EPEC for Veterans

Education in Palliative and End-of-life Care for Veterans

Trainer’s Guide

Module 6a

GI Symptoms

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Module 6a trainer’s notes

Principal message
Facility with the management and treatment of common physical symptoms encountered in end-of-life care is important if quality of life and relief of suffering are to be achieved.

Module overview
Module 6a presents an approach to the assessment and management of a number of gastrointestinal (GI) symptoms. It includes:

- Nausea and vomiting
- Constipation
- Diarrhea
- Bowel obstruction
- Ascites
- Musositis

Each section covers the pathophysiology, assessment, and management of common GI symptoms.

Preparing for a presentation

1. Assess the needs of your audience
Choose from the material provided in the syllabus according to the needs of your expected participants. It is better for participants to come away with a few new pieces of information, well learned, than to come away with a deluge of information, but remembering nothing.

2. Presentation timing
Allow sufficient time to collect participants’ demographic data and complete the pre-test.

The suggested timing for each part of this module is:

<table>
<thead>
<tr>
<th>Part</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>2-3 minutes</td>
</tr>
<tr>
<td>Presentation</td>
<td>35 minutes</td>
</tr>
<tr>
<td>Summary</td>
<td>2-3 minutes</td>
</tr>
<tr>
<td>Post-test &amp; Evaluation</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Total</td>
<td>44-46 minutes</td>
</tr>
</tbody>
</table>
3. Number of slides: 60 (for all the covered GI symptoms)

4. Preparing your presentation

The text in the syllabus was not designed to be used as a prepared speech. Instead, the slides have been designed to trigger your presentation. Although the slides closely follow the text of the syllabus, they do not contain all of the content. Their use presumes that you have mastered the content. You may want to make notes on the slide summary pages to help you prepare your talk in more detail and provide you with notes to follow during your presentation.

You will not want to use all of the slides for a single 45-minute session. You will only be able to cover 1 or possibly 2 of the symptoms well. By giving a handout, you can refer participants to it for the information you choose not to cover. Alternatively, you might choose to present this material in several sessions in order to cover all of the symptoms comprehensively.

Practice your presentation using the slides you have chosen, and speaking to yourself in the kind of language you expect to use, until it is smooth and interesting and takes the right amount of time.

5. Preparing a handout for participants

The syllabus text and slides in the Trainer’s Guide were designed to be reproduced and provided to participants as a handout, either in its entirety, or module by module. If the entire curriculum is not being offered, please include the following in each handout:

- EPEC for Veterans Front Cover Page
- EPEC for Veterans Acknowledgment Pages (to acknowledge the source of the material)
- Syllabus and slides for Module 6a

6. Equipment needs

- computer with DVD capability or separate DVD player
- flipchart and markers for recording discussion points

Making the presentation

1. Introduce yourself

If you have not already done so, introduce yourself. Include your name, title, and the organization(s) you work for. Briefly describe your clinical experience related to the information you will be presenting.
2. Introduce the topic
Show the title slide for the module. To establish the context for the session, make a few broad statements about the importance of managing symptoms as a clinical skill. Identify which symptoms you will be covering. Tell participants the format and time you will take to present the session. Identify any teaching styles other than lecture that you intend to use.

3. Review the session objectives
Show the slide with the session objectives listed. Read each objective and indicate those that you are planning to emphasize.

4. Show the trigger tape or present the clinical case
After reviewing the objectives for the session, show the trigger tape or present one of the clinical cases below. It has been designed to engage the audience and provide an appropriate clinical context for the session. It was not designed to demonstrate an ideal interaction, but to ‘trigger’ discussion.

Clinical case (Part 1: Nausea and vomiting)
P.T. is an 85-year-old farmer with diabetes, end-stage heart disease, gastroesophageal reflux disorder, chronic shoulder pain from a war injury, stage 4 chronic kidney disease, and a history of alcoholism. His shoulder pain is well controlled with extended-release morphine 30 mg PO bid, and gabapentin 300 mg PO q HS. However, he complains of constant nausea that limits his ability to eat.

Clinical case (Part 2: Constipation)
M.R. is 79-year-old Veteran with advanced COPD (O₂ dependent and wheelchair bound), mild Alzheimer disease with neuropathic phantom-limb (from a left below-the-knee amputation) who developed subacute onset of increased abdominal pain with intermittent nausea. He had been on long-acting morphine 60 mg PO q 12 hr and gabapentin 300 mg PO q 8 h for pain, and promethazine 12.5 mg PO q 6 hr prn for nausea. He had been eating, had flatus, and had been having a daily soft bowel movement. He denied fevers or chills. There was no other significant past medical history and review of systems was otherwise negative.

On exam, bowel sounds were present but diminished. There was gross abdominal distention that was dull to percussion, no shifting dullness and diffuse abdominal tenderness to palpation without rebound. Rectal exam revealed normal sphincter tone and soft, claylike stool in the vault.
Clinical case (Part 3: Diarrhea)

S.D. is a 79-year-old Korean war Veteran with a history of multiple transient ischemic attacks (TIAs) and cerebrovascular accidents (CVAs) resulting in right side weakness, who has also had 3 hospitalizations in the last year for congestive heart failure (CHF) exacerbations. He reports frequent watery stools. His daughter reports he is unusually unsteady on his feet when he gets up to walk. He has been incontinent once, and slipped and fell. He says he feels bloated and ‘gassy’ and that he is exhausted.

Clinical case (Part 4: Bowel Obstruction)

C. J. is a 72-year-old Korean Conflict Veteran with stage IV colon cancer (1 year s/p surgical resection of the primary lesion) who is admitted with both continuous and colicky abdominal pain, nausea and vomiting, and abdominal distension. The diagnosis of bowel obstruction is established based on clinical signs and symptoms and confirmed with abdominal x-rays demonstrating air-fluid levels. An exploratory laparotomy demonstrates the presence of mechanical obstruction and peritoneal carcinomatosis. Surgical intervention is technically impossible due to adhesion of the tumor to the abdomen wall and the presence of carcinomatosis.

Clinical case (Part 5: Ascites)

Q.H. is 44-year-old disabled truck driver admitted to a hospice program with hepatocellular carcinoma and ethanol-induced cirrhosis. A diminished albumin level and elevated prothrombin time are consistent with impaired hepatic synthetic function. Comorbidities related to cirrhosis include esophageal varices, a single, recent episode of hepatic encephalopathy, coagulopathy, and massive ascites. Although abstinent from ethanol for the preceding five years, he is not a liver transplantation candidate because of significant cardiopulmonary disease.

Medications include furosemide 40 mg PO tid, spironolactone 200 mg PO bid, lactulose 30 mg PO tid, thiamine 100 mg PO daily, folate 1mg PO daily, omeprazole 40 mg PO daily, citalopram 20 mg PO daily, albuterol inhaler 2 puffs q 4 h PRN, lisinopril 20 mg PO daily, and O₂ 2 l/min. The physical examination shows no jugular venous distension. The abdomen is obese, but shifting dullness and a fluid wave are demonstrable. There is no asterixis. Laboratory examination is remarkable for a partial prothrombin that is elevated by ≈ 4 seconds above normal.

Discussion

If the discussion is slow to start, you may want to ask more direct questions, like:

- Have they had similar patients?
- How did the patient react to the clinician’s questions?
- How did the clinician start? What was well done? What was missing?
• What did the clinician do to foster a comfortable atmosphere?
• How did the physician address the patient’s concerns?

Use the discussion to set the stage for the material to follow. Don’t let the discussion focus on a critique of the technical quality of the trigger tape or how ‘real’ the players seemed. If the participants don’t like something that was said or done in the trigger tape, ask them how they would do it themselves.

Setting limits to discussion time

Limit discussion of each scene of the trigger tape to no more than 5 minutes, then move on to the presentation. To help move on if the discussion is very engaged, try saying something like:

• Let’s hear two last points before we move on.
• Now that you have raised many of the tough questions, let’s see how many practical answers we can find.

5. Present the material

Recommended style: interactive lecture

An interactive lecture will permit you to engage your audience, yet cover 2 to 3 GI symptoms within 45 to 60 minutes. Identify the symptoms you plan to cover and select the slides to go with those symptoms. Use your own case vignettes to illustrate clinical applications for the information presented.

Alternative style: Case-based

If you have mastered the material and the method, a case-based approach to teaching this module can be very effective.

There is a case vignette at the beginning of each symptom in this module. Ask a participant to read the vignette. In a Socratic way, ask participants to help ‘solve’ the cases. Ask them questions about assessment and management. Ask them to explain the known pathophysiology that underlies the management of each symptom. Write points on the overhead or flipchart. Draw diagrams yourself. Don’t be concerned about your artistry, the points will come across.

Use the discussion to interweave the key take-home points from the syllabus.

6. Key take-home points

Nausea/vomiting

1. Nausea is better prevented than treated once it emerges.
2. Use antiemetic agents for their neurotransmitter blocking functions; combine them strategically.

3. Untreated nausea may become ‘learned’ and refractory to neurotransmitter-based antiemetics therapy.

**Constipation**

4. Assess what is normal for the Veteran before deciding on a treatment plan. Don’t wait for the Veteran to bring up the symptom – ask about it.

5. Combine agents with different mechanisms of action.

6. Titrate senna and bisacodyl to relieve and prevent opioid-induced constipation

7. Tailor pharmacologic treatment to the suspected underlying cause of constipation.

**Diarrhea**

8. Diarrhea can be a serious symptom and affect quality of life

9. Ask for specific details to ascertain the impact of the diarrhea.

10. Management of serious diarrhea begins with a thorough work-up and an opioid to slow peristalsis. Titrate to effect.

**Bowel Obstruction**

11. First, evaluate the Veteran with bowel obstruction for a definitive operative solution.

12. Stent placement may be a reasonable alternative in selected Veterans.

13. If the Veteran is inoperable, satisfactory symptom control is possible with medications.
   a. Antisecretory agents, such as octreotide, may be effective alone.
   b. Antidopaminergic antiemetics in combination with anticholinergics and opiates are an alternative.

