

EPEC

Education for Physicians on End-of-life Care

Trainer's Guide

Module 10

Common

Physical

Symptoms

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Module 10 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 10 presents an approach to the assessment and management of a number of common physical symptoms. After discussing general principles, the module moves to a discussion of the ethics that permit physicians to prescribe medications aimed at the relief of suffering, or any other therapy, that have known but unwanted consequences. It provides examples as to why the ethical reasoning known as the principle of double effect may not apply to most medical management of symptoms, even when opioids are used.

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:

Introduction	2-3 minutes
Video trigger tape & discussion	5-7 minutes
Presentation	35 minutes
Summary	2-3 minutes
<u>Post-test & Evaluation</u>	<u>5 minutes</u>
Total	45-50 minutes

3. Number of slides: 54

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 2 to 3 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 **Participant's Handbook** 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:

- the **EPEC Front Cover Page**
- the **EPEC Acknowledgment Pages** (to acknowledge the source of the material)
- the **EPEC Table of Contents** (to give each participant an overview of the EPEC curriculum)
- the syllabus and slides for **Module 10**

6. Equipment needs

- slide projector and screen
- video player and monitor or projector
- flipchart, or overhead projector with acetates, and markers for recording discussion points

Test your equipment beforehand to ensure that it works. Cue your video to the start of the segment you will use for the session.

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 video trigger tape

After reviewing the objectives for the session, show the video trigger tape. 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

Martha Stone is a 67-year-old woman with progressive pulmonary fibrosis. She has been having progressive shortness of breath and nausea for several months. She visits her physician.

Discussion

After the video, ask the participants for their comments about the issues and the interaction they have just seen. To affirm what they contribute, consider recording the important points on a flipchart or overhead projector.

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 questions?

- How did the physician ask questions? What was well done? What was missing?
- What did the physician do to foster a comfortable atmosphere?
- How did the physician address Ms Stone'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 videotape or how "real" the players seemed. If the participants don't like something that was said or done in the video, ask them how they would do it themselves.

Setting limits to discussion time

Limit discussion of the video 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 2 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.

Many participants will pick up that this is a "real" patient with a "real" doctor. Some find humor in her colorful personality. Don't let the group get carried away by this. Redirect the energy by probing into the case material presented. Ask participants to identify her emotions as she describes her symptoms (hint: she only describes anger—she can't seem to describe panic, anxiety, or fear, yet they are clearly operative).

5. Present the material

Recommended style: interactive lecture

An interactive lecture will permit you to engage your audience, yet cover 2 to 3 symptoms within 45 to 60 minutes. Identify the symptoms you plan to cover and select the slides to go with those symptoms. Use the case of Martha Stone to illustrate the symptoms of breathlessness and nausea. 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.

Turn off the projector and turn up the lights. Use a flipchart or overhead projector.

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

1. Initial therapeutic trials based on history, examination, and inference about the pathophysiology may provide both symptom relief and/or additional information as to the etiology and pathophysiology of the symptom.

Pearl: Accept the patient's self-report of his or her experience.

2. Where possible and consistent with the goals of care, treat the underlying cause, at the same time as you relieve physical symptoms.

Pearl: Assess how much the patient (as opposed to family) is bothered by symptoms. Frequently the patient is comfortable, but the family is distressed.

Ethical issues

3. It is the intent in offering a treatment greatly determines whether it is ethical medical practice.
4. Virtually all medical treatments have both intended effects and the risk of unintended, potentially adverse, secondary consequences.
5. Adequate symptom management can be achieved without causing death. Concerns that opioids used appropriately to manage symptoms will also hasten death or cause addiction are rarely relevant.

Breathlessness

6. Research has demonstrated that opioids will relieve the distress of breathlessness in many patients without a measurable effect on their respiratory rate, hemoglobin saturation, or blood gas concentrations when dosing guidelines are followed.

Pearl: Don't use pulse oximetry to assess relief of breathlessness.

7. Opioid treatment for dyspnea is consistent with good medical practice, and ethical when the intent is to relieve suffering. When dosing guidelines are followed it is exceedingly unlikely to cause drug abuse behaviors or premature death.
8. Benzodiazepines may relieve anxiety related to breathlessness.

Pearl: Nonpharmacologic techniques may also provide significant relief.

Nausea/vomiting

9. A thorough assessment of nausea and vomiting is crucial to understanding which of the potential etiologies is operative, what the likely pathophysiology is, and what the most appropriate therapy to prescribe would be
10. There are 6 different categories of antiemetic drugs

Constipation

11. Establish what the patient's normal bowel function is.
12. Constipation should be expected during opioid treatment, and prophylactic measures with stimulant or prokinetic laxatives should always be considered.
13. A thorough assessment of constipation is crucial to understanding which of the potential etiologies is operant, what the likely pathophysiology is, and what the most appropriate therapy to prescribe would be.

Pearl: The condition is easier to prevent than treat.

Potential pitfall: Misdirecting the radiologist. In assessing constipation with an x-ray, tell the radiologist that you are looking for the volume of stool present, not just signs of obstruction.

Anorexia/cachexia

14. Help family and caregivers distinguish between the normal progression of the disease, over which they have no control, and things they can do to help the patient feel better. Explore the emotional components and the meaning of the patient not eating, losing weight, or not having energy.

Pearl: Help families find an alternative way to express their desire to give care.

Fatigue/weakness

15. The physician can play an instrumental role in educating the patient and family about the nature of the symptom and giving the patient "permission" to rest.
16. Corticosteroids and psychostimulants may have a beneficial effect.

Fluids, edema

17. It is normal for some patients to develop relative hypotension, tachycardia, and reduced urine output in far-advanced phases of illness, especially in the presence of hypoalbuminemia.

Potential pitfall: Infusions of albumin are ineffective and very expensive.

18. For patients at the end of life, no amount of intravenous fluid and salt will return the intravascular volume to normal. Attempts to do so will create or exacerbate edema,

resulting in swollen limbs, skin breakdown, ascites, pleural effusions, and pulmonary edema.

Skin

19. Keep skin clean and dry.
20. Cover areas where prolonged urine or stool contact may occur.
21. Cover intact pressure points with thin hydrocolloid dressings.
22. Use appropriate pressure-reducing bed overlays to optimize weight distribution, reduce the risk of pressure ulcer development, and minimize contact pain.

Pearl: Prevention is easier and far less costly than treatment.

