A RESOURCE GUIDE FOR PALLIATIVE CARE EDUCATION

Part 2: Non-Pain Symptom Management

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**PREFACE**

There is a pressing need to improve palliative care education. This guide was developed to assist medical educators implement educational programs in key palliative care learning domains. The guide is meant to highlight the topics of greatest educational need, as identified by clinicians.

**DISCLAIMER**

The information in this book is not medical advice. Health care providers should exercise their own independent clinical judgment. Some of the information in this book cites the use of a product in dosage, for an indication, or in a manner other than that recommended in the product labeling. Accordingly, the official prescribing information should be consulted before any such product is used.

**LEARNING FORMATS USED IN THIS GUIDE**

**PRE-POST TESTS**

A brief test (5 minutes), (short-answers or fill in the blank) is included at the beginning of each topic domain. Answers are provided at the bottom and can be covered when copies are made for distribution. The test can be administered in one of the following ways:

- Used at the beginning of a teaching session to heighten learner awareness of the topic;
- Used at the conclusion of a teaching session for the learner and/or the teacher to gauge effectiveness of the learning experience and to demonstrate topics for further learning;
- Used at both the beginning and the end of a teaching session for the learner and/or the teacher to gauge effectiveness of the learning experience and to demonstrate topics for further learning; Note: using the same test both pre and post may create re-test bias in the responses.

**TEACHING OUTLINES**

Each topic domain contains a brief outline containing the essential topic information. The outlines are designed as quick reference guides, suitable for distribution for different types of learning opportunities—either as stand-alone guides, or as written material to accompany an educational experience, such as:

- a didactic lecture—small or large group setting
- teaching time during ward rounds
- a faculty development course
- a self-study guide

**CASE STUDIES**

The case study format is used to complement the content outlines to help learners:

- express their own feelings toward the attitudinal issues raised in each case (see Discussing attitudes, below);
- reveal deficits in knowledge;
• reinforce existing knowledge.

The cases are designed for small-group discussions, ideally no more than 12-15 participants, (e.g. ward rounds teaching time, small group conference, faculty development course). Each case can be discussed in 30-45 minutes depending upon the depth of discussion. Case studies are included in the following modules: Pain; Dyspnea; Delirium; Nausea; Constipation, Artificial Hydration/Nutrition.

SMALL GROUP WORKSHOP-Attitude Discussions
Small groups are excellent venues to discuss attitudinal issues. To optimally explore the personal attitudes that arise in discussing end-of-life care, it is essential that the small group environment feel comfortable and safe. Have each participant introduce themselves and then set basic small group ground rules. One suggestion to help engage all participants is to break the small group into pairs; have each pair work for 5-10 minutes on the questions and then reconvene the entire group, asking each pair to report their answers to the questions. Use of a blackboard or flip-chart can be helpful in keeping track of ideas, opinions. Listed below are key teaching points concerning the subject of attitude change (1).

• Exhortation, information and rational argument have a limited role in the learning or changing of attitudes.
• Recognize that attitudes involve ego-involvement.
  • Shared group attitudes are more resistant to change
  • There must be a willingness to change
• Effective teaching capitalizes on “teachable moments” when the learner is emotionally or intellectually aroused by a question, contradiction, or problem.
• Attitudinal development is fostered in situations in which
  • concrete knowledge and skills are taught that relate to the desired attitudes;
  • the learner is able to examine personal feelings/attitudes in an open and non-threatening dialog with peers;
  • the learner can be active and can engage with others around real problems;
  • the learner has an opportunity to practice the new behavior thus making a commitment;
  • the learner has the opportunity to reflect on the meaning, difficulties and rewards of attitudinal change.
• Role-playing and role-reversal encourages the learner to take an alternative perspective and may foster an empathic awareness of the other’s experience.
• Role models and mentors are crucial to the process of learning attitudes; especially when the learner is making a transition.
• Feedback about the learners progress towards explicitly desired attitudinal objectives can help promote self-reflection and self-learning.

1. Adapted from information provided by Susan Block, MD with assistance from Luann Wilkerson, Ed.D.

ROLE PLAYING AND EXPERIENTIAL EXERCISES
Role playing exercises have been designed to help practice critical end-of-life skills, to reinforce knowledge and as learner evaluation tools. The exercises can be done with dyads (doctor and patient/family) or triads (doctor, patient/family and observer/recorder). The exercise can also be used as an example—the facilitator acting as the doctor, showing “how to do it right”.

The teacher can reduce the inevitable anxiety that accompanies experiential activities such a role playing by encouraging participants to view the role play as a time for the group to
experiment with various approaches to common clinical dilemmas. In the process of experimenting, the learners will discover some approaches that work well, and other approaches that are less effective.

Role playing exercises have been designed to help practice critical end-of-life skills, to reinforce knowledge and as learner evaluation tools.
DYSPNEA

LEARNING OBJECTIVES

ATTITUDES

- Self-reflect on past experiences managing dyspnea near the end of life.
- Dyspnea is a common end-of-life symptom that has a significant negative impact on quality of life.
- Treating dyspnea with opioids is ethically appropriate if the intent is to relieve suffering.

KNOWLEDGE

- Describe at least two disease processes resulting in dyspnea from each of the following categories: a) obstructive airway diseases; b) parenchymal lung disease; c) pleural disease; d) vascular disease; e) cardiac disease; f) chest wall/respiratory muscle disease.
- Describe at least four non-drug treatments for dyspnea.
- Understand the role of opioids and benzodiazepines as drug therapy in managing terminal dyspnea.
- Understand the medical facts and ethical arguments concerning opioid induced respiratory depression, physician-assisted suicide, and euthanasia in relation to opioids used to treat dyspnea.