14. Diverting procedures may be needed for refractory symptoms.

**Ascites**

15. Increased portal pressures, direct secretion into the abdomen, or a combination of these two mechanisms can result in ascites.

16. Ascites related to portal hypertension is more likely to respond to diuretic therapy

17. Ascites related to malignancy usually requires paracentesis and an external catheter.

**Mucositis**

18. Provide adequate analgesia.
19. Cleansing with dilute soda or salt water frequently is as effective as chlorhexidine.

20. Offer easy to swallow foods and fluids. Veterans may need parental analgesia and hydration support if intake is severely impaired.

7. **Summarize the discussion**

Briefly review each part of the presentation. Recap 2 or 3 of the most important points that were discussed.

8. **Post-test/evaluation**

Ask the participants to evaluate the session.
Module 6a: GI Symptoms

Overall introduction

Most patients in palliative care suffer from a number of common symptoms as well as pain. This module discusses common GI symptoms experienced by Veterans in palliative care. These include:

- Nausea and vomiting
- Constipation
- Diarrhea
- Bowel obstruction
- Ascites
- Mucositis

Objectives

After studying this module, clinicians will be able to:

- discuss pathophysiology of common GI symptoms in palliative care;
- discuss assessment strategies; and
• describe management strategies.

Part 1: Nausea and vomiting

Clinical case

P.T. is an 85-year-old farmer with diabetes, end-stage heart disease, gastroesophageal reflux disorder, chronic shoulder pain from a war injury, stage 4 chronic kidney disease, and a history of alcoholism. His shoulder pain is well controlled with extended-release morphine 30 mg PO bid, and gabapentin 300 mg PO q HS. However, he complains of constant nausea that limits his ability to eat.

Introduction

Nausea is an unpleasant subjective sensation of being about to vomit. Vomiting is the reflex expulsion of gastric contents through the mouth. Nausea may be present without vomiting or vice versa.

The awareness of nausea, the experience of vomiting, the inability to keep food or fluids down, the associated acid and bitter tastes, and the unpleasant smells associated with vomiting can be distressing for Veterans, families, and caregivers. There are many potential causes for both nausea/vomiting in a Veteran with advanced chronic disease. In
this section, the management of the symptom of nausea is discussed and some specific etiologies are considered in that discussion.\(^3\)

Certain diagnoses and treatments are associated with significant rates of nausea and vomiting as follows: 33% for end-stage kidney disease, 17% for HIV, 40-70% for advanced cancer, 10-40% for opioid therapy. Radiation and chemotherapy-associated nausea/vomiting rates depend on the agents and fields affected.\(^1,4,5,6,7\)

**Pathophysiology**

Two organ systems are particularly important in nausea/vomiting: the brain and the GI tract. These are shown schematically in Figure 1 below.
The motor function of the GI tract is controlled at three levels: the parasympathetic and sympathetic nervous systems, enteric brain neurons, and smooth muscle cells. The gastric lining, the chemoreceptor trigger zone (CTZ) in the floor of the fourth ventricle, the vestibular apparatus, and the cortex are all involved in the intricate physiology of nausea. The neuromuscular reflex that constitutes the final common pathway after stimulation from one or more of these areas emanates from the vomiting center.8

Stimulation is mediated through the neurotransmitters serotonin, dopamine, acetylcholine, and histamine. All four neurotransmitters can be demonstrated in the chemoreceptor trigger zone. Although all are present in the lining of the GI tract, serotonin is particularly important. Acetylcholine and histamine are important in the vestibular apparatus.

Nausea/vomiting that is mediated by the cortex is more complex and is not associated with specific neurotransmitters. Cortical responses seem to be learned responses, e.g., the anticipatory nausea associated with chemotherapy, nausea related to anxiety, etc.

A thorough assessment of nausea and vomiting is crucial to understanding which of the potential etiologies is present, what the likely pathophysiology is, and what the most effective pharmacologic approach will be. Different causes will require different interventions if the symptoms are to be controlled effectively.

Ask the Veteran to describe the nausea with the following questions:

- “When does it occur?”
- “Is it acute or chronic?”
- “Intermittent or constant?”
- “Associated with sights or smells or events?”
- “What happens after eating?”
- “Do you vomit right after the food is swallowed [a cortical learned response or anxiety-related], after about 45 minutes [associated with delayed gastric emptying
or a ‘squashed stomach’ syndrome from an enlarged liver], or hours after eating [suggesting intestinal or bowel involvement]?"

- “Does vomiting make it better?”
- “What are your normal bowel patterns?” (Constipation is a frequently missed cause of chronic nausea.)
- “What medications have been tried? With what frequency?”
- “Have you stopped or started any other medications recently?”
- “Is the nausea associated with any particular medication? For example, do you become nauseous after each oxycodone pill or every time he/she takes an antibiotic?”

The physical examination and selected studies help confirm impressions from the history. For example, changing posture or head position may reproduce or worsen nausea, implicating the vestibular apparatus. Funduscopic examination may confirm increased intracranial pressure. Abdominal examination that shows the absence of bowel sounds suggests obstruction.

There are a range of diagnostic studies that can be considered. A plain x-ray of the abdomen looking for presence and quantity of stool and evidence of ileus is frequently useful. Abdominal ultrasound for enlarged liver or ascites assessment, CT scans of the head or abdomen, and motility studies may be useful in selected cases.

Three specific etiologies of nausea that are common in palliative care are discussed below: associated opioid-induced nausea, chemotherapy-associated nausea and radiation-associated nausea.

**Opioid-associated nausea**

Opioids are associated with nausea in 10-40% of patients. The mechanism is thought to be due to direct effects in the chemoreceptor trigger zone and the vestibular apparatus and gastric stasis. Antidopaminergics, antihistamines, anticholinergic and antiserotonergic drugs have all been observed to be effective. Fortunately, Veterans will generally develop pharmacological tolerance to this side effect within 5-7 days of initiating therapy, and the antiemetics can be discontinued. For some Veterans, changing to a different opioid is also effective.

Nausea that emerges after chronic use is most likely mediated through diminished GI tract motility and/or constipation causing pseudoobstruction. Management is best directed at increasing GI tract motility and relieving constipation. This includes the use of metaclopramide, and if that is unsuccessful, methylaltrexone. The details of methylaltrexone use are discussed in the section on Constipation later in this module.
Chemotherapy-associated nausea/vomiting

Three distinct types of chemotherapy-associated nausea/vomiting have been defined: acute, delayed, and anticipatory.\(^8\)

**Acute nausea/vomiting** occurs within the first 24 hours after chemotherapy. It usually starts within 1-2 hours and peaks at 4-6 hours.\(^8,12\)

**Delayed nausea/vomiting** occurs more than 24 hours after chemotherapy. With cisplatin, this peaks 48-72 hours after therapy and then gradually subsides for 2-3 days. It is also seen with carboplatin, cyclophosphamide, and the anthracyclines. The antiserotonergic and antidopaminergic medications have minimal effect on delayed nausea. The antineurokinin class is the first to show definitive, albeit small, effect on this syndrome.

**Anticipatory nausea/vomiting** is a conditioned response to previous experiences. If acute and delayed nausea are prevented, anticipatory nausea does not occur. Once it occurs, it is a learned response—it is not mediated by the usual emetic neurotransmitters. Management is challenging. Once established, benzodiazepines for their anxiolytic and amnestic properties are most useful. Psychotherapy with a focus on cognitive/behavioral interventions may be adjunctive.

Most writers have divided chemotherapeutic agents into five emetogenic categories based on the incidence of acute nausea (see Table 2 below). As can be seen, each regimen has a specific combination of antiemetic recommended for use. Although many Veterans in palliative care may not be getting active chemotherapy, knowledge of previous regimens and medications used to combat nausea may be helpful.
Table 2: Antiemetic regimens based on emetogenic potential of chemotherapy

<table>
<thead>
<tr>
<th>Emetogenic class</th>
<th>Medications</th>
<th>Incidence of nausea</th>
<th>Regimen to prevent nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Capecitabine, Rituximab</td>
<td>Minimal (&lt;10%)</td>
<td>PRN antidopaminergic</td>
</tr>
<tr>
<td>II</td>
<td>Gemcitabine, Paclitaxel</td>
<td>Low (10-30%)</td>
<td>Dexamethasone 20 mg orally x 1</td>
</tr>
<tr>
<td>III</td>
<td>Doxorubicin, Carboplatin</td>
<td>Mild (30-60%)</td>
<td>5 HT-3 inhibitor + Dexamethasone 20 mg orally x 1</td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td>Moderate (80-90%)</td>
<td>5 HT-3 inhibitor + lorazepam 1 mg orally + Dexamethasone 20 mg x 1</td>
</tr>
<tr>
<td>V</td>
<td>Cisplatin, high dose cyclophosphamide</td>
<td>High (&gt; 90%)</td>
<td>5 HT-3 inhibitor + lorazepam + Dexamethasone 20 x 1 + Aprepitant (NK inhibitor)</td>
</tr>
</tbody>
</table>

**Radiation-associated nausea**

The incidence of radiation-associated nausea is related to the irradiated region. It is generally mild in radiation therapy to the head and neck and extremities, moderate in radiation therapy to the thorax, abdomen and pelvis and severe in the setting of total body irradiation (TBI). In patients receiving TBI, pre-treatment with a 5 HT-3 antagonist is recommended. Dexamethasone is an adjunctive agent in this setting. For moderate nausea, treatment with a 5 HT-3 agent or dopamine antagonist is recommended.\(^{13,14}\)

**Bowel obstruction**

The nausea associated with bowel obstruction is associated with reverse peristalsis in response to accumulated fluid behind the obstruction. This is discussed in detail later in this module in the section on bowel obstruction.
This module focuses on the general symptomatic management of nausea/vomiting. It does not provide detail of all the possible causes or specific treatments to reverse each of these etiologies.