23. Treat superficial infections with topical metronidazole or silver sulfadiazine.
24. Manage odors by using kitty litter or other deodorizers.

Potential pitfall: Letting the patient become physically repellant. Unmanaged odors and ugly wounds can lead to poor-quality care as everyone avoids the patient.

Insomnia

25. Patients and families may be disturbed by insomnia, particularly day-night reversal.

Pearl: Avoid caffeine; assess alcohol use.

26. Antihistamines or benzodiazepines frequently manage insomnia effectively.

Potential pitfall: Causing confusion. Benzodiazepines can increase cognitive dysfunction, particularly in the elderly.

27. Low doses of a sedating neuroleptic (eg, chlorpromazine, 10-25 mg q hs) may be required to manage day-night reversal.
28. Trazodone may be particularly useful in the frail and elderly.

7. Summarize the discussion

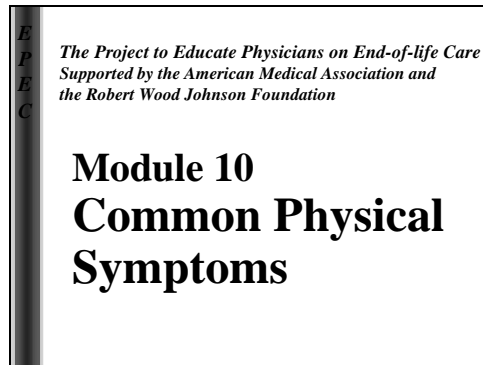
Briefly review each part of the presentation. Recap 2 or 3 of the most important points that were discussed.

8. Post-test/evaluation

Ask the participants to complete the post-test questions for Module 10 and evaluate the session.

Abstract

Slide 1



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*The Project to Educate Physicians on End-of-life Care
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**Module 10
Common Physical
Symptoms**

Many symptoms are commonly encountered in patients with advanced illness. This module discusses the assessment and management of breathlessness (dyspnea), nausea and vomiting, constipation, diarrhea, loss of appetite (anorexia)/weight loss (cachexia), edema, skin ulcers, insomnia, and fatigue (asthenia).

Each one can both be debilitating and prevent the patient and family from either continuing their lives or completing life closure. As with other aspects of medicine, management is tailored based on the underlying etiology and pathophysiology. When several symptoms occur together, they can be interrelated and management may become complex. The physician requires a working knowledge of therapy, drug interactions, and potential adverse effects to effectively relieve suffering and improve the patient's quality of life.

Key words

anorexia, asthenia, breathlessness, cachexia, constipation, diarrhea, dyspnea, edema, fatigue, insomnia, loss of appetite, nausea, skin ulcers, vomiting, weight loss

Objectives

Slide 2

Objectives

- Know general guidelines for managing nonpain symptoms
- Understand how the principles of intended / unintended consequences and double effect apply to symptom management
- Know the assessment, management of common physical symptoms

The objectives of this module are to:

- know general guidelines for managing nonpain symptoms
- understand how the principles of intended/unintended consequences and double effect apply to symptom management
- know the assessment and management of common physical symptoms

Clinical case on trigger tape

Martha Stone is a 67-year-old woman with progressive pulmonary fibrosis. She has been having progressive shortness of breath and nausea for several months. She visits her physician.

Introduction

During advanced stages of illness, particularly in end-of-life care, pain management appropriately receives a great deal of attention and emphasis. However, most patients are likely to suffer from a number of other symptoms besides pain. At times, these symptoms can be even more distressing to patients and families than pain. If unrelieved, they preclude any possibility of relieving psychological, social, and spiritual suffering, improving quality of life, or completing life closure.

Focusing on symptom control may make some physicians uneasy. Many regard symptoms simply as clues to lead the physician to diagnoses, and assume that the symptoms will improve as the disease gets better. While it is common for physicians to direct their efforts at curing or reducing disease, most do not understand the associated pathophysiology, appropriate pharmacology, or therapeutic interventions. When combined with misconceptions about the potential risks, interactions, or adverse effects of appropriate medications, symptoms are often very poorly controlled.

This module discusses basic approaches to the management of the physical symptoms that are commonly seen in medicine, and particularly in end-of-life care, including breathlessness (dyspnea), nausea/vomiting, constipation, diarrhea, anorexia/cachexia, fatigue, fluid balance/edema, pressure ulcers, and insomnia. There are multiple textbooks, journal articles, and conferences from which the physician who desires special expertise can learn more.

Several of the other EPEC modules present related topics. Module 3: Whole Patient Assessment discusses general approaches to patient assessment. Anxiety, delirium, and depression are discussed in detail in Module 6, pain is addressed in Module 4, and symptom management issues in the last hours of life, including terminal delirium and rattle, are discussed in Module 12.

General management guidelines

Slide 3

General management guidelines . . .

- History, physical examination
- Conceptualize likely causes
- Discuss treatment options, assist with decision making

Slide 4

. . . General management guidelines

- Provide ongoing patient, family education, support
- Involve members of the entire interdisciplinary team
- Reassess frequently

The general approach to managing any symptom is identical to the standard approach used to manage any illness. A thorough history, physical examination, and laboratory or radiologic investigations appropriate for the patient's situation are used to gain the best possible understanding of each symptom's etiology and underlying pathophysiology.

As symptoms are often interrelated with multiple concurrent medical problems, management can be challenging. As with any other illness, it is not acceptable to have an

unthinking approach to symptom management, as causes and appropriate therapies can vary widely.

Once the cause(s) and pathophysiology are known, intervention ideally includes therapy to relieve the symptom(s) as well as treat underlying causes. As many journal articles and textbooks have been written on the management of the underlying causes, this module will focus primarily on relieving the symptom itself.

When goals for care preclude disease management, symptom relief may be all that is required. When symptoms are debilitating or the patient is too weak, physicians will not be able to wait for the results of investigations before initiating therapy. Initial therapeutic trials based on history, examination, and inference about the pathophysiology may provide both symptom relief and/or additional information as to the etiology and pathophysiology.

As with pain management (see Module 4: Pain Management), if a symptom is present continuously, medication should be prescribed on a continuous or “around-the-clock” basis. Breakthrough doses may also be required.

Education and involvement of the patient and family as partners are key to successful management. Encourage patient and family to keep a diary when symptoms are out of control or adverse effects occur. When individual patient management becomes complex, physicians are encouraged to consult with local palliative medicine experts, and other members of the interdisciplinary team, to optimize therapies and minimize the risk of adverse events and drug interactions.