SKILLS

- Demonstrate communication skills in discussing the treatment of dyspnea with patients and families.
- Demonstrate communication skills necessary to take a thorough history from a patient with dyspnea.
- Construct a differential diagnosis for at least three patients with dyspnea.
- Develop an initial treatment plan for at least three patients with dyspnea.
- Demonstrate ability to choose and titrate an initial opioid dose and/or benzodiazepine.
- Demonstrate skill at treating dyspnea that is refractory to an initial treatment approach.
DYSPNEA

PRE / POST TEST

1. List three causes of dyspnea in the cancer patient related to direct tumor effects:
   a) 
   b) 
   c) 

2. List two causes of dyspnea that are not related to lung, pleura or cardiac pathology:
   a) 
   b) 

3. List three non-drug treatments for dyspnea:
   a) 
   b) 
   c) 

4. When using opioids to treat dyspnea, the drug of choice is:_______________

5. Write a prescription for emergency treatment of severe dyspnea in an opioid-naïve, 50 y/o dying patient, using morphine (dose, schedule, route):
   “___________________________________________________________________”

Answers
1. pleural effusion, post-obstructive pneumonia, SVC syndrome; 2. anxiety, anemia; 3. relaxation training, fan, open window; 4. morphine; 5. 2-4 mg IV MS q 10 minutes.
DYSPNEA

**DEFINITION**

Dyspnea is a subjective sensation of difficulty in breathing; an abnormally uncomfortable awareness of breathing. Dyspnea is experienced when there is an imbalance between the perceived need to breathe and the perceived ability to breathe.

**DIFFERENTIAL DIAGNOSIS**

1. Obstructive airway process
   - tracheal obstruction—intrinsic / extrinsic
   - asthma / COPD

2. Lung parenchymal / pleural disease
   - diffuse primary or metastatic cancer to lung or pleura
   - lymphangitic metastases
   - pneumonia
   - pleural effusion—malignant / other
   - pulmonary drug reaction
   - radiation pneumonitis

3. Vascular disease
   - pulmonary embolus
   - superior vena cava obstruction
   - pulmonary vascular tumor emboli

4. Cardiac disease
   - congestive heart failure
   - pericardial effusion—malignant / other
   - arrhythmia

5. Chest wall / respiratory muscles
   - primary neurological disease (e.g. ALS)
   - malnutrition

6. Other
   - anxiety
   - anemia

**TREATMENT**

**Non-Drug Therapy**

1. Oxygen—nasal cannula better tolerated than mask—especially in the terminal setting; Oxygen not always helpful—a therapeutic trial, based on symptom relief, not pulse oximetry, is indicated to determine usefulness;
2. Positioning—sitting up, leaning forward;
3. Increase air movement—open window, bedside fan;
4. Behavioral treatments—education, relaxation exercises, distraction;
5. Humidified air—especially for pts with distressing cough;
6. Noninvasive Positive Pressure Ventilation (mask)—often uncomfortable;
7. Pulmonary rehabilitation for chronic dyspnea (e.g. COPD);
Drug Therapy

1. Opioids: Particularly helpful when patients experience air hunger and heavy work of breathing. Starting dose depends on current/prior use. For opioid naïve patients with severe dyspnea, start with 2-5 mg IV or SQ morphine sulfate (MS), every 5 minutes (IV) or every 15 minutes (SC) until symptoms improve. MS is drug of choice (however, all opioids are effective) and can be administered by any route.

2. Anxiolytics: (Diazapam, Lorazapam, Midazolam) Particularly helpful when patients experience anxiety, panic, or a sense of suffocation. For severe dyspnea, give Valium 2-5 mg or Ativan 1 mg IV every 5-10 minutes until symptoms improve.

3. Cough suppressant: Opioids act centrally as cough suppressants, as does dextromethorphan, which is chemically related to opioids. Inhaled local anesthetics can also be used to suppress cough – aerosolized lidocaine: start with 2 cc of 2% Lidocaine (40 mg) q4h by inhalation, titrate dose upwards as needed. (Caution: lidocaine use may impair gag reflex, increasing risk of aspiration with eating/drinking, and will impair sense of taste).

4. Steroids: IV/PO dexamethasone/prednisone for bronchospasm, SVC syndrome, or diffuse parenchymal metastases.

5. Sedatives: Sedating major tranquilizers (chlorpromazine) or barbiturates (pentobarbital, phenobarbital) may be needed to control dyspnea/anxiety that cannot managed with opioids and benzodiazepines. (Chlorpromazine is strongly anticholinergic and thus may dry respiratory secretions, which may be helpful [see below] or harmful if the results are thick, tenacious secretions which are hard to clear).

6. Anticholinergic agents: Useful when dyspnea is accompanied by large amounts of thin/watery respiratory secretions (oral and lung). Centrally acting agents: scopolamine, chlorpromazine. Peripherally acting: glycopyrrolate. Note: centrally acting agents are more sedating and can cause delirium.

SPECIFIC TREATMENTS
Treat underlying cause when appropriate (e.g. anticoagulation for PE, diuretics for CHF).

ETHICAL CONSIDERATIONS
Health professionals and the public often mistakenly equate use of opioids to ease dyspnea at the end-of-life with euthanasia or assisted suicide. Ethically, the use of opioids is appropriate as long as the intent is to relieve distress, rather than shorten life. However, there is no evidence that reasonable and proper use of opioids and anxiolytics results in patients at the end-of-life ‘dying sooner’. Understanding the patient's wishes for end-of-life symptom control, and providing good communication with both family and other caregivers (e.g. nursing staff), regarding the use of these drugs, is essential to avoid misunderstanding.

REFERENCES
• Smith GP. Terminal sedation as a palliative care: revalidating a right to a good death. Cambridge Quarterly of health Care Ethics. 1998; 7:382-387.
MANAGEMENT OF DYSPNEA

CASE STUDY

Faculty Guide (2 parts)

OBJECTIVES

1. Review the assessment of dyspnea.
2. Develop a differential diagnosis for dyspnea.
3. Develop a patient management plan for dyspnea.
4. Review ethical implications of dyspnea management.