In the management of nausea/vomiting, it is frequently not possible to identify or specifically correct the underlying etiology. Time-limited therapeutic trials may provide both relief and clues to underlying causes. When causes are known, the burden of the disease-modifying intervention may also outweigh its potential benefit.

Table 1 relates major causes of nausea/vomiting to their principal site of action and lists the “11 M’s” of emesis. This clarification is intended to set the stage for the rational use of the antiemetics, which can be classified by their principal site of action.
<table>
<thead>
<tr>
<th>Etiology</th>
<th>Pathophysiology</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metastases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral</td>
<td>Increased ICP, direct CTZ effect</td>
<td>Steroids, mannitol, anti-DA/Hist</td>
</tr>
<tr>
<td>Liver</td>
<td>Toxin buildup, mechanical</td>
<td>anti-DA/Hist/steroids</td>
</tr>
<tr>
<td><strong>Meningeal irritation</strong></td>
<td>Increased ICP</td>
<td>Steroids</td>
</tr>
<tr>
<td><strong>Movement</strong></td>
<td>Vestibular stimulation</td>
<td>Anti-Ach or Antihistamine</td>
</tr>
<tr>
<td><strong>Mentation (anxiety)</strong></td>
<td>Cortical</td>
<td>Anxiolytics, e.g., benzodiazepines</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>CTZ, vestibular effect, GI tract</td>
<td>Anti-DA, prokinetic agents, stimulant laxatives</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>CTZ, GI tract</td>
<td>Anti-5HT/DA, steroids, anti-NK</td>
</tr>
<tr>
<td><strong>Mucosal irritation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>gastritis</td>
<td>Cytoprotective agents/antacids</td>
</tr>
<tr>
<td>Hyperacidity, GERD</td>
<td>gastritis, duodenitis</td>
<td>Antacids/cytoprotectants</td>
</tr>
<tr>
<td><strong>Mechanical obstruction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraluminal</td>
<td>Constipation, obstipation, laxatives/stimulants/enemas</td>
<td>Reversible—surgery/stent</td>
</tr>
<tr>
<td>Extrapoluminal</td>
<td>Tumor, fibrotic stricture</td>
<td>Irreversible—manage fluids, steroids, inhibit secretions with octreotide, scopolamine</td>
</tr>
<tr>
<td><strong>Motility</strong></td>
<td>GI tract, CNS</td>
<td>Prokinetic agents, stimulant laxatives</td>
</tr>
<tr>
<td>Opioids, ileus, other medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td>CTZ</td>
<td>Anti-DA/Hist, rehydration, steroids</td>
</tr>
<tr>
<td>Hypercalcemia, hyponatremia, hepatic/renal failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Microbes</strong></td>
<td>GI tract</td>
<td>Antibacterials, antivirals, antifungals, antacids</td>
</tr>
<tr>
<td>Local irritation, e.g., esophagitis, gastritis from <em>Candida, H pylori</em>, herpes, CMV</td>
<td>CTZ</td>
<td>Anti-DA/Hist, antibacterials, antivirals, antifungals, antacids</td>
</tr>
<tr>
<td>Sepsis</td>
<td>CTZ</td>
<td>Anti-DA/Hist</td>
</tr>
<tr>
<td><strong>Myocardial</strong></td>
<td>Vagal stimulation, cortical, CTZ</td>
<td>Oxygen, opioids, anti-DA/Hist, anxiolytics</td>
</tr>
<tr>
<td>Ischemia, congestive heart failure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Legend:**  
- anti-Ach = Acetylcholine antagonists  
- anti-DA = Dopamine antagonists  
- anti-5HT = Serotonin antagonists  
- CTZ = Chemoreceptor trigger zone  
- GUT = Gastrointestinal tract  
- ICP = Intracranial pressure  
- NK = Neurokinin
The following are the five classes of antiemetic medications:

- antidopaminergic drugs;
- antiserotonergic drugs;
- antihistamines;
- anticholinergics; and
- neurokinin antagonists.

In addition, there are adjunctive drugs that, while not directly antiemetics, treat specific causes of nausea such as hyperacidity or gut dysmotility or whose mechanism of action is poorly understood.

If a cause of the nausea cannot immediately be determined, empiric therapy with a dopamine antagonist can be helpful while workup is ongoing. If a cause is known, a specific antiemetic can be chosen to block the implicated receptor. It is generally better to schedule the antiemetic around the clock, rather than as needed. If this does not fully resolve the symptoms, adding another antiemetic that works via a different mechanism can be helpful. Sequential combination therapy may be required in some Veterans.

**Medications**

**Dopamine antagonists**

Medications...  

Dopamine-mediated nausea is probably the most common form of nausea, and the most frequently targeted for initial symptom management. These medications are phenothiazines or butyrophenone neuroleptics and have the potential to cause drowsiness and extrapyramidal symptoms.

Medication dosing options include:

- Haloperidol 0.5–2.0 mg PO, IV, SC q 6 h, then titrate; up to 20 mg total per day
- Metoclopramide 10–20 mg IV, PO q 6 h; and
- Prochlorperazine 10–20 mg PO q 6 h or 25 mg PR q 12 h or 5–10 mg IV q 6 h.
Histamine antagonists (antihistamines)

Antihistamines typically used to control nausea may also cause sedation.\textsuperscript{15} In some Veterans, this adverse effect may be an added benefit. They may also cause confusion and delirium, especially in the elderly, and so should be used judiciously.\textsuperscript{16} Because the antihistamines also have anticholinergic properties, they may do ‘double duty’ as a single agent and cover both mechanisms.

Medication and dosing options include:

- Diphenhydramine 25–50 mg PO q 6 h;
- Hydroxyzine 25–50 mg PO q 6 h; and
- Meclizine 25–50 mg PO q 6 h. May be especially effective in vestibular nausea.

Acetylcholine antagonists (anticholinergics)

If a motion-related component is elicited, the vestibular apparatus is implicated. In addition, opioids and anesthetics can trigger acetylcholine-mediated nausea in the vestibular apparatus.\textsuperscript{10}

For management, consider the following:\textsuperscript{17}

- Scopolamine 1-3 transdermal patches q 72 h or 0.1-0.4 mg SC, IV q 4 h or 50-200 mcg/h by continuous IV or SC infusion.

Serotonin antagonists

Serotonin (hydroxytryptophan) subtype 3 (commonly abbreviated HT-3) has been particularly implicated in chemotherapy-associated nausea. This class of medications can be effective if serotonin is a mediator, but they are often more expensive than the other classes. For each medication, there is a plateau in therapeutic efficacy; titration beyond gives no improvement in outcome. Outside the setting of prophylaxis before chemotherapy and radiation therapy, they can be useful for refractory nausea of diverse types, but are typically tried after other medications have failed.\textsuperscript{18} Although thought to be free of side effects, 5HT3 antagonists can cause constipation, headache, fatigue and possibly QT prolongation.
Medication and dosing options include:

- Granisetron 1 mg PO/IV daily or bid, and
- Ondansetron 4 mg PO/IV q 4-6 h or 8 mg PO/IV tid (also available as an orally dissolvable tablet).

**Neurokinin antagonists**

The newest class of antiemetics called neurokinin antagonists are substance p antagonists that mediates its effect at the neurokinin-1 receptor, is used in combination with a serotonin inhibitor and dexamethasone for highly emetogenic chemotherapy with significant potential for ameliorating delayed nausea and vomiting and postoperative nausea and vomiting.\(^{19}\) Cost limits the use of these agents outside of these prescribed settings.

Dosing options include:

- Aprepitant 125 mg PO day 1 followed by 80 mg days 2 and 3, and
- Fosaprepitant 115 mg IV (equivalent to 125 mg PO of Aprepitant).

**Prokinetic agents**

A ‘sluggish’ or dyskinetic gut, due to carcinomatosis, opioid therapy, other medications, etc. may be a profound source of nausea/vomiting in Veterans with advanced disease.\(^{5,20}\) Another situation where this may be a mechanism of nausea is in the presence of an enlarged liver, due to metastases or congestion in the case of heart failure. Ascites or peritoneal disease may cause ileus and pseudo obstruction. Constipation can be an exacerbating factor.

Medication and dosing options include:

- Metoclopramide 5-20 mg PO or IV q 6 h (AC & HS).
**Antacids**

Hyperacidity, with or without gastroesophageal reflux and/or gastric or duodenal erosions, may produce considerable nausea, heartburn, acidity, or bitter taste. It may also be associated with vomiting. Possible therapies include:

- Antacids, such as Maalox or Mylanta, 1-2 tablespoons PO q 2 h PRN,
- H₂ receptor antagonists, e.g., cimetidine 800 mg PO q HS, famotidine 40 mg PO q HS, ranitidine 150 mg PO q HS, and
- Proton pump inhibitors, e.g., omeprazole 20 mg PO daily or bid, lansoprazole 30 mg PO daily or bid, pantoprazole 40 mg PO daily.

**Other medications**

This heterogeneous class of medications has unclear mechanisms of action, but may have benefits in some Veterans. They are often used when more mechanism-based therapies such as described above have been unsuccessful. Consider the following:

- Dexamethasone 6-20 mg PO daily,
- Lorazepam 0.5-2 mg PO, Buccal, SC q 4-6 h, or
- Tetrahydrocannabinol 2.5-5 mg PO bid-tid.

**Summary**

Acute and chronic nausea are associated with poor quality of life. Management requires: a solid knowledge of the pathophysiology, including neurotransmitters; a careful evaluation to target likely etiologies; and skillful administration of medications, frequently in combination and titrated to effect.