As etiologies and pathophysiology may change, frequent reassessment is critical, particularly when symptoms recur. As changes in the patient’s condition can occur rapidly, caregivers should be prepared to respond quickly.

Intended vs unintended consequences

Slide 5

Intended vs unintended consequences

- Primary intent dictates ethical medical practice

Many physicians believe that medications used to manage symptoms have an unusually or unacceptably high risk of an adverse event that may shorten a patient’s life, particularly when he or she is frail or close to the end of his or her life. Instead of fully

understanding and discussing the potential benefits and risks of these therapies with their patients, taking into account their goals for care, this fear of an adverse unintended consequence often leads clinicians to withhold treatment or dose inadequately, thus leaving their patients suffering unnecessarily.

When offering a therapy, the intent in offering a treatment that greatly determines whether it is ethical medical practice:

- if the intent in offering a treatment is desirable or helpful to the patient and the primary outcome is good (such as cure or relief of suffering), but there is a potential, adverse, secondary effect (such as death), then the treatment is probably still ethical if there was proper informed consent
- if the intent is not desirable or will harm the patient and the primary outcome is bad, the treatment is probably unethical

Concerns about intended vs unintended consequences are most commonly invoked around such issues as the treatment of pain or dyspnea with opioids. However, all medical treatments have both intended effects and the risk of unintended, potentially adverse, secondary consequences. Some examples are listed in the following table:

Intended vs Unintended Consequences

Therapy	Intended, Primary Effect	Potential Adverse, Secondary Consequences
TPN for short gut syndrome	Improved nutritional status	Sepsis, death
Chemotherapy	Cure or reduce the burden of cancer	Immune suppression, cytopenias, death
Amiodarone	Prevent arrhythmia	Promote arrhythmia, death
Epidural administration of analgesia	Reduce pain	Sepsis, death
Stopping all lab tests	Reduce burden of investigation for patient	Electrolyte imbalance, death
Operation to repair broken hip	Reduce pain, improve function	Cardiac arrest, death during surgery

Principle of double effect

The principle of double effect refers to an ethical construct when a person takes an action with an expected good outcome but with an unavoidable, known bad effect as well. The

primary intended effect can sometimes justify the action. When a physician uses a treatment for an ethical, intended effect where the potential outcome is good (eg, relief of a symptom), knowing that there may also be a dire, undesired, secondary effect such as death, this principle of double effect is commonly cited. In symptom control, however, it rarely applies. The secondary adverse consequence of death is not likely to occur.

Concerns about symptom management

Concerns that the principle of double effect may be an issue when managing symptoms are raised by the fact that, like other medical treatments, there is a risk that treatments to control symptoms could produce adverse consequences including death, either when improperly used or, very rarely, when properly used. Also, in suffering states of life-threatening illness, death may seem appealing and what is ordinarily intuitive may become complex. For many interventions, such as chemotherapy, total parenteral nutrition (TPN) for short gut syndrome, surgery, and noninterventions such as stopping all laboratory tests or avoiding surgery, we make decisions knowing there is a risk of adverse events, in particular death. As long as (a) the intent is to relieve suffering and not hasten death, (b) death is a possible and not inevitable outcome of the interventions, and (c) there is fully informed consent, the action need not be ethically suspect.

In contrast, if symptom control involves treatments that are intended to cause death as the means to relieve suffering, then there is ethical concern. If the patient seeks hastened death by physician-assisted suicide or euthanasia, the clinical and ethical issues are different. Some of these issues are addressed in Module 5: Physician-Assisted Suicide.

Fortunately, these difficult circumstances need not occur. Adequate symptom management can be achieved without causing death. If the reason for offering a medication such as an opioid is to relieve suffering (eg, pain, breathlessness), and accepted dosing guidelines are followed, the risk of a potentially dangerous adverse secondary effect is minimal. The risk of respiratory depression is vastly over estimated. Patients will become drowsy and confused and lose consciousness long before their respiratory rate is compromised.

Symptoms can be well controlled with the interventions outlined in this module and those in Module 4: Pain Management, Module 6: Depression, Anxiety, Delirium, and Module 12: Last Hours of Living. None of these recommendations, properly used, will cause death. In this, they are like all other medical interventions; concerns about unintended consequences are no greater than normal and concerns about double effect rarely apply.

Breathlessness (dyspnea)

Slide 6

Breathlessness (dyspnea) . . .

- May be described as
shortness of breath
a smothering feeling
inability to get enough air
suffocation

Slide 7

. . . Breathlessness (dyspnea)

- The only reliable measure is patient self-report
- Respiratory rate, pO₂, blood gas determinations DO NOT correlate with the feeling of breathlessness
- Prevalence in the life-threateningly ill: 12 – 74%

Case vignette

M.S. is a 67-year-old accountant with advanced pulmonary fibrosis. She experiences severe breathlessness with minimal activity around the house. She experiences little benefit from bronchodilators. She would like to be able to do things for herself.

Breathlessness can be one of the most frightening and distressing symptoms for patients, families, and caregivers. The sense of drowning or being smothered can be terrifying for everyone. Fortunately, for the majority of patients, relief can be relatively straightforward. Yet physicians' lack of understanding of breathlessness and the medications to manage it, and the fear of adverse effects, frequently lead to inadequate relief and unnecessary suffering for the patient, family, and caregivers.

Breathlessness, like pain, is a symptom, not a sign. Its prevalence is variable (12%–74%), depending on the diagnosis and the stage of the illness. Research has shown that measures of respiratory rate, oxygen saturation, blood gas levels, and professional and family members' perceptions do not correlate with the patient's perception of breathlessness. Thus, as we have no objective assessments, we must accept the patient's self-report of his or her experience. Some patients may not report breathlessness. However, when asked

about walking, they may indicate that breathlessness prevents them from walking at their usual pace or distance.

Families and caregivers need to be aware that what they see may be very different from the patient's experience. Time spent to understand the patient's wishes for symptom control, and to communicate management strategies to the patient, family, and caregivers, will minimize misunderstanding and onlookers' distress.