PART I--TEACHING POINTS:

• the need for rapid assessment—this patient cannot wait 1 hour to assess the effectiveness of any changes—the assessment must be continuous until the patient is more comfortable;
• a pulse oximeter reading will likely not change the therapeutic strategy in this case—as the goal is to relieve the symptom, not to treat an O₂ saturation reading;
• use of oxygen masks are often very disturbing to patients with severe dyspnea, especially in the terminal setting, where they should generally be avoided;

Clearly, a rapid assessment for reversible causes is needed
• is the oxygen working?, is the oxygen tubing kinked?
• is there an acute anxiety event in progress?
• is there a new increase in pain?
• is there a pneumothorax?

See outline for list of pharmacological and non-pharmacological options. Non-drug treatments can include:
• increasing the delivered oxygen;
• opening a window or bringing in a fan;
• bedside relaxation techniques.

An appropriate set of drug orders include:
• IV or SQ morphine 4 mg q5-15 minutes PRN;
• IV or Sublingual lorazepam 1 mg q 30 min PRN;

PART II--TEACHING POINTS:

The fear of using drug therapy, drugs with the potential for respiratory depression, to ease the distress of dyspnea, often leads to inadequate symptom control. Health professionals and the public often mistakenly equate use of drugs to ease dyspnea at the end-of-life with euthanasia or assisted suicide. Ethically, the use of these drugs is appropriate, as long as the intent is to relieve distress, rather than shorten life. NOTE: As long as patient or proxy agrees to therapy, there is no justification for...
withholding symptomatic treatment to a dying patient out of fear of potential respiratory depression. Having said this, it should also be pointed out that there is no evidence that reasonable and proper use of such agents (opioids, anxiolytics) results in patients at the end-of-life dying sooner. All major United States medical, ethical and religious organizations recognize the imperative to treat distressing symptoms in the dying patient. All recognize and accept the concept of “double effect”—so that if the intent is to relieve distressing symptoms (and medications are administered and titrated in keeping with reasonable standards of care) and the patient dies, this is considered good medical care, not euthanasia. In contrast, euthanasia is defined as the intent to end a patient’s life through an active means. Although this seems like a fine distinction, the key concept and distinction is the physician’s intent. Understanding the patient's wishes for end-of-life symptom control and good communication with both family and other caregivers (e.g. nursing staff) regarding how and why drugs to relieve distressing dyspnea are administered, is essential to avoid misunderstanding.
Part I
Mr. J has been on your inpatient service for the past four days—admitted with end-stage pulmonary fibrosis. Over the past three weeks he has experienced increasing dyspnea—prompting this admission. On admission his respiratory rate was 24-32, pulse of 110 and pulse oximetry was 89% saturated on 2 liters oxygen by nasal prongs. An evaluation revealed no reversible causes of dyspnea and the pulmonary consultant believes the dyspnea is irreversible, caused by the underlying lung disease. The patient has previously expressed a wish for a No Code status. Current treatments for the dyspnea include oxygen by nasal prongs and hand-held inhalers. He also takes sustained action morphine 60 mg q12 for pain, with good relief of back pain from spinal compression fractures (secondary to long-term steroid use) and has an order for 15 mg of immediate release morphine q 2 PRN pain.

On the fourth hospital day while you are making rounds, a nurse interrupts to tell the team that Mr. J is breathing at a rate of 50/min and is very agitated, sitting on the edge of bed gasping for air. The team goes immediately to see Mr. J and confirms the above findings. The resident tells the nurse to 1) check pulse oximetry, 2) increase the oxygen to a 50% face mask, and 3) call him in one hour to report any changes.

Questions

1. What should be included in your assessment of this acute exacerbation of dyspnea?
2. Is the proposed treatment plan appropriate, if not, why?
3. Suggest an alternative treatment approach; specify non-drug and drug orders (drug/dose/schedule);

Part 2
A new set of orders are discussed which includes morphine 4 mg IV q 10 minutes, prn dyspnea. However, the intern looks very uncomfortable and finally expresses concern saying: “I understand the medical issues here but it still feels like we are doing nothing more than performing euthanasia.”

Question

1. How should you respond to this concern? What arguments will you use? What educational or public policy statements can you use to support the opioid orders?
DELIRIUM

PRE / POST TEST

1. List three findings from the history and mental status examination that distinguish delirium from dementia:
   a) 
   b) 
   c) 

2. List three common metabolic causes for delirium:
   a) 
   b) 
   c) 

3. List three common classes of drugs that can cause delirium:
   a) 
   b) 
   c) 

4. List three non-drug measures that are helpful with a delirious patient:
   a) 
   b) 
   c) 

5. List the two classes of drugs most useful in treating delirium:
   a) 
   b) 

6. Write a prescription for emergency treatment of severe delirium (drug, dose, schedule, route):
   “_____________________________________________________________”

Answers
1. Dementia: long history, normal state of arousal, primary issue is loss of memory; 2. Elevated Calcium, Low Glucose, Renal Failure; 3. Benzodiazepines, opioids, anti-cholinergics; 4. Frequent reminders of date, lights on, family at bedside; 5. Major and minor tranquilizers; 6. Haldol 2 mg po q 8 and 1 mg q1 PRN.
DELIRIUM AT THE END-OF-LIFE

Delirium (a.k.a. acute confusional state) refers to an altered level of consciousness (a.k.a. state of arousal) with associated features of: reduced attention and memory, perceptual disturbances (hallucinations and/or delusions), incoherent speech, and altered sleep/wake cycle.

- Delirium occurs to some degree in virtually all patients before death;
- The cause is often multifactorial, an exact etiology cannot be established in 40% or more of patients;
- Unlike delirium in other situations (acute illness in geriatric patients, for example) delirium in patients close to death is often not reversible;
- Delirium presents as either a: agitated/hyperactive delirium: climbing out of bed, pulling out IVs, picking at air, mumbling speech; or a hypoactive--hypoalert delirium—quiet, very sleepy, mumbling speech.