**Key take-home points**

1. Nausea is better prevented than treated once it emerges.
2. Use antiemetic agents for their neurotransmitter blocking functions; combine them strategically.
3. Untreated nausea may become ‘learned’ and refractory to neurotransmitter-based antiemetics therapy.
**Part 2: Constipation**

**Clinical case**

M.R. is a 79-year-old Veteran with advanced COPD (O₂ dependent), mild Alzheimer disease with neuropathic phantom-limb (from a left below-the-knee amputation) who developed subacute onset of increased abdominal pain with intermittent nausea. He had been on long-acting morphine 60 mg PO q 12 hr and gabapentin 300 mg PO q 8 h for pain, and promethazine 12.5 mg PO q 6 hr prn for nausea. He had been eating, had flatus, and had been having a daily soft bowel movement. He denied fevers or chills. There was no other significant past medical history and review of systems was otherwise negative.

On exam, bowel sounds were present but diminished. There was gross abdominal distention that was dull to percussion, no shifting dullness and diffuse abdominal tenderness to palpation without rebound. Rectal exam revealed normal sphincter tone and soft, claylike stool in the vault.

**Introduction**

**Constipation** refers to stools that are decreased in frequency or quantity and may be difficult to evacuate.

Possible causes of constipation include congenital, mechanical, endocrine/metabolic, neurological, psychological, and medication-related. Intrinsic or extrinsic luminal compression from masses can mechanically lead to constipation. Endocrine/metabolic causes include diabetes, hypothyroidism, and hypercalcemia. Nerve function can be perturbed by diseases such as Parkinson’s, direct invasion by tumor, or from paraneoplastic syndromes. Psychologic conditions such as depression have been linked to an increased incidence of constipation. Finally, medications such as calcium channel blockers, anticholinergic agents, antiserotonergic agents, and opioids can be associated with constipation.
In addition to discomfort and pain, constipation can cause nausea, emesis, delirium, and urinary retention. The volume of gas and stool may synergize with other space-occupying processes such as ascites or tumor to worsen pain. Constipation’s synergism with other abdominal processes can limit diaphragmatic excursion, worsening dyspnea. Furthermore, constipation can evolve into impaction and occasionally bowel obstruction.

In the general population, the baseline prevalence of constipation is high and increases with age. In advanced medical illness the combination of underlying disease and medication often lead to a dramatic increase in occurrence. For example, when opioids are used for pain and/or dyspnea, prevalence of constipation approaches 90%.

**Pathophysiology**

Normal gastrointestinal function is mediated through endocrine, paracrine, autocrine, and neuronal forms of cellular communication. The GI tract has its own intrinsic nervous system in the form of the myenteric and submucosal plexi. Additionally, there is extrinsic input via the autonomic nervous system. These inputs mediate fight or flight responses and other emotional factors that are known to affect bowel function. The GI tract has its own pacemaker cells, the interstitial cells of Cajal, which generate rhythmic electrical activity. Complex communication and coordination is required to produce segmental contractions that mix luminal contents or produce peristaltic contractions that move luminal contents forward.

Many agents mediate this communication including peptides like vasoactive intestinal peptide (VIP), nitric oxide, and modified amino acids such as serotonin. Over 80% of the body’s serotonin (5-HT) resides in the gastrointestinal tract and there are over 21 serotonin receptor subtypes. The 5-HT4 receptor subtype is known to play a key role in intestinal motility. Finally, acetylcholine is the neurotransmitter ultimately responsible for smooth muscle cell contraction.

Disruption of this complex communication at the level of pacemaker cells, nerves, muscle, or transmitters can lead to constipation.

The *gastrocolic reflex* is an example of the integration of this complex communication. Food contents trigger the release of transmitters such as cholecystokinin that induces colonic peristalsis. Local stimulation of the colon can trigger peristalsis as well. Luminal
distention causes enterochromaffin cells lining the GI tract to release serotonin that leads to a cascade of messengers ending in peristalsis. In most people, this predictably occurs one to two hours after they wake and eat breakfast.

Opioids interact with the GI tract via receptors (mu and kappa subtypes) that are located throughout its length. Opioids are predominantly mu agonists and contribute to constipation in two major ways: (1) diminishing gastrointestinal secretions and (2) reducing productive forward peristalsis.

**Assessment**

- Specifically ask about bowel function
- Establish what is normal for patient

Most importantly, ask about bowel function. Veterans may not initiate discussion on this topic especially in the setting of decreased oral intake where many mistakenly believe it is normal to not have a bowel movement. Then put current function in context of what is normal for the Veteran.

The Rome II criteria represent a definition of constipation originally derived for research purposes. These criteria highlight physical characteristics of stool, frequency of bowel movements, and subjective perceptions of distress as important to the definition, as well as a component of chronicity. Although they are principally used in research protocols to investigate medications for constipation, the criteria are important for clinicians to note. They are the following:

- straining with defecation;
- hard stool;
- a sensation of incomplete evacuation;
- a sensation of anorectal obstruction; and
- fewer than 3 bowel movements/week.

Although a diagnosis of constipation is made when there are ≥ 2 of the above symptoms for 12 weeks (may be noncontiguous, but in one year) by the criteria, in the acute palliative care setting Veterans may have had symptoms for a shorter time.
A presentation of diarrhea may lead to a diagnosis of fecal impaction. Liquid stool from the right colon or stool may leak around the hard stool of fecal impaction and mimic the presentation of diarrhea. A careful history may reveal that such a Veteran had been experiencing constipation before the onset of loose stools.

During the abdominal exam, assess for bowel sounds, distention, ascites, and masses that could be tumors or stool. A rectal exam will provide neurologic information by assessing sphincter tone. Moreover, if stool is present, information about consistency can be gleaned and a low impaction that requires manual disimpaction can be detected.

Laboratory assessment may be useful to look for hypothyroidism, diabetes, dehydration, hypercalcemia, or other electrolyte abnormalities. A flat plate of the abdomen may help to assess for obstruction or colonic stool load.

**Management**

This module focuses on symptomatic management of constipation. It will not detail the treatment of underlying causes, as these can be found in many textbooks and journal articles.30,31,32

**Non-pharmacologic strategies**

**Toileting strategies**

It is useful to synergize pharmacologic interventions with normal physiologic processes. To improve outcomes, time interventions with a Veteran’s normal toileting schedule and take advantage of the gastrocolic reflex after meals (usually 8-9 a.m.).

**Activity**

Activity has been shown to correlate with an improvement in constipation.33

**Dietary issues**

Nutritional intake including hydration, hot beverages, caffeine, and prune juice have all been shown to help constipation in some patients.
Pharmacologic strategies

Fiber/fluids

In general, a greater volume of stool in the lumen stretches the colon and luminal stretch triggers peristalsis. Hydration and high dietary fiber content are usually advantageous. In Veterans with opioid-induced constipation or with advanced medical illness and suboptimal hydration, avoid excessive supplemental dietary fiber as it may actually worsen constipation. If fiber laxative is appropriate, consider a dosing regimen of the following:

- Psyllium 15 ml daily, mix with at least 240 ml of water.

Stool softeners

Stool softeners, e.g., docusate sodium, are detergents that break up the fat content of stool, allowing water to penetrate more effectively. As a result, stool stays moister and softer. Stool softeners may also increase luminal fluid secretion. They do not affect peristalsis.

The following is a standard dosing regimen:

- Sodium or calcium docusate 100-200 mg PO daily to tid.

Stimulant laxatives

Stimulant laxatives

- Prune juice
- Senna
- Bisacodyl
Stimulant laxatives such as senna and bisacodyl predominantly increase intestinal propulsive activity through unknown mechanisms. Senna is a prodrug and becomes active only upon reaching the colon where bacteria metabolize it. Bisacodyl is activated in the small intestine and may cause more cramping.

Dosing options include:

- Senna 1-3 tablets PO daily to tid, or
- Bisacodyl 5-10 mg PO, PR daily to tid.

For opioid-associated constipation, it is standard to prescribe a combination of senokot and bisacodyl commonly called Senokot-S. Starting dose is 1 tab po bid but can be increased up to 4 tab po bid.

**Osmotic agents**

Osmotic agents, e.g., magnesium salts, lactulose, sorbitol, and polyethylene glycol, pull water into the bowel lumen along with other luminal contents. This helps keep the stool softer and more voluminous. Extensive use of magnesium containing osmotics can lead to magnesium toxicity, especially in the setting of renal dysfunction. Some Veterans find the disaccharide osmotics such as lactulose and sorbitol to be unpalatable. Moreover, when they reach the colon, bacteria can metabolize them leading to gas production and bloating. Studies have shown lactulose and sorbitol to be equally efficacious; however, sorbitol is more cost effective.  

Polyethylene glycol exists both as an oral liquid and a tasteless, odorless powder. The powder can be mixed with foods or liquids increasing palatability. It is not metabolized by colonic flora and therefore there may be less gas bloating. Compared to lactulose, studies have shown polyethylene glycol to be more effective and better tolerated.

Dosing options include:

- Magnesium hydroxide (milk of magnesia) 15-30 ml PO daily to qid routinely or PRN;
- Polyethylene glycol 17 g or 15-30 ml PO daily to bid routinely or PRN;
- Lactulose 15-60 ml PO daily to tid routinely or PRN;
• Sorbitol 15-60 ml PO daily to tid routinely or PRN; and
• Magnesium citrate 50-150 ml PO daily to tid PRN.

Lubricants/enemas

Lubricating suppositories and enemas work mechanically to soften hard, dry stool. Examples include glycerin suppositories, oil enemas, and sodium phosphate small volume enemas. Large volume enemas, in addition to lubricating and softening the distal leading edge, can cause luminal distention and trigger peristalsis and defecation.

Dosing options include:
• Glycerin suppository 1 PR daily to bid PRN;
• Phosphate enema 1 PR daily to bid PRN;
• Oil enema, mineral oil 15-30 ml PR, retain for as long as possible; followed by 500-1,000 ml tap water as tolerated daily to bid PRN; and
• Tap water enema 500-1,000 ml tap water as tolerated daily to bid PRN.

Anal topical anesthetics

Veterans experiencing significant anal/rectal pain from hemorrhoids, muscle spasm, fissures or impaction may benefit from a topical anti-inflammatory and/or anesthetic applied to the involved areas routinely or before each bowel movement to reduce inflammation, pain and pruritus.