Causes of breathlessness

Slide 8

Causes of breathlessness

- Anxiety
- Airway obstruction
- Bronchospasm
- Hypoxemia
- Pleural effusion
- Pneumonia
- Pulmonary edema
- Pulmonary embolism
- Thick secretions
- Anemia
- Metabolic
- Family / financial / legal / spiritual / practical issues

Many different illnesses can impair respiration and leave the patient with a sense of being breathless. Some of the common mechanisms include anxiety, airway obstruction, bronchospasm, hypoxemia, pleural effusion, pneumonia, pulmonary edema, pulmonary embolism, thick secretions, anemia, metabolic disorders, and family/financial/legal/spiritual issues. Each may itself have many different etiologies.

Management of breathlessness

Slide 9

Management of breathlessness

- Treat the underlying cause
- Symptomatic management
 - oxygen
 - opioids
 - anxiolytics
 - nonpharmacologic interventions

As many other writers have focused on treatment of the underlying causes, this module focuses on the symptomatic management of breathlessness. A brief summary of approaches to the symptomatic management of airway obstruction, bronchospasm, pleural effusion, thick secretions, and anemia may be found in the appendix of this module.

When patients report air hunger, it is frequently not possible to identify and/or correct the underlying etiology. Therapeutic trials based on known history are frequently focused on symptomatic relief only. In patients with advanced disease, the burden of investigations and disease-modifying interventions may outweigh any potential benefit.

There are 3 widely used medical approaches for the symptomatic relief of breathlessness: oxygen, opioids, and anxiolytics. Nonpharmacologic interventions may also contribute significantly to the patient's and family's sense of well-being.

Oxygen

Slide 10

Oxygen

- Pulse oximetry not helpful
- Potent symbol of medical care
- Expensive
- Fan may do just as well

As breathlessness is frequently perceived to be a lack of air, it would seem to be quite reasonable to suppose that the administration of supplemental oxygen would relieve a patient's sense of air hunger. Yet, research has shown that the majority of patients who report breathlessness are not hypoxemic and measures of hypoxemia (eg, pulse oximetry, blood gas determination) do not correlate with the patient's self-report. Thus, do not follow pulse oximetry or blood gases to assess relief. These tests do not reliably reflect breathlessness or its relief. They may be uncomfortable and/or expensive, and divert the focus away from the symptom. It does not help symptom management to know that the oxygen saturation is 86% if the patient feels fine.

If a patient is breathless, a therapeutic trial of supplemental oxygen may be beneficial. After all, the goal is to make the patient feel better. However, clinicians should be aware that there is likely a placebo effect in nonhypoxemic patients. Supplemental oxygen is frequently viewed as a potent symbol of contemporary medical care. In addition, it is important to know that cool air moving across the patient's face, eg, from compressed air or from a fan, may relieve the sense of breathlessness. This is likely due to the physiologic effect of stimulating the V2 branch of the fifth cranial nerve that has a central inhibitory effect on the sensation of breathlessness. Portable oxygen is expensive and is not reimbursed by all insurance payers. Nevertheless, if the patient reports relief, use supplemental oxygen if possible.

Opioids

Slide 11

Opioids

- Relief not related to respiratory rate
- No ethical or professional barriers
- Small doses
- Central and peripheral action

Research has demonstrated that opioids will relieve the distress of breathlessness in many patients without a measurable effect on their respiratory rate or blood gas concentrations. The precise mechanism by which opioids exert this effect is unclear. There may be both central and peripheral effects.

In the opioid-naive patient, doses lower than those used to relieve pain may be effective. Sample prescriptions follow. When an effective dose has been established, convert to an extended-release preparation to simplify dosing. When using opioids, always anticipate adverse effects, particularly constipation.

While nebulized opioids have been widely reported to be effective in anecdotal reports and phase II studies, in placebo-controlled studies, they have not yet been demonstrated to be superior to nebulized saline.

When opioids are used to manage breathlessness, pharmacologic tolerance is not a clinically significant problem. In some patients, the symptom relief may also be associated with a measurable increase in exercise tolerance and mobility. If opioid dosing guidelines are followed (see Module 4: Pain Management), respiratory depression has not been demonstrated at the doses used to relieve breathlessness.

Concerns that opioids used to manage symptoms will hasten death or cause addiction are not relevant. Opioid treatment for dyspnea is consistent with good medical practice, and, when widely accepted dosing guidelines are followed, are unlikely to be associated with hastened death or abuse behaviors.

Sample opioid prescriptions

Mild dyspnea

For mild dyspnea in patients taking no opioid analgesics treatment options include:

- hydrocodone, 5 mg tab q 4 h with a breakthrough dose of 5 mg q 2 h prn
- acetaminophen, 325 mg, with codeine, 30 mg (1 tab) q 4 h with a breakthrough dose of 30 mg q 2 h prn
- for children or elderly who may require lower doses, consider hydrocodone/acetaminophen syrup, 1–3 mL q 4 h with a breakthrough dose equivalent to the q 4 h dose offered q 2 h prn

Severe dyspnea

In the opioid-naive patient treatment options include:

- morphine (as elixir or tablets), 5–15 mg q 4 h and titrate
- oxycodone, 5–10 mg q 4 h and titrate
- hydromorphone, 0.5–2 mg q 4 h and titrate

In patients receiving an opioid on a fixed schedule, an additional dose of a short-acting opioid (eg, morphine) equivalent to 30%–50% of the amount of the baseline opioid taken over 4 hours can be tried q 1 h, and titrated to effect. Opioids can be administered IV or SC for urgent situations or when the oral route is not available or advisable.

Chlorpromazine and promethazine have both been reported improve breathlessness, particularly when combined with opioids.

Anxiolytics

Slide 12

Anxiolytics

- **Safe in combination with opioids**

lorazepam
0.5-2 mg po q 1 h prn until settled
then dose routinely q 4–6 h to keep settled

Breathlessness, particularly when it is acute or severe, may cause severe anxiety and panic. Opioid and nondrug therapies may relieve both breathlessness and resultant anxiety. Consequently, their use is recommended as first-line pharmacologic therapy for

breathlessness. However, the opioids themselves, particularly with continued dosing, are not particularly anxiolytic.

Some patients who are breathless and anxious may need treatment for their anxiety. Although the management of anxiety is discussed in detail in Module 6: Depression, Anxiety, Delirium, pertinent aspects will be reviewed again here.