DIFFERENTIAL DIAGNOSIS
- metabolic—hypoxia, hypercalcemia, hypo or hypernatremia, hypoglycemia, liver or renal failure, dehydration;
- CNS pathology—metastases, infarction, bleeding, infection, seizures;
- drug withdrawal—alcohol, benzodiazepines, barbiturates;
- drug toxicity—benzodiazepines, anticholinergics, opioids, steroids, illicit drugs, alcohol;
- other—systemic infections, fever, heart failure, imminent death, urinary retention or constipation, sleep deprivation, hyperviscosity.

ASSESSMENT
- perform a history and physical examination with a detailed mental status examination;
- distinguish between delirium and dementia; dementia refers to a loss of intellectual function with diminished memory, thinking and judgment (a.k.a. executive functions);
- determine if the patient is in danger of harming themselves or others and if the cognitive dysfunction is distressing to the patient;
- where clinically appropriate, a complete evaluation includes blood, urine, spinal fluid, and radiographic studies to evaluate for metabolic causes, infection or CNS pathology;
- evaluate first for the most easily reversible and common causes: hypoxia, drug effects, metabolic problems such as hypoglycemia, hypoxia, infections, and seizures;
- use a cognitive assessment scale e.g. (mini-mental score).

TREATMENT

Non-Drug Therapy
- frequent reminders of time and date;
- a quiet, well lit room, use a night light;
- ask a family member or health professional to be present continuously to help allay fears and provide patient support;
- physical restraints should be rarely necessary; use only as a brief temporizing measure while instituting non-drug and drug treatments;
- re-hydration—in selected cases, correction of dehydration may improve delirium, especially when delirium is caused by accumulation of opioid metabolites.

Drug Therapy

A. Review current medications. Consider discontinuing suspect medications (drug associated with delirium that were recently started) or switching to less deliriogenic agents. NOTE: Opioids required for management of pain or dyspnea should not be discontinued abruptly. Consider switching to a different opioid or lowering the dose to see if the delirium improves, while monitoring pain/dyspnea relief.
B. A decision should be made as to whether the primary goal of therapy is to clear the sensorium (reverse or ameliorate the delirium) or to provide symptomatic relief for distress and agitation associated with delirium. Relatively non-sedating neuroleptics, such as haloperidol, can be helpful if the goal is to clear the sensorium. Where the delirium is thought to be refractory to such efforts or where such efforts have not been successful, symptomatic relief with a sedating neuroleptic (e.g. chlorpromazine) and anxiolytic agents is often appropriate.

**Neuroleptics (Caution: patients with active seizure disorders)—**

- **haloperidol (Haldol)** 0.5-2 mg PO, IV, SQ (SQ infusion--start at 1 mg/hr)
- **chlorpromazine (Thorazine)** 12.5-50 mg PO, PR, IV, IM

**Benzodiazepines**

- lorazepam (Ativan) 0.5-2.0 mg PO, IV
- diazepam (Valium) 2-10 mg PO, IV, IM
- midazolam (Versed) 2-10 mg IV, SQ; (SQ infusion--start at 1 mg/hr)

**Starting treatment**—Neuroleptics should be used as first-line drugs since benzodiazepines can cause a paradoxical reaction with increasing agitation. There is no current data that newer anti-psychotics are of any benefit compared to the older drugs. If trying to clear the sensorium, consider using haloperidol 1-2 mg PO or SQ q6h with a 1-2 mg q1 hr PRN; titrate upwards as needed (NOTE: contraindicated in Parkinson’s Disease; watch for EPS side-effects.) More sedating neuroleptics, such as chlorpromazine, may be used when sedation is indicated. Starting dose: 25-50 mg q6h PO, PR, IM with 25 mg q1 hr PRN dose; titrate upwards as needed. Benzodiazepines will not help clear the sensorium (and often worsen delirium). They are useful in this setting primarily for their sedating effects.

**REFERENCES**

MANAGEMENT OF DELIRIUM

CASE STUDY

Faculty Guide

OBJECTIVES

1. Review the major components of the delirium assessment.
2. Develop a differential diagnosis for delirium.
3. Develop a patient management plan for delirium.
4. Correctly administer a delirium assessment scale.

TEACHING POINTS

• “Confusion” is a common but imprecise term that can include delirium, dementia, hallucinations, delusions, etc.

• Nighttime cognitive changes (sundowning) are very common in hospitalized patients, especially the elderly, and patients with fever or metabolic disturbances, borderline cognitive function, or those receiving psychoactive medications, particularly benzodiazepines. A diagnosis and appropriate treatment cannot be established without an appropriate assessment.

• Discontinuing the morphine will lead to opioid withdrawal and is not appropriate as no assessment has been done. Ativan (lorazepam) will cause temporary sedation but also has the potential for worsening cognitive deficits and potentiating CNS depressant effects of other psychoactive drugs.

• An appropriate assessment would include a basic neurological examination including a bedside mini-mental exam, review of recent medication changes and assessment for evidence of infection. Further work-up is dependent on the clinical situation and the patient goals (e.g. evaluating potential metabolic change only if treatment would be instituted).

• Treatment options include:
  1) re-orientation, leaving a light on;
  2) use of a major tranquilizer such as haloperidol PRN, for disturbing hallucinations or concern about physical harm;
  3) avoid benzodiazepines; continue opioids.
Case

Mr. J is ending a four day hospital stay for evaluation of progressive dyspnea due to metastatic lung cancer. He is now breathing comfortably on 3 L oxygen and 30 mg of extended release morphine Q12 h. He has been receiving the MS Contin for one week with no toxicity except constipation. The night before planned discharge to home with home hospice care, he becomes “confused”. The houseofficer is called at 2 am and orders 1.0 mg of IV lorazepam and discontinues the morphine.

Questions

1. Describe an appropriate initial assessment for this patient.
2. Develop a rank-ordered differential diagnosis for this patient.
3. Do you agree with the stated treatment plan?—if not, design a new plan.
NAUSEA

LEARNING OBJECTIVES

ATTITUDE

• Self-reflect on past good and bad experiences managing nausea/vomiting.
• Nausea is a common end-of-life symptom that has a significant negative impact on quality of life.