The following is a standard dosing regimen:
• Lidocaine, 2-5% spray or jelly PRN. Maximum 200 mg/24 hour.
Constipation can be treated and prevented in almost all Veterans who require opioid therapy. Prevention and early detection is still the mainstay of treatment, and much easier than management of opioid-induced constipation. When an opioid is initially prescribed, start every Veteran on a combination of a stool softener and stimulant laxative (senokot-S) at the same time. Titrate doses to effect. Add osmotic laxatives, and use enemas as needed.

All opioids cause some degree of constipation. Whereas a pharmacological tolerance to many of opioids’ adverse effects develops, it never seems to develop to the constipating effects. Dietary interventions alone, e.g., fiber and fluids, are usually not sufficient. Bulk-forming agents, e.g., psyllium, may cause worsened constipation in a Veteran who cannot drink sufficient fluid. Most experts recommend a combination of a stimulant laxative, e.g., senna or bisacodyl, and a softener, e.g., docusate, to manage the condition. Prokinetic medications, such as metoclopramide, have been advocated for refractory cases. The following is a standard dosing option:

- Metoclopramide 5-20mg PO, SC, IV q 6 h.

Systemically active opioid antagonists such as naltrexone and naloxone have been shown to be useful in the management of constipation, but they also reverse opioids’ analgesic effects. A newer agent, methylnaltrexone has recently been approved. It is dosed based on weight, generally at:

- Methylnaltrexone 8-12 mg SC qod.
It will often result in a bowel movement within ½ hour of administration and has been shown to not reverse the analgesic effect of opioids. Its major adverse effect is cramping. Its use is also limited by cost and the need for injections.

**Summary**

Constipation is a common condition that causes significant morbidity. Reversible causes can be removed if identified. The complex control of laxation is being elucidated and new agents are being developed based on this knowledge. Currently, there are multiple categories of pharmacologic agents that work in different ways that can be successfully synergized to control constipation. Using these agents in concert with physiological processes such as the gastrocolic reflex and daily patterns of bowel movement can further enhance success. It remains true that the easiest and the best treatment for constipation is primary prevention.

**Key take-home points**

1. Assess what is normal for the Veteran before deciding on a treatment plan. Don’t wait for the Veteran to bring up the symptom – ask about it.
2. Combine agents with different mechanisms of action.
3. Titrate senna and docusate to relieve and prevent opioid-induced constipation.
4. Tailor pharmacologic treatment to the suspected underlying cause of constipation.
Part 3: Diarrhea

Clinical case

S.D. is a 79-year-old Korean war Veteran with a history of multiple transient ischemic attacks (TIAs) and cerebrovascular accidents (CVAs) resulting in right side weakness, who has also had 3 hospitalizations in the last year for congestive heart failure (CHF) exacerbations. He reports frequent watery stools. His daughter reports he is unusually unsteady on his feet when he gets up to walk. He has been incontinent once, and slipped and fell. He says he feels bloated and ‘gassy’ and that he is exhausted.

Introduction

Diarrhea is defined as stools that are looser than normal and may be increased in frequency. It may be acute (< 14 days), persistent (>14 days), or chronic (> 30 days). Diarrhea can lead to dehydration, malabsorption, fatigue, hemorrhoids, and perianal skin breakdown. Secondarily, it can lead to electrolyte abnormalities and dehydration. It can also be embarrassing for the Veteran and affect his/her sense of dignity.

Most cases of acute diarrhea are viral and self-limited. Clues to consider bacterial causes include stools containing blood and mucus, fever, severe abdominal pain, recent antibiotic use, or hospitalization (i.e., due to C. difficile).

When diarrhea is severe, it can lead to significant dehydration, renal failure, and electrolyte abnormalities that may be life threatening.

Prevalence

The prevalence of chronic diarrhea in the general population in developed nations has not been well established, but seems to be around 5%. As a general rule, the principal causes of diarrhea vary by the population and the setting in which they are seen. In developing countries, diarrhea is often due to infections, although functional disorders, malabsorption, and inflammatory bowel disease are also found. In developed countries,
the most common causes are irritable bowel syndrome, inflammatory bowel disease, and malabsorption syndromes. Diarrhea is commonly associated with chemotherapeutic regimens and can be the dose-limiting adverse effect of 5-fluorouracil and capecitabine, and irinotecan; diarrhea occurs in 30-90% of patients receiving these chemotherapeutic agents. It is also seen in association with methotrexate and cisplatin. Diarrhea may also been seen as an acute sequela or chronic sequela of radiation therapy to the GI tract. Additionally, diarrhea may be a consequence of comorbid conditions that a Veteran has such as: malabsorption, inflammatory bowel disease or irritable bowel syndrome.

**Pathophysiology**

Diarrhea may be secretory, osmotic, inflammatory or infectious or a result of abnormal motility of the GI tract. With normal GI function, approximately two liters per day of fluid is ingested. In addition, five to seven liters or more of fluid are secreted into the gut lumen from the stomach, small intestine, and from exocrine sources such as the pancreas. This fluid is reabsorbed in the large intestine. Loose stools can occur when as little as 100 ml of fluid is not absorbed in the large intestine. Disruption of the complex orchestration of communication at the level of pacemaker cells, nerves, muscle, or transmitters can lead to diarrhea.

**Assessment**

A thorough medical history can guide appropriate evaluation. Important components of the history include:
• establish the Veteran’s normal bowel habit;
• elicit a description of the stool that is different from normal, i.e., consistency or frequency, urgency, fecal soiling, greasy stools that float, presence of blood, color, volume, etc;
• duration;
• nature of onset (sudden or gradual);
• travel history;
• risk factors for human immunodeficiency virus infection;
• weight loss;
• diarrhea with fasting or at night (suggests secretory);
• family history of irritable bowel syndrome;
• systemic symptoms, e.g., fever, joint pain, mouth ulcers, eye redness;
• chemotherapy, laxatives, and over-the-counter medications and supplements; and
• dietary history, including sorbitol-containing candies, specific food associations such as dairy products.

On physical examination, look for fever, perineal irritation and signs of dehydration, i.e., poor skin turgor, dry/cracking mucous membranes, and orthostatic hypotension.42

**Specific types of diarrhea**

**Medication-related diarrhea**

A thorough medication review should be performed to identify and eliminate pharmacologic causes of diarrhea. Education of Veterans and caregivers on the appropriate use of laxatives should also be pursued to minimize inappropriate usage. The following are medications that can be associated with diarrhea to specifically look for:

• Magnesium containing antacids;
- Cholinergic agents, e.g., donepezil;
- Antibiotics, antiretrovirals;
- Beta-blockers and some antiarrhythmics;
- NSAIDS, colchicine;
- GERD agents (H2 blockers and PPIs);
- Theophylline;
- Vitamin, mineral supplements and herbal agents; and
- Inappropriate use of laxatives.

**C. Difficile**

Recently hospitalized Veterans or those residing in a long-term care facility who present with diarrhea and abdominal pain should prompt the consideration to evaluate and treat *C. Difficile*. This is a growing and prevalent cause of nosocomial-acquired diarrhea; specific major risk factors include antibiotic exposure, hospitalization, and advanced age. Diagnosis is typically made by stool assay for *C. Difficile* toxin. Treatment includes:

- Metronidazole 500 mg po tid, or
- Vancomycin 250 mg po qid.

**Diarrhea associated with enteral-feeding and dietary supplements**

Many Veterans with advanced neurologic illnesses such as dementia, stroke and less commonly with general debility may have had a gastrostomy tube placed for supplemental nutritional support. These supplements, i.e., Ensure or other products, can lead to diarrhea related to the Veteran’s inability to fully digest the feeding and the lack of bulk. These Veterans often will have diarrhea but not be able to self-report. Family and other caregivers will report this problem as it relates to need to change the Veteran’s pads/diapers. Left uncontrolled, diarrhea from the tube feeding can exhaust caregivers and lead to problems with skin breakdown as well and maintenance of the Veteran’s dignity at life’s end.

The clinicians should review with the Veteran/family as appropriate the goals of care as they relate to the tube feeding and in some cases discontinuing tube feedings or changing formulations may be appropriate.
Pancreatic insufficiency-associated diarrhea

Veterans treated with total pancreatectomy, i.e., a Whipple Procedure, frequently experience diarrhea due to maldigestion and steatorrhea due to exocrine pancreatic insufficiency. This is treated with a low fat diet and administration of exogenous pancreatic enzymes. Several commercial preparations are microencapsulated so that they are stomach acid-resistant to avoid enzyme inactivation. As a general rule, 30,000 IU of pancreatic lipase, swallowed during each meal will serve to reduce steatorrhea.

**Management**

This module focuses on symptomatic management of diarrhea. It will not detail the treatment of underlying causes (including medication related causes), as these can be found in many textbooks and journal articles.  

**Non-pharmacologic**

Consider the following non-pharmacologic treatments:

- assure adequate hydration: oral rehydration solutions that contain sodium chloride, e.g., soups, red juices with salt, and sport drinks may be adequate. Subcutaneous hypodermoclysis or intravenous rehydration is rarely necessary;
- avoid gas-forming foods, particularly lactose; acute diarrhea is frequently associated with transient lactose intolerance; and
- increase bulk, e.g., psyllium, bran, pectin.

**Pharmacologic**

For the transient or mild diarrhea consider the following:

- Attapulgite (Kaopectate) 30 ml or 2 tablets PO PRN, or
- Bismuth subsalicylate 30 ml or 2 tablets PO every 30 minutes PRN up to a maximum of eight doses. This has both anti-inflammatory and antibacterial actions.
For persistent diarrhea (rule out infectious causes first) consider the following:

- Codeine 15-30 mg PO q 4 h PRN to decrease peristalsis;
- Diphenoxylate/atropine 5 mg (2 tablets) PO q 6 h; maximum 20 mg/24h; diphenoxylate is a central opiate, while atropine is an anticholinergic agent which dries the bowel and decreases peristalsis;
- Loperamide 4 mg (2 tablets) initially, then 2-4 mg PO q 6 h to a maximum of 16 mg/24 h; this is a peripheral acting opioid (decreases peristalsis) that may be used with acute diarrhea even if there is a low grade fever, as long as there is not blood in the stool;
- Cholestyramine 4 g PO qd – qid, a bile-acid binding agent; or
- Tincture of opium, 0.5 ml PO q 4 h and titrate to effect; this is alcoholized morphine at approximately 10 mg/ml; very bitter tasting; and more potent than loperamide and diphenoxylate.