Benzodiazepines are highly effective anxiolytic medications. Use formulations that have relatively longer half-lives to avoid pronounced peak and trough effects that may lead to rebound anxiety. Begin with low doses and titrate to effect. These medications may be combined safely with opioids. Suggested benzodiazepines include:

- lorazepam, 0.5–2.0 mg po, SL, against the buccal mucosa, or IV q 1 h prn until settled, then dose routinely q 4–6 h to keep settled
- diazepam, 5–10 mg po, IV q 1 h until settled, then dose routinely q 6–8 h prn
- clonazepam, 0.25–2.0 mg po q 12 h
- midazolam, 0.5 mg IV q 15 min until settled, then by continuous SC or IV infusion

Nonpharmacologic interventions

Slide 13

Nonpharmacologic interventions . . .

- Reassure, work to manage anxiety
- Behavioral approaches, eg, relaxation, distraction, hypnosis
- Limit the number of people in the room
- Open window

Slide 14

Nonpharmacologic interventions . . .

- Eliminate environmental irritants
- Keep line of sight clear to outside
- Reduce the room temperature
- Avoid chilling the patient

. . . Nonpharmacologic interventions

- **Introduce humidity**
- **Reposition**
 - elevate the head of the bed
 - move patient to one side or other
- **Educate, support the family**

Additional relief of breathlessness may be provided by a variety of nonpharmacologic interventions. When possible, coordinate treatments with the family and other caregivers. Work closely with the patient and family to provide understanding and support, and explain the various interventions. Include other members of the interdisciplinary team to increase interaction, minimize loneliness, explore issues of meaning and value, and provide counseling for family, financial, legal, spiritual, or practical issues that may be adding to anxiety. Limit the number of people in the patient's room. Reduce the room temperature (without chilling the patient). Open a window and keep an unobstructed line of sight between the patient and the outside. Eliminate environmental irritants such as smoke. Maintain sufficient humidity in the air the patient is breathing. Reposition the patient by elevating the head of his or her bed, or moving him or her to one side or another. Try relaxation, distraction, or hypnotic therapy. Complementary and alternative medical approaches may help some patients.

In some instances, nonpharmacologic therapies may be effective without other medications. However, in the highly anxious patient, combination therapies are usually necessary.

Family member/caregiver reactions

Standing next to a person who is breathing at 36 breaths/min, with a pulse oximeter beeping and oxygen rushing through tubing, is anxiety producing for almost anyone. Family members and caregivers frequently take on the anxiety of the patient. In turn, their anxiety may make the patient's breathlessness worse.

When managing breathlessness, it is important to distinguish between the patient's distress and that of family members and caregivers. Minimize the number of machines and sounds. Titrate medications to relieve the patient's report of distress, not someone else's perception of it.

As patients approach the last hours of their lives, be sure to educate family members and caregivers about the breathing patterns they may witness. Remind them that what they see may be very different from what the patient experiences (see Module 12: Last Hours of Living).

Nausea/vomiting

Slide 16

Nausea / vomiting

- **Nausea**
 - subjective sensation
 - stimulation
 - gastrointestinal lining, CTZ, vestibular apparatus, cerebral cortex
- **Vomiting**
 - neuromuscular reflex

Case vignette

P.T. is a 92-year-old farmer with colon cancer metastatic to the liver. Right upper quadrant pain is well controlled with extended-release morphine, 60 mg po bid, and dexamethasone, 4 mg po q am. However, he complains of constant nausea that limits his ability to eat.

Nausea and/or vomiting are commonly associated with many advanced diseases. Nausea is an unpleasant subjective sensation that results from stimulation of the gastrointestinal lining, the chemoreceptor trigger zone in the base of the fourth ventricle, the vestibular apparatus, or the cerebral cortex. Vomiting is a neuromuscular reflex that constitutes a final common pathway after stimulation of one or more of these areas. The awareness of nausea, the inability to keep food or fluids down, the associated acid and bitter tastes, and the unpleasant smells associated with vomitus can be very distressing for patients, families, and caregivers.

Causes of nausea/vomiting

Slide 17

Causes of nausea / vomiting

● Metastases	● Mechanical obstruction
● Meningeal irritation	● Motility
● Movement	● Metabolic
● Mental anxiety	● Microbes
● Medications	● Myocardial
● Mucosal irritation	

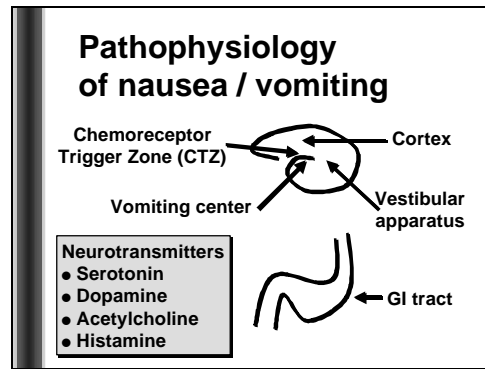
While there are multiple potential causes for both nausea and vomiting (see the table that follows), fortunately, symptomatic relief is relatively easy to achieve if the right

medications are chosen. Unfortunately, as with most symptoms, lack of physician understanding and unsophisticated prescribing frequently lead to inadequate relief and unnecessary suffering for the patient, family, and caregivers.

A thorough assessment of nausea and vomiting is crucial to understanding which of the potential etiologies is operant, what the likely pathophysiology is, and what would be most appropriate to prescribe. Different causes will require very different interventions if the symptoms are to be controlled effectively.

Pathophysiology of nausea/vomiting

Slide 18



There are 2 organ systems that are particularly important in nausea and vomiting: the brain and the GI tract. These are shown schematically. The gastric lining, the chemoreceptor trigger zone in the base of the fourth ventricle, the vestibular apparatus, and the cortex are all involved in the intricate physiology of nausea. The vomiting center is where the neuromuscular reflex that constitutes the final common pathway after stimulation from one or more of these areas emanates.

Stimulation is mediated through the neurotransmitters serotonin, dopamine, acetylcholine, and histamine. All 4 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 and vomiting that is mediated by the cortex is more complex and is not associated with specific neurotransmitters. Cortical responses seem to be learned responses (eg, the anticipatory nausea associated with chemotherapy, nausea related to anxiety, etc).

Management of nausea/vomiting

Slide 19

**Management of
nausea / vomiting**

- Dopamine antagonists
- Antihistamines
- Anticholinergics
- Serotonin antagonists
- Prokinetic agents
- Antacids
- Cytoprotective agents
- Other medications

This module focuses on the general symptomatic management of nausea and 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 and vomiting, it is frequently not possible to identify or specifically correct the underlying etiology. 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.