KNOWLEDGE

• Understand the role of the cerebral chemoreceptor trigger zone and vomiting center in the mediation of nausea and vomiting.
• Describe three anatomic sites that send afferent input to the medullary vomiting center.
• Know at least two causes of nausea and vomiting from each of the following categories: gastrointestinal, CNS, drugs, metabolic and psychological.
• Identify one drug, understand its mechanism of action and relative cost, from each of the following classes: a) dopamine antagonist, b) serotonin antagonist, c) glucocorticoid, d) benzodiazepine, e) cannabinoid, f) antihistamine, g) neurokinin-1 antagonist.
• Understand the role of behavioral treatments for nausea.

SKILLS

• Demonstrate communications skills necessary to take a thorough history from a patient with nausea.
• Construct a differential diagnosis for at least three patients with nausea.
• Develop an initial treatment plan for at least three patients with nausea.
• Demonstrate skill at treating nausea that is refractory to an initial treatment approach.
• Understand resources for managing nausea refractory to standard pharmacological management.
• Prescribe anti-emetics in a cost-effective manner.
NAUSEA AND VOMITING

PRE / POST TEST

1. List three anatomic sites that send afferent input to the medullary vomiting center:
   a) 
   b) 
   c) 

2. List four gastrointestinal causes of nausea:
   a) 
   b) 
   c) 
   d) 

3. List the most appropriate class of anti-emetic drugs to use in the following conditions:
   a) elevated intra-cranial pressure:________________________
   b) gastric stasis:________________________
   c) hypercalcemia:________________________
   d) middle ear infection:________________________

4. List one drug that can be used as a continuous infusion for refractory nausea:
   a) 

Answers
1. Frontal cortex, CTZ, vagus nerve; 2. gastritis, bowel obstruction, ulcer, gastric stasis; 3. steroid, promotility drug, dopamine antagonist, anti-histamine; 4. metoclopramide or chlorpromazine.
NAUSEA AND VOMITING

MECHANISM OF VOMITING

Vomiting Center—control center in medulla for coordinating the efferent output of vomiting motor sequence (vomiting reflex).

Sources of afferent input to the Vomiting Center:

- chemoreceptor trigger zone (CTZ)—entry point for emetogenic blood or CSF–borne substances—located in the area postrema outside the BBB; (morphine, hypercalcemia, uremia);
- cerebral cortex–limbic system (e.g. anxiety—anticipatory nausea);
- visceral afferent—(vagal) stimulation—pharynx, GI tract (mechanoreceptors, chemoreceptors, responding to inflammation);
- midbrain ICP receptors—(e.g. raised intracranial pressure);
- vestibular system—(e.g. neurotoxins, morphine, infections).

DIFFERENTIAL DIAGNOSIS

Gastrointestinal—Mechanical obstruction (constipation, intrinsic/extrinsic obstruction), Dysmotility (gastric and bowel stasis, squashed stomach syndrome (compression of stomach, usually by enlarged liver), inflammation (GI infection, GERD, gastritis, abdominal carcinomatosis, acute effect of abdominal radiation or chemotherapy)

CNS—elevated ICP, posterior fossa tumors/bleed, infectious, or neoplastic meningitis;

Drugs—opioids 1–3, chemotherapy 1,4, SSRIs 1, NSAIDs 4, antibiotics 4, iron 4

Metabolic—hypercalcemia, liver failure, renal failure;

Psychological—anxiety, pain, conditioned response (e.g. anticipatory nausea/vomiting).

1. Nausea via stimulation of CTZ
2. Nausea via gastric/gut slowing
3. Nausea via stimulation of vestibular system
4. Nausea via stimulation of gut chemo receptors and vagal afferents

TREATMENT

Non-Drug Therapy

- Behavioral treatments—relaxation, imagery, distraction, music;
- Nasogastric drainage or percutaneous gastrostomy—indicated mainly for gastric stasis obstruction or bowel obstruction refractory to conservative management;
- Fluid management—patients with GI obstruction may benefit from restricting oral fluids and/or discontinuing IV fluids to decrease GI fluid output and vagal stimulation.

Drug Therapy

There are many anti-emetics to choose from. Although often used in a trial and error fashion, certain disorders will respond best to a drug from a specific drug class. These include:

- Movement-related nausea: Antihistamine
- Anxiety/anticipatory nausea: Benzodiazepine
- Tumor-related elevated intracranial press.: Glucocorticoid
- Gastric stasis: Metoclopramide**
- Stimulation of CTZ (drugs, uremia): Dopamine or serotonin antagonist
- Constipation: Laxative

** Indirectly causes acetylcholine release, which stimulates motility. This action antagonized by drugs with anticholinergic properties such as promethazine or chlorpromazine.
## Specific drugs

### Dopamine Antagonists
- **prochlorperazine (Compazine)** PO, IV, IM 10 mg q6; PR 25 mg supp q12
- **chlorpromazine (Thorazine)** PO, IV, IM 25-50 mg q6; PR 25 mg supp q6 (also anticholinergic)
- **haloperidol (Haldol)** PO, IV, SQ, IM 0.5-2 mg q6
- **thiethylperazine (Torecan)** PO, IV 10 mg q8

### Serotonin Antagonists
- **ondansetron (Zofran)** IV 10 mg q8; PO 4-8 mg Q8h
- **granisetron (Kytril)** IV 10 mcg/kg qd, PO 1 mg qd or bid
- **dolasetron (Anzemet)** IV or PO dose is 100 mg qd

### NK1 Inhibitor
- **aprepitant (Emend)** 125 mg day one, 80 mg day 2-3 post chemotherapy
  only approved indication is for highly emetogenic chemotherapy