For persistent, severe secretory diarrhea, consider parenteral fluid support as needed and appropriate to treat or prevent dehydration and octreotide, a synthetic congener of somatostatin. Octreotide blocks secretion at the epithelium of the small and large bowel as well as the secretory organs like the pancreas. For a more detailed explanation of octreotide action, see the section on bowel obstruction later in this module. For octreotide dosing, consider the following:

- Octreotide 50 mcg SC q 8-12 h, then titrate up to 500 mcg q 8 h SC, or 10-80 mcg q 1 h by continuous SC, IV infusion.
Summary

After managing underlying pathophysiology, symptomatic management of diarrhea involves measures that either thickens the stool, slow peristalsis to permit more time for water absorption, or agents to decrease secretion of fluid into the gut.

Key take-home points

1. Diarrhea can be a serious symptom and affect quality of life.
2. Ask for specific details to ascertain the impact of the diarrhea.
3. Management of serious diarrhea begins with a thorough work up and an opioid to slow peristalsis. Titrate to effect.
Part 4: Bowel Obstruction

Clinical case

C. J. is a 72-year-old Korean Conflict Veteran with stage IV colon cancer (1 year s/p surgical resection of the primary lesion) who is admitted with both continuous and colicky abdominal pain, nausea and vomiting, and abdominal distension. The diagnosis of bowel obstruction is established based on clinical signs and symptoms and confirmed with abdominal x-rays demonstrating air-fluid levels. An exploratory laparotomy demonstrates the presence of mechanical obstruction and peritoneal carcinomatosis. Surgical intervention is technically impossible due to adhesion of the tumor to the abdomen wall and the presence of carcinomatosis.

Introduction

Slide 33

Bowel obstruction

Definition: mechanical or functional obstruction of the progress of food and fluids through the GI tract.

Prevalence

- range from 6% (ovarian cancer) to 48% (colorectal cancer)

Prognosis – poor if inoperable

Bowel obstruction is the mechanical or functional obstruction of the progress of food and fluids through the gastrointestinal tract. It causes nausea, vomiting, and abdominal pain.

Compression of the bowel lumen develops slowly and often remains partial. Gastrointestinal symptoms caused by the sequence of distension, secretion, and motor activity of the obstructed bowel, occur in different combinations and intensity, depending on the site of obstruction, and tend to worsen over time.44,45,46

Bowel obstruction can be partial or complete, single or multiple, due to benign or malignant causes. For malignant bowel obstruction the prevalence varies widely based on the type of cancer the Veteran has. For example the rate can range from 6% in ovarian and other gynecological cancers to 48% in colorectal cancer.44,45,46,47,48

The prognosis of Veterans with both mechanical and functional obstruction due to advanced cancer who have received maximal surgical, chemotherapeutic, and radiological treatment is poor.
Several mechanisms may be involved in the onset of bowel obstruction and there is variability in both presentation and etiology.

An obstruction may be functional or mechanical. Functional obstruction is a disorder of intestinal motility. It can be caused by infiltration of the mesentry or celiac plexus by cancer (carcinomatosis), paraneoplastic neuropathy, chronic intestinal pseudo-obstruction due to diabetes mellitus, other neurological disorders, and constipating medications. Fecal impaction, dehydration and constipating medications, e.g., opioids and anticholinergics, are all likely to contribute to the development of gastrointestinal obstruction or to worsening of clinical picture. A mechanical obstruction is due to either an intraluminal or extraluminal mass that causes obstruction.

A history of crampy abdominal pain, abdominal fullness, and postprandial nausea with or without vomiting or hiccups is suggestive of obstruction. The time of vomiting after eating may be suggestive of the site of obstruction. Nausea and vomiting about 45 minutes after meals suggests a gastric outlet or duodenal obstruction. Nausea with or without vomiting that is several hours after eating correlates with large bowel obstruction. Passage of gas or stool per rectum argues against obstruction, as some peristalsis must be present.
Physical examination may show an absence of bowel sounds (when auscultated for several minutes). High pitched or rushing bowel sounds have traditionally been associated with impending obstruction, although the sounds are neither sensitive nor specific when compared with radiographic ‘gold standard’ assessments.

An upright abdominal x-ray is the first investigation in Veterans with suspected bowel obstruction to document the dilated loops of bowel, air-fluid levels, or both. An abdominal CT scan is useful for evaluating the site of obstruction, overall extent of disease, to perform staging, and to assist in the choice of surgical, endoscopic, or pharmacological intervention for the management of the obstruction.45

**Management**

Place choices for the management of malignant bowel obstruction in the context of the clinical situation. Veterans with good performance status and localized tumor may benefit from treatments that require some discomfort for their administration, e.g., surgery. Veterans with more advanced disease and a prognosis of weeks to live should be spared extensive evaluation and treated medically.

**Surgery**

Palliative surgery can reverse malignant bowel obstruction. However, published data show that, in advanced cancer, the operative mortality is 5-32% and reobstruction rates vary from 10-50%.49 Not all Veterans are fit for surgery and cases need to be carefully reviewed to assess the potential benefits and risk present in each case.

Several authors have emphasized that prognostic criteria are needed to select patients who are likely to benefit from surgical intervention. The available data suggest that poor prognostic factors that preclude a surgical approach include the following:

- intestinal motility problems due to diffuse intraperitoneal carcinomatosis;
- ascites requiring frequent paracentesis;
- advanced cachexia;
- previous radiotherapy of the abdomen or pelvis;
• palpable intra-abdominal masses and liver involvement, or distant metastases, pleural effusion or pulmonary metastases;
• multiple partial bowel obstruction with prolonged passage time on radiograph examination; and
• poor general performance status.44,45,46

Stents
Stents are an evolving intervention for palliative care of malignant bowel obstruction.50,51,52,53,54,55 Radiologic or endoscopic enteral stent placement has been reported to be an effective alternative for palliation of high risk surgical candidates with malignant gastric outlet, small bowel, large bowel, and rectal obstruction. Most reports are retrospective single institution studies of highly selected patients. Potential complications include stent migration, perforation, biliary obstruction, and need for subsequent endoscopic, radiologic and surgical interventions.50,51,53

Nasogastric suction and percutaneous gastrostomy
Nasogastric suction decompresses the stomach and/or intestine and intravenous fluids correct fluid and electrolyte imbalance before surgery, or while a decision is being made. However, nasogastric suction is no longer the principal therapy to manage malignant bowel obstruction once surgical relief of obstruction has failed or is not considered possible. The tube often becomes occluded and requires flushing and/or replacement. During long-term drainage, a nasogastric tube interferes with coughing to clear pulmonary secretions and may be associated with nasal cartilage erosion, otitis media, aspiration pneumonia, esophagitis, and bleeding. This treatment can also create considerable discomfort in Veterans who are already distressed. When obstructive symptoms cannot be controlled by medications, percutaneous gastrostomy is an effective and acceptable alternative to the prolonged use of a nasogastric tube. 44,45,46

Pharmacological management
The pharmacological management of bowel obstruction focuses on the treatment of nausea, vomiting, pain, and other symptoms without the use of a nasogastric tube.
**Analgesics**

Opioids are usually used to control abdominal pain. The dose is gradually increased using standard opioid dosing guidelines until symptom control is achieved (see EPEC for Veterans Module 4: Pain Management).44,45,46

**Anti-nausea agents**

Haloperidol is an effective antidopaminergic antiemetic. It can be combined with scopolamine and an opioid in the same solution for simpler administration parenterally. The following is a standard dosing regimen:

- Haloperidol 1 mg IV/SC q 6-8 h.

**Antisecretory agents**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Scopolamine</td>
<td>0.5-200 mcg/hr cont. infusion or 0.1 mg SQ q 6 h</td>
<td>Anticholinergic effects may be dose-limiting; titrate daily</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>0.2-0.4 mg SQ q 1 to 4 h; titrate</td>
<td>Anticholinergic effects possible</td>
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Three antisecretory medications have been used in the setting of bowel obstruction: scopolamine, glycopyrrolate and octreotide.

**Scopolamine** decreases peristalsis in smooth muscle and the secretions in the GI tract, and lessens the resulting pain.56,57,58,59,60 Dry mouth is reported to be the most significant adverse effect and can often be managed by sucking ice cubes or hard candies, and drinking small sips of water.

Standard dosing regimens include:

- Scopolamine 0.1-0.4 mg SC q 6 h or 50-200 mcg/hr continuous infusion, and
• Scopolamine patch q 3 days.

**Glycopyrrolate** can be used with similar effects and properties. It is a quaternary ammonium anticholinergic agent that also has limited lipid solubility and less risk of both central nervous system and ocular effects. The onset of its action is 35-45 minutes when given subcutaneously and minutes when given intravenously.

A common dosing range is the following:

• Glycopyrrolate 0.2-0.4 mg SC q 6 h or 0.02 mg/hr continuous infusion.

**Octreotide** is a synthetic analogue of somatostatin. Somatostatin and its analogues have been shown to inhibit the release and activity of GI hormones, modulate gastrointestinal function by reducing gastric acid secretion, slow intestinal motility, decrease bile flow and reduce splanchnic blood flow. It reduces GI secretions and increases absorption of water and electrolytes. The inhibitory effect of octreotide on both peristalsis and GI secretions reduces bowel distension and the secretion of water and sodium by the intestinal epithelium, thereby reducing vomiting and pain.