The table that follows will help to relate major causes of nausea/vomiting (11 M's of emesis) to their principal site of action. It is intended to set the stage for the rational use of the antiemetics, which can be classified by their principal site of action.

Empiric therapy with antiemetics usually begins with a single medication targeting the presumed mechanism of nausea/vomiting. The dose should be optimized before a second medication with a different mechanism of action is added. Sequential combination therapy may be required in some patients.

Management of Nausea/Vomiting		
Etiology	Pathophysiology	Therapy
Metastases Cerebral (increased ICP) Liver	increased ICP, direct CTZ effect toxin buildup	steroids, mannitol, anti-DA/Hist anti-DA/Hist
Meningeal irritation	increased ICP	Steroids
Movement	vestibular stimulation (may be worse with morphine)	anti-Ach
Mentation, eg, anxiety	Cortical	anxiolytics, eg, benzodiazepines, THC
Medications Opioids Chemotherapy Others (NSAIDs, see Mucosal Irritation)	CTZ, vestibular effect, GUT CTZ, GUT CTZ	anti-DA/Hist, anti-Ach, prokinetic agents, stimulant cathartics anti-5HT/DA, steroids anti-DA/Hist
Mucosal irritation NSAIDs Hyperacidity, gastroesophageal reflux	GUT, gastritis GUT, gastritis, duodenitis	cytoprotective agents antacids
Mechanical obstruction Intraluminal Extraluminal	Constipation, obstipation Tumor, fibrotic stricture	manage constipation reversible —surgery irreversible —manage fluids, ster- oids, inhibit secretions with octreotide, scopolamine
Motility Opioids, ileus, other medications	GUT, CNS	prokinetic agents, stimulant laxatives
Metabolic Hypercalcemia, hyponatremia, hepatic/renal failure	CTZ	anti-DA/Hist, rehydration, steroids
Microbes Local irritation, eg, esophagitis, gastritis from <i>Candida</i> , <i>H pylori</i> , herpes, CMV Systemic sepsis	GUT CTZ	antibacterials, antivirals, antifungals, antacids anti-DA/Hist, antibacterials, antivi- rals, antifungals
Myocardial Ischemia, congestive heart failure	Vagal stimulation, cortical, CTZ	Oxygen, opioids, anti-DA/Hist, anxiolytics
Legend: anti-Ach = Acetylcholine antagonists anti-DA = Dopamine antagonists	anti-Hist = Histamine antagonists anti-5HT = Serotonin antagonists CTZ = Chemoreceptor trigger zone	GUT = Gastrointestinal tract ICP = Intracranial pressure THC = Tetrahydrocannabinol

Dopamine antagonists

Slide 20

Dopamine Antagonists

- Haloperidol
- Prochlorperazine
- Droperidol
- Thiethylperazine
- Promethazine
- Perphenazine
- Trimethobenzamide
- Metoclopramide

Dopamine-mediated nausea is probably the most common form of nausea, and the most frequently targeted for initial symptom management, even when the precise mechanism of nausea is not known. These medications are phenothiazines or butyrophenone neuroleptics and have the potential to cause drowsiness and extrapyramidal symptoms, particularly in young women. Haloperidol is less sedating. Medication dosing options include:

- haloperidol, 0.5–2.0 mg po, IV, SC q 6 h, then titrate
- prochlorperazine, 10–20 mg po q 6 h or 25 mg pr q 12 h or 5–10 mg IV q 6 h
- droperidol, 2.5–5 mg IV q 6 h
- thiethylperazine, 10–20 mg po q 6 h
- promethazine, 12.5–25 mg IV, 25 mg po/pr q 4–6 h
- perphenazine, 2–8 mg po, IV q 6 h
- trimethobenzamide, 250 mg po q 6–8 h, 200 mg pr q 6–8 h
- metoclopramide, 10–20 mg po q 6 h

Histamine antagonists (antihistamines)

Slide 21

**Histamine antagonists
(antihistamines)**

- Diphenhydramine
- Meclizine
- Hydroxyzine

All antihistamines typically used to control nausea may also cause sedation. In some patients, this adverse effect may be an added benefit. Because the antihistamines also have anticholinergic properties, they may do “double duty” as a single agent and cover both mechanisms. Consider using:

- diphenhydramine, 25–50 mg po q 6 h
- meclizine, 25–50 mg po q 6 h
- hydroxyzine, 25–50 mg po q 6 h

Acetylcholine antagonists (anticholinergics)

Slide 22

**Acetylcholine antagonists
(anticholinergics)**

- Scopolamine

Opioids and anesthetics can trigger acetylcholine-mediated nausea in the vestibular apparatus. A medication from this class may be added to other antiemetics in empiric therapy. Consider:

- scopolamine, 0.1–0.4 mg SC, IV q 4 h or
1–3 transdermal patches q 72 h or
10–80 µg/h by continuous IV or SC infusion

Serotonin antagonists

Slide 23

Serotonin Antagonists

- Ondansetron
- Granisetron

Serotonin has been particularly implicated in chemotherapy-associated nausea. This class of medications can be exceedingly effective, but they are very expensive. They can be useful for refractory nausea of diverse types but are typically tried only when other medications have failed. They should be promptly stopped if they are not effective after a short trial. Medication and dosing options include:

- ondansetron, 8 mg po tid
- granisetron, 1 mg po q d or bid

Prokinetic agents

Slide 24

Prokinetic agents

- Metoclopramide
- Cisapride

A “sluggish” or dyskinetic gut (due to carcinomatosis, opioid therapy, other medications, etc) may be a profound source of nausea and vomiting in patients with advanced disease. A large liver may be causing a “squashed stomach.” Ascites or peritoneal disease may be causing pseudo-obstruction. Constipation can be an exacerbating factor. Medication and dosing options include:

- metoclopramide, 10–20 mg po q 6 h
- cisapride, 10–20 mg po q 6 h

Antacids

Slide 25

Antacids

- Antacids
- H₂ receptor antagonists
 - cimetidine
 - famotidine
 - ranitidine
- Proton pump inhibitors
 - omeprazole
 - lansoprazole

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, 1–2 tablespoons q 2 h prn
- H₂ receptor antagonists (cimetidine, famotidine, ranitidine)
- proton pump inhibitors (omeprazole, lansoprazole)