### Glucocorticoids
- **dexamethasone** PO, IV 2-10 mg q6-q12 (dosing is empiric)

### Benzodiazepines
- **lorazepam (Ativan)** PO, IV 0.5-2 mg q6 (helps to prevent anticipatory N/V)

### Cannabinoids
- **dronabinol (Marinol)** PO 2.5-10 mg q6 (poorly tolerated in elderly)

### Anti-histamines and Anti-Cholinergics
- **promethazine (Phenergan)** PO, IV 25 mg q6; PR 12.5-50 mg supp q6; (antihistaminic, anticholinergic)
- **diphenhydramine (Benadryl)** PO, IV 25-50 mg q6 (antihistaminic/anticholinergic)
- **hydroxyzine (Vistaril)** PO, IM 25-50 mg q6 (antihistaminic/anticholinergic)
- **scopolamine** Patch 1.5 mg over 3 days (anticholinergic)

### Pro-Motility
- **metoclopramide (Reglan)**—standard oral dose of 10 mg is ineffective against most nausea, but it is useful for treating gastroparesis. High-dose IV 1-3 mg/kg is effective against chemotherapy-induced nausea. (Weak antidopaminergic, 5HT₃ antagonism, principal effect – stimulates acetylcholine release)

### Drugs for continuous infusion
- Chlorpromazine—start at 1.0 mg /hr IV, titrate up in 1 mg increments, typical response at 1- 3 mg/hr but can go higher—upper dose defined by unacceptable side effects
- Metoclopramide—start at 1.0 mg/hr IV or SQ

### REFERENCES
- Nausea and Vomiting Resource: http://www.nauseaandvomiting.co.uk/
MANAGEMENT OF NAUSEA / VOMITING

CASE STUDY

Faculty Guide

OBJECTIVES

1. Review the assessment of nausea / vomiting.
2. Develop a differential diagnosis for nausea / vomiting.
3. Develop a patient management plan for nausea / vomiting.

TEACHING POINTS

- The care team knows more about the work-up for suspected cancer than they do about the patients’ chief complaint and subsequent symptom management.

- The complaint of “nausea” may represent one of many different sensations/symptoms/syndromes including: GI reflux, anorexia, labyrinthine dysfunction, regurgitation, bowel obstruction, medication effects, anxiety (butterflies), etc. The assessment provided in the case is incomplete to determine exactly what the patient means by “nausea”. Only through a more detailed assessment can a differential diagnosis be established.

- The patient has constant nausea—if felt to be of gastrointestinal cause, around-the clock anti-emetics, at least for 24 hours, may be more appropriate than prn orders. There should be better assessment and documentation of response after a PRN anti-emetic is given to know if the prescribed medication is effective.

- Prochlorperazine (Compazine) is a reasonable starting drug for nausea where a dopamine antagonist may be helpful (see outline) or for nausea of unclear etiology. When this is not successful, re-assessment is needed and targeted drug therapy used whenever possible. Gastric compression and associated dysmotility (squashed stomach syndrome due an enlarged liver) is a possible cause of the nausea. Early satiety with eating would be a strong hint in favor of dysmotility. Metoclopramide, a prokinetic, could be considered as an alternative drug in this case.
Case

Mrs. L is admitted to your service late one evening because of 4 days of nausea and poor oral intake. She has a past history of Dukes C1 colon cancer with no known metastases. Her physical exam is significant for mild pallor, dehydration and a hard, enlarged, nodular liver. Abdominal x-rays showed a non-specific gas pattern and an enlarged liver. Trauma surgery saw the patient in the ER prior to admission and did not feel this was a surgical abdomen.

You think that Mrs. L has metastatic colon cancer. IV fluids were begun, an abdominal CAT scan was ordered along with a GI consult for a liver biopsy and an Oncology consultation to discuss potential chemotherapy options. On rounds the next morning Mrs. L says that she is still nauseated and that this feeling is constant. Admission orders include: prochlorperazine (Compazine) 10 mg POq6 PRN nausea. Review of the nursing notes show that only one dose of prochlorperazine was given shortly after admission (12 hours ago) and that there has been no recorded vomiting.

Questions

1. Describe a differential diagnosis for nausea in this patient.
2. Is this an appropriate initial treatment plan? If not describe changes you would make?
3. If the nausea fails to respond to prochlorperazine what would you do next?
CONSTIPATION

LEARNING OBJECTIVES

ATTITUDE

• Self-reflect on the management of constipation in patients near the end-of-life.
• Constipation is a common end-of-life symptom that has a significant negative impact on quality of life.

KNOWLEDGE

• Describe at least five symptoms commonly associated with constipation.
• Describe at least two causes of constipation from each of the following categories: a) mechanical obstruction; b) drugs; c) metabolic; d) neurologic; e) misc.
• Know when to order diagnostic tests to help establish the cause of constipation.
• Understand the mechanism of action and common side-effects of drugs from the following categories: a) bulk laxatives; b) large bowel stimulants; c) detergent laxatives d) osmotic laxatives; e) lubricants; and f) pro-kinetic drugs.
• Describe which drugs are not indicated for patients with poor mobility/poor oral intake.
• Understand when it is appropriate to begin prophylactic constipation treatment.

SKILLS

• Demonstrate communications skills necessary to take a thorough history from a patient with constipation.
• Construct a differential diagnosis for at least three patients with constipation.
• Demonstrate awareness of when to order abdominal x-rays.
• Develop an initial treatment plan for at least three patients with constipation.
• Demonstrate ability to choose and titrate an initial drug management plan.
• Demonstrate skill at treating constipation that is refractory to an initial treatment approach.
• Describe how to prescribe a prophylactic bowel regimen in a patient starting opioid analgesics.
CONSTIPATION
PRE / POST TEST

1. List three classes of drugs that cause constipation:
   a) 
   b) 
   c) 

2. List one drug (generic and trade name) from each of the following laxative categories:
   a) bowel stimulant:______________________________
   b) detergent laxative:____________________________
   c) osmotic laxative:______________________________
   d) bulk laxative:______________________________

3. List one laxative that is generally not recommended because of side effects:
   a)

4. Bulk laxatives are contraindicated in patients who cannot increase their:
   ________________________________

5. A good prophylactic drug regimen for patients starting opioid analgesics would be (write drug(s), dose(s) and schedule):
   ________________________________

Answers
1. Iron, vinca alkaloids, anti-cholinergics; 2. bisacodyl, docusate, mag citrate, lactulose, Metamucil; 3. castor oil; 4. Fluid intake; 5. senna 2 tabs q day.
CONSTIPATION

DEFINITION

Acute: Less than 6 months, decrease in frequency or increase in difficulty initiating a bowel movement.