Octreotide is administered as a 50-100 mcg dose, usually given q 8 hr. The dose can be titrated upward until symptom control is achieved, usually at 0.6-0.9 mg/day. Octreotide is significantly more effective and faster than scopolamine in reducing the amount of GI secretions in patients with a nasogastric tube and in reducing the intensity of nausea and the number of vomiting episodes in patients without a nasogastric tube. Moreover octreotide may prevent the development of irreversible bowel obstruction in Veterans with recurrent episodes of obstruction.
Common dosing regimens include:

- Octreotide 50-100 micrograms SC q 8 h, and
- Long-acting depot form of octreotide (Sandostatin LAR) 30 mg IM monthly.

If the Veteran has clearly irritable bowel obstruction then the long acting depot form of octreotide is recommended, especially in the long-term care setting.

**Corticosteroids**

In the setting of tumor related obstruction corticosteroids are believed to reduce peritumoral inflammatory edema and improve intestinal motility as well as reduce associated nausea. There is also a suggestion that corticosteroids may help resolve malignant bowel obstructions. To date, no controlled clinical trials have been carried out and the various administration routes and dosing of these medications have not been standardized.\(^{45,61}\)

However, the following is one common dosing plan:

- Dexamethasone 20-40 mg IV daily for 4 day trial.

**Hydration and total parenteral nutrition**

In Veterans with inoperable bowel obstruction carefully assess the amount of fluid you will administer. High levels of oral or parenteral fluids may result in more bowel secretions. As a result, keep a balance between the efficacy of the treatment and the risk of adverse effects such as increased vomiting, abdominal distension, and pain.

The intensity of dry mouth and thirst are independent of the quantity of both oral and parenteral hydration.\(^{63}\) Hypodermoclysis is a simple technique for rehydration that offers many advantages over the intravenous route.\(^{63}\) Some Veterans with a distal bowel obstruction will tolerate and find some oral fluid intake to be pleasurable.

The role of total parenteral nutrition in the management of patients with inoperable bowel obstruction has been controversial.\(^{64}\) It should be considered in light of overall goals of care.
The optimal treatment of bowel obstruction in Veterans is still a debated issue. Veterans are usually considered suitable candidates for surgery when survival is expected to be more than two months. Although surgery has been the primary treatment for malignant obstruction, it is now recognized that some Veterans with advanced disease or those in a general poor condition are unfit for surgery and require alternative management to relieve distressing symptoms. A number of treatment options are now available for Veterans with advanced and terminal cancer that develop intestinal obstruction. Medical treatment by continuous subcutaneous or intravenous administration of opioids, corticosteroids, anticholinergic medications, octreotide, and antiemetic medications can be an effective approach in controlling pain, nausea, and vomiting in Veterans with inoperable gastrointestinal obstruction. Consider nasogastric suction or percutaneous gastrostomy for Veterans with refractory symptoms and/or upper bowel obstruction who do not respond satisfactorily to pharmacological measures alone. Aim efforts of the clinical team at both symptom control as well as the care of other aspects of the Veteran’s suffering, including psychological distress and spiritual concerns.

**Key take-home points**

1. First, evaluate the Veteran with bowel obstruction for a definitive operative solution.
2. Stent placement may be a reasonable alternative in selected Veterans.
3. If the Veteran is inoperable, satisfactory symptom control is possible with medications.
   a. Antisecretory agents, such as octreotide, may be effective alone.
   b. Antidopaminergic antiemetics in combination with anticholinergics and opiates are an alternative.
4. Diverting procedures may be needed for refractory symptoms.
Part 5: Ascites

Clinical case

Q.H. is 44-year-old disabled truck driver admitted to a hospice program with hepatocellular carcinoma and ethanol-induced cirrhosis. A diminished albumin level and elevated prothrombin time are consistent with impaired hepatic synthetic function. Comorbidities related to cirrhosis include esophageal varices, a single, recent episode of hepatic encephalopathy, coagulopathy, and massive ascites. Although abstinent from ethanol for the preceding five years, he is not a liver transplantation candidate because of significant cardiopulmonary disease.

Medications include furosemide 40 mg PO tid, spironolactone 200 mg PO bid, lactulose 30 mg PO tid, thiamine 100 mg PO daily, folate 1mg PO daily, omeprazole 40 mg PO daily, citalopram 20 mg PO daily, albuterol inhaler 2 puffs q 4 h PRN, lisinopril 20 mg PO daily, and O2 2 l/min. The physical examination shows no jugular venous distension. The abdomen is obese, but shifting dullness and a fluid wave are demonstrable. There is no asterixis. Laboratory examination is remarkable for a partial prothrombin that is elevated by \( \approx 4 \) seconds above normal.

Introduction

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**Ascites**

- Definition: accumulation of fluid in the abdomen
- 10% caused by malignancy
- Other etiologies:
  - heart failure
  - cirrhosis
  - renal failure

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**... Ascites**

- Prognosis:
  - mean survival with malignant ascites < 4 months
  - if chemo-responsive cancer (e.g. new dx ovarian ca) 6 months – 1 year
Ascites is the accumulation of fluid in the abdomen. Its formation may be a direct result of a malignant process or secondary to an unrelated comorbidity. Ascites may contribute to dyspnea, early satiety, fatigue, and abdominal pain. Because the pathophysiology of fluid collection varies, treatment strategies differ. An understanding and clinical differentiation of the mechanisms responsible for ascites are important for rational management.

**Prevalence and prognosis**

Approximately 85% of patients have ascites as a result of cirrhosis while 15% are due to nonhepatic causes such as cancer, heart failure, nephritic syndrome, nephrotic syndrome pericardial disease and tuberculosis, and 5% have two or more causes. Among cancers, epithelial malignancies, particularly ovarian, endometrial, breast, colon, gastric, and pancreatic carcinomas, cause over 80% of malignant ascites. The remaining 20% are due to malignancies of unknown origin.

In general, the presence of ascites portends a poor prognosis. In cirrhosis, new ascites suggests a two-year survival rate of 50%. The mean survival in cirrhosis with malignant ascites is generally less than 4 months. However, with ascites due to a malignancy that is relatively sensitive to chemotherapy, e.g., newly diagnosed ovarian cancer, the mean survival may be significantly better, i.e., 6–12 months.

**Pathophysiology**

- **Normal physiology:**
  - intravascular pressure = extravascular pressure
  - no extravascular fluid accumulation
- **Ascites:**
  - fluid influx increases
  - fluid outflow decreases
  - fluid accumulates

- **Elevated hydrostatic pressure (e.g., congestive heart failure, cirrhosis)**
- **Decreased osmotic pressure (e.g., nephrotic syndrome, malnutrition)**
- **Fluid production > fluid resorption (infections, malignancy)**
Complex mechanisms are responsible for ascites. Increased hydrostatic pressure or hepatic obstruction, e.g., heart failure, cirrhosis, metastatic cancer, decreased osmotic pressure, e.g., malnutrition, nephrotic syndrome, and increased production, e.g., carcinomatosis, infection, can all cause ascites. Increased portal pressure leads to transudation of fluid across the splanchnic bed into the abdominal cavity. Diminished intravascular oncotic pressure, i.e., decreased osmotic pressure from conditions such as malnutrition, and nephrotic syndromes, results in passive migration of fluid into the abdominal cavity due to solute gradients.

In the setting of cancer, tumor cells on the peritoneal surface directly interfere with normal venous and lymphatic drainage, causing fluid to ‘leak’ into the abdomen. A humoral vascular permeability factor that allows exudation of fluid from the peritoneal vessels has also been identified.\(^67\) Chylous ascites can result from the lymphatic obstruction commonly seen in lymphoma.

**Assessment**

A history of dyspnea, fatigue, anorexia, early satiety, nausea, vomiting, pain, or diminished exercise tolerance in the setting of weight gain, increases in abdominal girth (with or without protrusion of the umbilicus), a sensation of fullness or bloating, and early satiety suggests the presence of ascites. Some Veterans simply describe a vague generalized abdominal discomfort or a feeling of heaviness with ambulation. Increased intra-abdominal pressure can produce esophageal reflux symptoms. Delayed gastric emptying may prompt complaints of indigestion, nausea, and vomiting.

The diagnosis is supported by physical findings of bulging flanks, flank dullness (if fluid accumulation is > 1,500 ml), shifting dullness, and a fluid wave. To monitor changes in ascites volume, measure abdominal girth at the umbilicus or another landmark. Assess for jugular venous distention. If present, it may indicate a cardiac cause of ascites.
A plain x-ray of the abdomen may demonstrate a hazy or 'ground-glass' pattern. Ultrasound or computed tomography will identify as little as 100 ml of free fluid, and will be helpful if loculation is present.

Management

Every intervention has associated burdens and benefits that need to be realistically considered and discussed, so assess overall goals for a Veteran’s care before making specific choices for managing ascites. No treatment is needed for the Veteran who is asymptomatic. Establish prognosis, expected response to management of the underlying conditions, and preferences for treatment before any plan of care is instituted. Refractory ascites is uncommon (10%) and most Veterans can be managed using noninvasive measures. 65
Sodium and fluid balance

When portal hypertension is present, dietary management may be helpful. Symptoms may be improved with sodium restriction. Limiting sodium intake to 2 grams per day is an attainable goal for a motivated Veteran, but does make food less palatable. Depending on the Veteran’s prognosis and goals of care, it may be better to liberalize the sodium intake and control ascites through other methods. Veterans with ascites are also prone to develop dilutional hyponatremia. In Veterans with advanced disease whose treatment goals are purely palliative, fluid restriction to 1 liter per day is usually intolerably burdensome.