Cytoprotective agents

Slide 26

Cytoprotective agents

- Misoprostol
- Proton pump inhibitors (omeprazole, lansoprazole)

Mucosal erosion secondary to NSAIDs may be associated with significant nausea. Consider use of:

- misoprostol, 200 µg bid–qid
- proton pump inhibitors (omeprazole, lansoprazole)

Other medications

Slide 27

Other medications

- Dexamethasone
- Tetrahydrocannabinol
- Lorazepam

- Octreotide

This heterogeneous class of medications has unclear mechanisms of action, but uncontested benefits in some patients. Consider:

- dexamethasone, 6–20 mg daily
- tetrahydrocannabinol, 2.5–5 mg po tid
- lorazepam, 0.5–2 mg po q 4–6 h

The symptoms of bowel obstruction represent a special case. With complete obstruction, accumulation of intraluminal fluid from epithelial sources is principally responsible for the symptoms of bloating, crampy abdominal pain, nausea, and vomiting. Octreotide, a synthetic analog of somatostatin, selectively inhibits secretion of fluids and electrolytes into the gut lumen. It may be started by continuous IV at 10 µg/hr or intermittent subcutaneous injection. A standard regimen is:

- octreotide 100 µg q 8-12 h, titrate q 24 to 48 h to effect

Constipation

Slide 28

Constipation

<ul style="list-style-type: none">● Medications<ul style="list-style-type: none">opioidscalcium-channel blockersanticholinergic● Decreased motility● Ileus● Mechanical obstruction	<ul style="list-style-type: none">● Metabolic abnormalities● Spinal cord compression● Dehydration● Autonomic dysfunction● Malignancy
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Case vignette

A.R. is a 46-year-old mother of 2 with advanced ovarian cancer widespread within the abdomen. Ascites is present on examination. Bowel sounds are present. Pain is well controlled with transdermal fentanyl, 25 µg/h. However, she complains of persistent constipation.

Constipation can be defined as “discomfort associated with reduced frequency of bowel movements.” It is usually associated with an increase in stool consistency that leads to difficulty in defecating. There are many causes of constipation, including medications (eg, opioids, calcium-channel blockers, anticholinergics), decreased mobility, ileus, mechanical obstruction, dehydration, metabolic abnormalities, spinal cord compression, autonomic dysfunction, malignancy, etc.

The cause in a given patient is often not carefully assessed. If left unmanaged, it can lead to considerable patient distress. The consequences of unmanaged constipation include abdominal pain, bloating, nausea and vomiting, overflow incontinence, tenesmus, fecal impaction, or even bowel obstruction.

Management of constipation

Slide 29

Management of constipation

<ul style="list-style-type: none">• General measures<li style="padding-left: 20px;">establish what is "normal"<li style="padding-left: 20px;">regular toileting<li style="padding-left: 20px;">gastrocolic reflex	<ul style="list-style-type: none">• Specific measures<li style="padding-left: 20px;">stimulants<li style="padding-left: 20px;">osmotics<li style="padding-left: 20px;">detergents<li style="padding-left: 20px;">lubricants<li style="padding-left: 20px;">large volume enemas
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General approaches

Examination, investigation, and treatment should be tailored to the presentation, stage, and context of the person and illness. For most patients near the end of life, correction of the underlying pathophysiologic cause of constipation is often not possible or appropriate. The following general measures may be helpful.

Establish what the patient considers normal bowel function. There is a wide range of "normal" number of bowel movements per day or per week, consistency, color, and volume. Have the patient toilet regularly at the same time each day. Take advantage of the gastrocolic reflex that occurs after eating. Have the patient sit upright if possible.

Specific approaches

For medical management of constipation, suggested cathartics are listed in order of usual preference in patients with advanced illness, poor mobility, and decreased oral intake. Clinicians frequently fail to dose-escalate a particular modality. This leads to the sense that "nothing works" when, in fact, nothing has been tried to its maximal therapeutic dose.

Stimulant laxatives

Slide 30

Stimulant laxatives

- Prune juice
- Senna
- Casanthranol
- Bisacodyl

Stimulant laxatives irritate the bowel and increase peristaltic activity. Consider:

- prune juice, 120–240 mL q d or bid
- senna, 2 po q hs, titrate to effect (up to 9 or more per day)
- casanthranol, 2 po q hs, titrate to effect (up to 9 or more per day)
- bisacodyl, 5 mg po, pr q hs, titrate to effect

Osmotic laxatives

Slide 31

Osmotic laxatives

- Lactulose or sorbitol
- Milk of magnesia (other Mg salts)
- Magnesium citrate

Osmotic laxatives draw water into the bowel lumen. They maintain or increase the moisture content of stool and increase the overall stool volume. Consider:

- lactulose, 30 mL po q 4–6 h (sorbitol is cheaper alternative), then titrate
- milk of magnesia (or other Mg salts), 1–2 tablespoons 1–3 times per day
- magnesium citrate, 1-2 bottles prn

Detergent laxatives (stool softeners)

Slide 32

**Detergent laxatives
(stool softeners)**

- Sodium docusate
- Calcium docusate
- Phosphosoda enema prn

Detergent laxatives facilitate the dissolution of fat in water and increase the water content of stool. Consider:

- sodium docusate, 1–2 po q d–bid, titrate to effect
- calcium docusate, 1–2 po q d–bid, titrate to effect
- phosphosoda enema prn

Prokinetic agents

Slide 33

Prokinetic agents

- Metoclopramide
- Cisapride

Prokinetic agents stimulate the bowel’s myenteric plexus, and increase peristaltic activity and stool movement. Consider:

- metoclopramide, 10–20 mg po q 6 h
- cisapride, 10–20 mg po q 6 h

Lubricant stimulants

Slide 34

Lubricant stimulants

- Glycerin suppositories
- Oils
 - mineral
 - peanut

Lubricant stimulants lubricate the stool and irritate the bowel, thus increasing peristaltic activity and stool movement. Consider:

- glycerin suppositories
- oils:
 - mineral
 - peanut

Large-volume enemas

Slide 35

Large-volume enemas

- Warm water
- Soap suds

Large-volume enemas soften stool by increasing its water content. They also distend the colon and induce peristalsis. Consider:

- warm water

The addition of soap suds further irritates the colon and induces peristalsis. (NB. Too much soap suds may damage the bowel wall.)