Chronic: Greater than 6 months, less than 3 BM’s per week.

BOWEL FUNCTION

Four interrelated factors contribute to bowel function: 1) water content of stool, 2) gut motility, 3) solid stool content (fiber, bacteria etc.) and 4) resistance (or lack thereof) to passage of stool.

1. Water Content: ~8-9 L/day fluid enters the gut; only 1 L/day reaches colon after small bower resorption. Daily stool content is ~200 ml/day; +/- 100 cc/day will lead to constipation or diarrhea. Slow gut transit results in more water being absorbed (constipation). Fast transit results in less water being absorbed (diarrhea). The presence of osmotically active particles in the gut results in water being retained in the stool (looser stools).

2. Motility. Gut motility is affected by extrinsic nerve stimulation and intrinsic systems speeding up or slowing down the gut. Greater motility is associated with looser stools (less water absorbed) and decreased motility with harder stools.

A. Extrinsic System
   • Sympathetic outflow: Slows gut motility. T5-L2: Inhibitory function via noradrenaline;
   • Parasympathetic outflow: Speeds up gut motility. Cranial distribution via Vagus N (stomach-splenic flexure); Sacral (S2-S4) (descending colon to anus): Promotes peristalsis and gut fluid secretion.
   • Supratentorial Control: medial prefrontal and anterior cingulate gyrus: timing and initiation of defecation.

B. Intrinsic System
   Binding of certain gut receptors increase gut motility (acetylcholine, motilin) and others decrease motility (mu (opioid) receptors, dopamine). Nerve plexi in the wall of the gut respond to signals from these and other receptors. Mechanical stretch stimulates motility.

3. Stool volume. Increased stool volume results in increased motility (up to a point). Where the diet is lacking in fiber, bulk fiber can alleviate constipation by increasing stool volume. However, excessive gut dilation impedes motility. Bulk laxatives, especially when taken with inadequate water or where there is a primary motility disorder, can result in large impactions.

4. Resistance to stool passage. Mechanical obstruction and pain with defecation (and resulting anal tightening) interfere with stool passage. Conversely lubricants (mineral oil enemas) and detergent laxatives (docusate) may reduce resistance and ease stool passage.

SYMPTOMS COMMONLY ASSOCIATED WITH CONSTIPATION

• increased passage of gas
• abdominal pain; rectal pain
• change in stool caliber
• oozing of liquid or stool
• anorexia; early satiety, nausea
DIFFERENTIAL DIAGNOSIS

1. Mechanical obstruction
   - intraluminal—colon cancer
   - extraluminal—malignant ascites/ peritoneal carcinomatosis (ovarian, colon), scaring

2. Drug-Induced
   - opioids: fentanyl and methadone may be less constipating than others
   - anticholinergics / tricyclic antidepressants / neuroleptics / anti-histamines
   - chemotherapy, esp. Vinca drugs: (Vincristine, Vinblastine)
   - 5HT₃ antagonist antiemetics
   - L dopa
   - calcium channel antagonists
   - iron / aluminum containing antacids / barium
   - laxative abuse

3. Metabolic
   - hypercalcemia; hypokalemia
   - diabetes (neuropathy); hypothyroidism; uremia

4. Neurological
   - spinal cord injury: high (quad): constipation common; Cauda equina injury: bowel atony with severe constipation and overflow incontinence due to parasympathetic denervation of sigmoid/rectum
   - paraneoplastic autonomic neuropathy (e.g. small cell lung cancer, carcinoid tumors)
   - polymyositis

5. Miscellaneous
   - dehydration / inactivity / bed rest
   - confusion / depression
   - pain on defecating--hemorrhoids, anal fissure, infection
   - generalized pain
   - irritable bowel syndrome
   - loss of normal bowel routine
   - inadequate privacy/positioning (use of bed pan)

MANAGEMENT

General measures
   - prophylaxis whenever possible
   - reverse treatable causes
     - rectal examination to exclude fecal impaction
     - abdominal exam / x-rays may be needed to exclude bowel obstruction
   - restore daily bowel routine
   - increase fluids and activity as much as tolerated by clinical condition

Drug therapy—drug classification

Large bowel stimulants (senna, bisacodyl, cascara, casanthranol, phenolphthalein)
   - directly increases bowel motility (requires intact nerve plexi to work);
   - requires transformation in liver (phenolphtalein, bisacodyl) or gut (senna, cascara);
   - abdominal cramps and increased gas are common;
   - senna, available as granules, pills or liquids, is commonly used in "natural" preparations;

Detergent laxatives (docusate, castor oil) also referred to as "wetting agents"
   - decreases surface tension, allows greater absorption of water/fat into dry stool;
   - docusate is a weak laxative (available as a sodium salt (Colace), or calcium salt (Surfak);
• docusate should rarely be used as a sole agent for constipation. A recent systematic review suggests that docusate also has minimal added value when used in addition to other more potent laxatives;
• docusate tastes bad (like concentrated soap). Liquid docusate should not be given by mouth. Pills may dissolve in patients’ mouths (dementia patients high-risk) and should be avoided in this population.