Diuretics

Diuretic therapy is useful for some Veterans, particularly those with a component of portal hypertension. The goal of diuretic therapy is to achieve a gradual diuresis that does
not exceed the capacity for mobilization of ascitic fluid. Mobilize only enough fluid to promote comfort. In Veterans with ascites and peripheral edema, the edema will act as a fluid reservoir to buffer the effects of a rapid contraction of plasma volume. A net diuresis of approximately one liter per day is safe. Symptomatic orthostatic hypotension from intravascular volume contraction is more likely to occur in Veterans without edema. In this group, a net diuresis of 500 ml per day is more reasonable. Overly aggressive diuretic therapy in Veterans with ascites due to cirrhosis can lead to a pre-renal state and potentially hepatorenal syndrome.

In Veterans with ascites for whom diuretics may be helpful, the renin-angiotensin-aldosterone system is activated. Therefore, the initial diuretic of choice is a distal tubule aldosterone antagonist. Examples include:

- Spironolactone 100-400 mg/day,
- Amiloride 10-40 mg/day, and
- Triamterene 100-300 mg/day.

Because these diuretics are relatively potassium sparing, advise Veterans to avoid potassium salt substitutes.

Start with a ratio of 100 mg of spironolactone to 40 mg of furosemide. Adjust the ratio and the doses to maintain normokalemia. The dosages can be increased in parallel until the goals of therapy have been attained (not to exceed maximal doses, i.e., spironolactone 400 mg PO daily and furosemide 240 mg PO daily), or until therapy is limited by adverse effects. Alternately, substitute ethacrynic acid, 50-200 mg PO daily instead of furosemide.

The sequential addition of diuretics is usually recommended. Although there is no evidence to support the combined use of multiple types of diuretics at the beginning of therapy, this may be an appropriate management strategy in a population with limited life expectancy and distressing symptoms. Precious time may be gained by starting with a spironolactone/furosemide combination in the ratios described above.

Diuretic therapy may be excessively burdensome in Veterans with limited mobility, urinary tract outflow symptoms such as hesitancy and frequency, poor appetite and poor oral intake, or complex polypharmacy. Injudicious use of diuretics can result in incontinence with attendant self-esteem and skin care issues, sleep deprivation from frequent urination, fatigue from hyponatremia and/or hypokalemia, and falls caused by postural hypotension.
Paracentesis may be the only therapeutic modality that is effective, particularly for Veterans with malignant ascites. The symptom response is much faster than when diuretics are used alone.

If the ascites is in equilibrium with the systemic circulation, as is the case with portal hypertension, there is some risk of hemodynamic compromise when a large volume paracentesis is performed. This is not true for Veterans with malignant ascites. Colloid plasma volume expansion, e.g., 6-8 grams of albumin per liter of ascites removed, has been used to avoid this complication, but its use remains controversial. Albumin is expensive, but it is not known to cause harm. Large-volume therapeutic paracentesis (≥ 5 liters) with concurrent colloid infusion is a simple procedure and is associated with minimal morbidity or mortality. However, the use of albumin does require IV access which may be difficult and cause pain. In addition, therapeutic paracentesis may be safely done in the home or in a care setting that does not readily support IV albumin. Therefore, albumin infusion should not be a barrier to having paracentesis for the Veterans comfort. Clinicians may opt to use colloid for large volume paracentesis of ascites due to portal hypertension until more definitive guidelines exist. More recently, midodrine has been studies as an alternative agent to albumin. It is less costly and appears to be as effective as albumin in a small randomized study.69

Implanted external catheters

Tenckhoff or other implanted abdominal catheters may be beneficial for selected Veterans who require repeated large-volume paracentesis for comfort and whose prognosis warrants an invasive procedure.70 Under local anesthesia, an externally draining catheter is placed in the peritoneal cavity.

This drain can be conveniently accessed intermittently by clinicians, or even by trained family members. The comfort and advantage of the smaller, less obtrusive devices is offset by their tendency to occlude or lead to infection. To date, there are no studies comparing implanted catheters with serial paracentesis in patients with either cirrhotic or malignant ascites. Complications such as cellulitis, peritonitis, and fibrin clots have been reported.
Transjugular intrahepatic portosystemic shunt

The transjugular intrahepatic portosystemic shunt (TIPS) is a procedure performed by interventional radiologists that creates a side-to-side shunt that effectively relieves portal hypertension. For Veterans with cirrhosis and refractory ascites who have relatively good hepatic and renal function, TIPS is considered the treatment of choice. However, shunt malfunction rates of up to 40% have been reported. In two cases of malignant portal and hepatic vein occlusion, TIPS improved ascites and quality of life.\(^7\)

As with any palliative management option, the decision to pursue invasive surgical procedures is dependent on the Veteran’s goals and the disease context. Hepatic encephalopathy may be exacerbated after TIPS procedures as the liver is bypassed and agents that are normally filtered out (ammonia) are shunted directly into the systemic vasculature. Veterans are likely to have been referred for or received a TIPS procedure before referral to hospice and palliative care services. It is important for clinicians to understand these procedures since discussion of past and present treatment options and their role in ongoing therapy is often part of the discussion of goals of care.\(^6\)

**Summary**

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Ascites is associated with a poor prognosis. In some Veterans, diuretics may help in management. Many Veterans, however, will require paracentesis to relieve symptoms. In selected Veterans, placement of a permanent catheter may be warranted.

**Key take-home points**

1. Increased portal pressures, direct secretion into the abdomen, or a combination of these two mechanisms can result in ascites.
2. Ascites related to portal hypertension is more likely to respond to diuretic therapy
3. Ascites related to malignancy usually requires paracentesis and an external catheter.
Oral mucositis is a common complication of both chemotherapy and radiation therapy. The overall incidence of oral mucositis is approximately 40% in patients who receive standard dose chemotherapy. However, the incidence varies with the medication, doses, and schedules used and occurs in up to 100% of patients undergoing high-dose chemotherapy with hematopoietic stem cell transplantation.

Mucositis is generally self-limiting. The prognosis is generally good if the comorbidities such as pain, decreased oral intake, fluid deficits, and dental caries are also managed. However, mucositis has an impact on overall treatment outcomes, such as infection, length of stay, and mortality in patients undergoing stem cell transplants. In general, the combination of neutropenia and mucositis increases the risk of infection.

**Mucositis** is a mucosal barrier injury, characterized clinically by oral erythema, ulceration, and pain following the use of known stomata-toxic therapy. The timing and location of the oral lesions help differentiate mucositis from oral infections and graft versus host disease. Oral viral infections frequently coincide with fever and are typically localized and involve keratinized mucosa of the hard palate, gingival, and dorsal tongue. Oral ulcers secondary to graft versus host disease are seen in patients who have undergone allogeneic stem cell transplantation and may develop after hematologic recovery. These ulcers are often lichenoid in character and may be associated with xerostomia.
Pathophysiology and assessment

Oral mucositis is caused by direct injury from radiation or chemotherapy therapy, secondary infection, or graft versus host disease (GVHD). The pathophysiology of mucositis reveals it to be a complex problem that is not simply a result of injury to the basal epithelial stem cells. It is a multistage process including initiation, message generation, amplification of signaling, ulceration, and healing.\textsuperscript{77}

Chemotherapy-induced mucositis most commonly involves the soft palate, antrum of the tongue/floor of the mouth, and buccal mucosa. Chemotherapy-induced mucositis generally presents 5-7 days after treatment and resolves within 2 days to a few weeks.\textsuperscript{78} While chemotherapy-induced mucositis tends to be acute, radiation-induced mucosal injury has a more chronic course.

Radiation therapy related mucositis is a function of the cumulative dose delivered. Mucositis is generally first seen after 15-20 Gy have been delivered to the mucosa. At about 30 Gy, ulcerative mucositis develops. Mucositis due to radiation typically lasts 6 weeks.\textsuperscript{79}
Overall there are limited opportunities in specific Veteran populations to prevent mucositis. The Multinational Association for Supportive Care in Cancer (MASCC) Mucositis Study Group published original guidelines in 2004 and 2007 that provide clinical approaches to mucositis prevention and treatment.\textsuperscript{80,81} The \textit{prevention} of oral mucositis is an important goal. The following four theoretical approaches have been articulated and are the subject of ongoing research although no specific preventive treatment is available:\textsuperscript{82}

- Reduce mucous membrane exposure to the cytotoxic agent (cryotherapy);
- Reduce infectious and inflammatory complications (antimicrobials);
- Modify epithelial proliferative capabilities (human keratinocyte growth factor (palifermin); and
- Reduce and inhibit pro-inflammatory cytokines (benzydamine).

Once mucositis begins, treatment is supportive. Little has been shown to change the overall course of mucositis. General measures such as oral hygiene and dietary modification, topical local anesthetics, and systemic analgesics have been recommended. Other options are currently being studied.

\textbf{Oral hygiene}: Good oral hygiene appears to reduce the severity of oral mucositis. Patients should: brush gently with a soft-bristled toothbrush using fluoride containing toothpaste two or three times daily; Floss gently, daily to remove food buildup; Rinse the
mouth every 4 hours with a dilute saline and baking soda solution (½ teaspoon salt plus ½ teaspoon baking soda in a cup of warm water); chlorhexidine appears no better than sterile saline. While this may be soothing, it has not been formally evaluated; remove dentures at night.

**Limit food contact:** limit the amount of time food is allowed to come into contact with the oral mucosa. Recommend foods that require little or no chewing. Advise against foods that are irritating, e.g., acidic, spicy, salty, coarse, or dry.

**Pain relief** is challenging. Local anesthetics provide some pain relief but rigorous studies are lacking. Systemic analgesics are frequently used. Patient-controlled analgesia (PCA) with an opioid has been recommended. Follow standard opioid dosing guidelines.

Since the efficacy of the treatments for mucositis is limited, appropriate counseling becomes very important. These conversations should focus on setting expectations regarding the degree of anticipated pain relief while reassuring the patient about the expected time course and eventual resolution of the symptoms.

**Summary**

1. Provide adequate analgesia.
2. Cleansing with dilute soda or salt water frequently is as effective as chlorhexidine.
3. Offer easy to swallow foods and fluids. Veterans may need parental analgesia and hydration support if intake is severely impaired.
References


