences in Communication Styles

Nurses – descriptive and detailed

Physicians – use brief statements, summarizing salient patient information

- Bullet points
- Headlines

Communication styles, training, gender, cultural differences, prior relationships, hierarchy, past experience

What makes you CRAZY in this clip…

https://www.youtube.com/watch?v=tM1CKK0MOoo

SBAR Model

Dr. Michael Leonard, physician leader for patient safety at Kaiser Permanente (Denver)

- Introduced a model of structured communication that helps clinicians have a shared mental model for the patient's clinical condition

An effective tool for all types of communication handoffs

- S – Situation
- B – Background
- A – Assessment
- R – Recommendation

SBAR Model

Situation – the problem

Background – brief, related, to the point

Assessment – what you found, what you think

Recommendation – what you want

Prior to Contacting Clinician

- Assess patient, review chart
- Make sure you have all relevant clinical information
- Know admitting diagnosis, date of admission, patient’s age
- Current medications, lab results

S - Situation

- State what is happening at the present time that has warranted the SBAR communication.
- Identify yourself, your title, your agency/employer
- “I am calling about [patient’s name]…
- I’m calling because [patient’s name] is [what is going on now]

S - Situation

"Hello, this is Lynn McPherson, the clinical pharmacist at University Ambulatory Care.

I am calling about your patient Mr. Jones, who is experiencing increased pain in his feet."

B - Background

- Explain circumstances leading up this situation. Put the situation in context for the reader/listener.
- State the admission diagnosis, patient's age, date of admission.
- State the pertinent medical history/clinical information.
- Brief synopsis of the treatment to date.

B - Background

- Medical history/clinical information may include:
  - Current medications, IV fluids, labs
  - Allergies
  - Vital signs
  - Code status
  - HPI (symptom analysis)

Symptom Analysis

- P (palliative/precipitating/previous therapy)
- Q (quality)
- R (region/radiating)
- S (site/severity)
- T (temporal)
- U (YOU - associated symptoms)

B - Background

"Mr. Jones is a 72 year old man with an 18 year history of type 2 diabetes. He also has a history of depression and hypertension.

His A1c has fallen from 9.2 to 7.8 with the addition of sitagliptin to his regimen of metformin and glipizide.

He continues to complain of pain in both feet on the bottoms and the tops. He complains of numbness and tingling in his feet, and occasional burning.

B - Background

On physical exam he shows decreased sensation to monofilament testing, ankle and knee jerks, decreased two point discrimination and vibratory sensation.

He rates the pain as a best of 4, a worst of 8, and an average of 6. Pain prevents him from getting a good night's rest.

On his last clinic visit he wanted to try ibuprofen, and unsurprisingly, this did not reduce the pain."

A - Assessment

- Analysis and considerations of options.
- What you found or think is going on
- “I believe the patient is experiencing [insert your impression]…or
- I have no idea what is causing this.”

A - Assessment

“I believe Mr. Jones is experiencing painful diabetic neuropathy in both feet.”

R - Recommendation

- Recommend what action you would like to occur.
- “I believe the patient should be referred for [whatever you think]
- I recommend beginning antibiotic therapy.
- I recommend changing the analgesic regimen to [new regimen].”

R - Recommendation

- “I recommend we discontinue the ibuprofen and begin an agent shown to be effective in treating painful diabetic neuropathy.
- Mr. Jones tells me he would also welcome a therapeutic intervention for his depression, so I recommend we begin duloxetine 20 mg po qd (Cymbalta) which will likely be beneficial for both the depression and neuropathic pain.
- We can titrate the duloxetine to 60 mg over the next week or two
- What do you think of this plan?”

Let’s try it again Pharmacist John…

https://www.youtube.com/watch?v=fsazEArBy2g

Let’s call Dr. Long again…

- SITUATION
  - Hello Dr. Long. This is Lynn the hospice nurse, calling about our patient Mrs. Smith, because we are not achieving her pain goal.
- BACKGROUND
  - Mrs. Smith is 67 years old, and she’s been on our program for about 3 weeks.
  - She was admitted with a diagnosis of breast cancer.
  - She’s on MS Contin 30 mg po q12h and using Roxanol 10 mg every 2 hours, about 5 or 6 times a day.
  - She tells me the pain is in her right ribs, and she can point right to the painful area. The pain doesn’t radiate to any other locations.
  - She rates the pain as a 5/10 if she holds perfectly still, but a 10+ if she twists or turns, or when she rolls over on her right side at night. The pain is especially bad first thing in the morning when she wakes up.
  - The patient describes it as sharp and achy.

Let’s call Dr. Long again…

- BACKGROUND
  - She’s tried a heating pad and ice packs with no success.
  - The Roxanol only brings the pain down about 0.5-1 points on the 0-10 scale.
  - She tells me the pain prevents her from getting a good night’s rest because she can’t roll over on her right side, and she has to hold herself so rigidly so she won’t twist her torso by accident.
  - She also tells me the pain is so bad it frequently makes her cry.
  - She doesn’t want to ambulate so she tries not to drink much so she won’t have to go to the bathroom and she doesn’t want to leave the house at all.

Let’s call Dr. Long again…

- ASSESSMENT
  - It sounds to me like metastatic bone pain.
  - I know we don’t have a bone scan, but I think this is a definite possibility.
- RECOMMENDATION
  - She’s only taking the morphine, but it doesn’t seem to be helping this particular pain very well.
  - If it is metastatic bone pain, how about adding dexamethasone, 4 mg bid? She doesn’t have diabetes, or any serious gastrointestinal issues.
  - What do you think?

And Dr. Long would say…

Element of Symptom Analysis	
Precipitating	Twisting or turning, especially when she rolls over on her right side at night.
Palliating	She's tried a heating pad and ice packs with no success.
Previous treatment or therapy	The Roxanol only brings the pain down about 0.5-1 points on the 0-10 scale.
Quality	The patient describes it as sharp and achy.
Region/radiation	She tells me the pain is in her right ribs, and she can point right to the painful area. The pain doesn't radiate to any other locations.
Severity	She rates the pain as a 5/10 if she holds perfectly still, but a 10+ if she twists or turns, or when she rolls over on her right side at night.
Temporal	The pain is especially bad first thing in the morning when she wakes up.
Associated Symptoms	She tells me the pain prevents her from getting a good night's rest because she can't roll over on her right side, and she has to hold herself so rigidly so she won't twist her torso by accident. She also tells me the pain is so bad it frequently makes her cry. She doesn't want to ambulate so she tries not to drink much so she won't have to go to the bathroom and she doesn't want to leave the house at all.

Tell me the Eight Elements of Symptom Analysis

P - (palliative/precipitating factors and previous therapy)

Q - (quality)

R - (region/radiating)

S - (severity)

T - (temporal)

U - (YOU- associated symptoms, impact on ADL's)

Survey Time!

- Please click this link (also emailed to you) and take this quick survey.

https://tinyurl.com/kauaihospice02

Well that’s a giant pain in the neck! Assessing and reporting on physical complaints!

Mary Lynn McPherson, PharmD