**NOTE**: castor oil is not recommended due to expense, bad taste, bowel stimulant effects.

**Bulk laxatives** (psyllium, methylcellulose, polycorbophil, bran)
• soluble and insoluble fiber supplements; inexpensive;
• requires increased fluid intake for activity;
• abdominal cramps, increased gas and allergic reactions can occur;
• best use in ambulatory pts with reasonable gut motility without bowel obstruction who can take large volumes of liquid.
• **NOTE**: when used without increased fluid intake, constipation will worsen;

**Osmotic laxatives** (lactulose, sorbitol, glycerin, Golytely, Miralax, mannitol)
• non-absorbable sugars—work via osmotic effect in small and large bowel;
• lactulose is expensive, bad tasting, increases abd. gas; sorbitol is a less expensive alternative; (Taste improved by mixing with apple juice);
• GoLytely, Miralax (Polyethylene Glycol)used as a bowel prep can be given in smaller doses for constipation; MiraLax (powder) has an advantage of being completely tasteless and can be added to any volume of fluids or food;

**Saline laxatives** (magnesium citrate or phosphate, sodium phosphate)
• contain poorly absorbed salts and work osmotically. They also increases gastric, pancreas and small bowel secretions;
• **NOTE**: do not use magnesium or phosphate products in renal failure; do not use sodium products in heart/liver/kidney failure;
• glycerin suppositories osmotically draw in water and lubricate hard stool.

**Prokinetic drugs** (bethanecol, neostigmine, metoclopramide)
• Decreases bowel transit time via increased motility. Of limited utility for colonic hypomotility due to toxicities (bethanecol, neostigmine – cholinergic, metoclopramide – dopaminergic).

**Lubricant** (mineral oil)
• can cause malabsorption, perianal irritation, and lipoid pneumonia aspiration with oral intake; Enemas may be useful for hard stools encountering resistance in passage.
• **NOTE**: Do not give orally or administer with docusate products

**Enemas / Suppositories**
• bisacodyl supp. (10 mg)--action in 15-60 minutes
• glycerin supp.--action in 30 minutes
• sodium phosphate enema (Fleet)
• tap water, oil retention, soap suds enemas

**Opioid Antagonists** (methylnaltrexone)
• Peripheral opioid mu antagonist indicated for treatment of opioid-induced constipation in patients with advanced illness who are receiving palliative care.

**Other**
• Octreotide has shown efficacy in managing constipation from the paraneoplastic autonomic neuropathy in small cell lung cancer.

"Natural" Laxatives
Many home recipes and/or natural food stores have products that contain a combination of raisins, prunes, applesauce, figs, and dates, with or without senna (a.k.a. “Power Pudding”).

Improving Palliative Care. Weissman DE, Ambuel B and Hallenbeck, J. Copyright 2007, Medical College of Wisconsin.
Trade Names--all available Over The Counter except for lactulose and PEG products

- Metamucil, Perdiem, Fiberall (psyllium);
- Citrucel (methylcellulose)
- Fiberall, Fibercon (calcium polycarbophil)
- MOM (magnesium phosphate)
- Colace (docusate sodium); Surfak (docusate calcium)
- Senokot (senna); Senokot S (senna and docusate)
- Peri-Colace (docusate and casanthranol)
- Ducolox (bisacodyl); Carter's (bisacodyl)
- Nature's remedy (cascara)
- Ex-Lax, Feen-a-Mint (phenolphthalein); Correctol, Doxidan (phenolphthalein and docusate)
- Haley MO (mineral oil and magnesium hydroxide)
- Magnesium citrate (magnesium citrate)
- Chronulac, Cephulac (lactulose)
- Fleets Enema (sodium phosphate)

**DRUG THERAPY--MANAGEMENT PLAN**

**NOTE:** the following agents should generally be avoided: mineral oil, castor oil, phenolphthalein

1. **For prophylaxis (e.g. pt. starting opioids) or for recent constipation start:**
   - a) psyllium product--**NOTE:** only if patient able to increase fluid intake;
   - b) senna product or MOM; docusate can also be added;
   - c) increase dose of each product as needed (no upper dose limit except MOM in patients with renal failure); if no BM at 8-12 Senokot/day or 60-80 cc MOM/day go to 2.

2. **For constipation refractory to 1. check for fecal impaction (see 4.); start:**
   - a) bisacodyl (Ducolax) po 5 mg; up to 3 tabs tid;
   - b) if no response use 1 Ducolax supp.

3. **For constipation refractory to 2. check for fecal impaction (see 4.); start:**
   - a) magnesium citrate 8 oz. or
   - b) lactulose or sorbitol or Miralax or Fleet enema
   - c) methylnaltrexone in opioid induced constipation

4. **For patients impacted:**
   - a) use sedatives/analgescics to relieve stress/pain of disimpaction;
   - b) lubricate rectum--glycerin supp. or oil-retention enema;
   - c) manually disimpact rectum;
   - d) enemas to clear rectum;
   - e) increase daily oral laxative program.

**REFERENCES**

MANAGEMENT OF CONSTIPATION

CASE STUDY

Faculty Guide

OBJECTIVES

1. Describe the assessment of constipation.
2. Develop a differential diagnosis for constipation.
3. Develop a patient management plan for constipation.

TEACHING POINTS

• The differential in this patient is likely to include:
  a) opioid use
  b) inactivity
  c) spinal cord damage from compression fractures
  d) loss of normal bowel routine
  e) inadequate privacy/positioning (use of bed pan)
  f) pain

• Emphasize the importance of constipation as a source of patient suffering; understand the need for close attention to bowel habits, especially when opioids are used;
• Emphasize the need for frequent (QD) patient assessment of bowel function;
• Assessment should include a description of what the patient means by “constipation” and if there are other associated symptoms (e.g. straining, gas);
• Assessment should include an abdominal and rectal examination, especially in the this patient, to assess rectal tone and to rule out impaction;
• Docusate is a very weak laxative—acts only as a mild detergent (wetting) agent;
• Regular use of a bowel stimulant (MOM or senna) is needed for patients taking opioids;
• Increasing fiber is not indicated unless patients can increase fluid intake;
• Review Content Outline for suggested treatment schema for this patient.
Case

Mrs. H is in the hospital for pain management after suffering vertebral compression fractures. She has been receiving oxycodone with acetaminophen, 2 tabs every four hours. By the third hospital day her pain is well controlled and she is ready for discharge but on rounds that morning, she says that her biggest problem is constipation. She has not had a BM for 10 days and she is feeling very “bloated”. The medication sheet lists docusate sodium 1 tablet qd.

Questions

• Describe a differential diagnosis for constipation in this patient
• Write a new orders for management of constipation for this patient