- soap suds (irritates colon to induce peristalsis)

Constipation from opioids

Slide 36

Constipation from opioids . . .

- Occurs with all opioids
- Pharmacologic tolerance developed slowly, or not at all
- Dietary interventions alone usually not sufficient
- Avoid bulk-forming agents in debilitated patients

Slide 37

. . . Constipation from opioids

- Combination stimulant / softeners are useful first-line medications
 - casanthranol + docusate sodium
 - senna + docusate sodium
- Prokinetic agents

Constipation should be expected during opioid treatment, and prophylactic measures should always be considered. The condition is easier to prevent than treat, and prophylactic laxatives are reasonable in the elderly, debilitated patient who may have other coexisting causes of constipation. An effective regimen to maintain bowel function will enable patients to have both pain relief and normal bowel movements. New-onset abdominal pain and/or nausea and vomiting in a patient taking opioids may be due to unrecognized constipation. Abdominal x-rays may be needed to confirm the diagnosis. Warn the radiologist that you are looking for the volume of stool present, not just signs of obstruction.

While opioids cause constipation, they are not the only medication to do so. Other medications also commonly cause constipation, including calcium-channel blockers, and any medication with anticholinergic adverse effects (such as tricyclic antidepressants) may be causing or exacerbating the problem (see Module 4: Pain Management).

Diarrhea

Case vignette

S.D. is a 79-year-old tax attorney with advanced congestive heart failure. He is debilitated and has difficulty with mobility. Due to a curative resection of a large transverse mass some years ago, he has chronic diarrhea. Getting up to go to the bathroom 12 to 15 times per day is exhausting.

Diarrhea can be defined as stools that are looser than normal and that may be increased in numbers. If persistent, diarrhea can lead to dehydration, malabsorption, fatigue, hemorrhoids, and perianal skin breakdown.

Causes of diarrhea

Slide 38

Causes of diarrhea

- Infections
- GI bleeding
- Malabsorption
- Medications
- Obstruction
- Overflow incontinence
- Stress

Potential causes of diarrhea include infections, GI bleeding, malabsorption, medications, obstruction, overflow incontinence, stress, etc.

Management of diarrhea

Slide 39

Management of diarrhea

- Establish normal bowel pattern
- Avoid gas-forming foods
- Increase bulk
- Transient, mild diarrhea
 - attapulgite
 - bismuth salts

Management of persistent diarrhea

- Loperamide
- Diphenoxylate / atropine
- Tincture of opium
- Octreotide

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

General approaches

- establish normal bowel habits (there is wide variation)
- avoid gas-forming foods, particularly lactose
- increase bulk (eg, psyllium, bran, pectin)

Specific approaches

For the medical management of transient or mild diarrhea consider:

- attapulgate, 30 mL or 2 tabs prn
- bismuth salts, 15–30 mL bid–qid

For persistent and bothersome diarrhea, slow peristalsis consider:

- loperamide, 2–4 mg po q 6 h, or higher
- diphenoxylate/atropine, 2.5–5.0 mg po q 6 h or higher
- tincture of opium, 0.7 mL po q 4 h and titrate

For persistent, severe secretory diarrhea consider:

- octreotide, 50 µg SC q 8–12 h, then titrate up to 500 µg q 8 h SC, or higher, or 10–80 µg q 1 h by continuous SC, IV infusion
- parenteral fluid support, as needed and appropriate

Anorexia/cachexia

Slide 41

Anorexia / cachexia

- Loss of appetite
- Loss of weight

Case vignette

M.C. is a 53-year-old obstetrician with widely metastatic breast cancer to bone, liver, and lung. Her disease is slowly progressive despite chemotherapy and hormonal therapy. She has lost 60 pounds in the past 4 months, and complains of a poor appetite.

Anorexia (loss of appetite) and cachexia (loss of weight) are frequently accompanied by generalized fatigue (asthenia). These symptoms occur in many illnesses, particularly when the disease process is advanced. Wasting syndromes are often seen with certain malignancies, heart and pulmonary disease, renal and hepatic failure, and chronic infections, including Acquired Immune Deficiency Syndrome (AIDS).

The specific etiology of these symptoms is not well understood. However, they are a significant cause of distress to patients and, even more so, to families and caregivers. Loss of appetite and weight in a patient are often construed as evidence of “failure” to provide adequate care. Alternately, attentive families may believe that they are doing something wrong. Many patients and families conclude that, if only the patient would eat more, he/she would resume his/her former weight and vigor. Sadly, this is not usually possible, even with parenteral or enteral nutrition (see Module 11: Withholding, Withdrawing Therapy). These symptoms typically represent progression of disease and are not reversible.

Loss of appetite, weight, and energy are not strictly the result of malnutrition; providing nutrition, even parenterally, does not change the course of the disease. Helping patients and families understand these distinctions often diminishes guilt, hostility, or conflict. The physician and members of the health care team can then help the patient and family focus on things that may be useful.

Assessing for dysphagia, odynophagia, medication effects, or infections that may be causing or exacerbating the problem may be worthwhile. There are therapies that may improve appetite and add weight, although none affect longevity. The resumption of

eating for enjoyment, and the sense of normalcy that it promotes, may be worth the attempt and expense if it improves the patient's and family's sense of well-being.

Management of anorexia/cachexia

Slide 42

Management of anorexia / cachexia . . .

- Assess, manage comorbid conditions
- Educate, support
- Favorite foods / nutritional supplements

Slide 43

. . . Management of anorexia / cachexia

- Alcohol
- Dexamethasone
- Megestrol acetate
- Tetrahydrocannabinol (THC)
- Androgens

General approaches

There are several approaches to the general management of loss of appetite, weight loss, and fatigue. Assess and manage comorbid conditions such as anxiety, nausea, dehydration, constipation, and oral or systemic infections. Educate and support the family and caregivers. Help them distinguish between the normal progression of the disease, over which they have no control, and things they can do to help the patient feel better. Explore the emotional components and the meaning of the patient not eating, losing weight, or not having energy. Assess how much the patient (as opposed to family) is bothered by symptoms. Frequently the patient is comfortable, but the family is distressed.

Offer the patient favorite foods and nutritional supplements if the patient enjoys them. Eliminate dietary restrictions. Reduce portion sizes and make food look appetizing. Avoid odors that the patient finds disagreeable.

Specific approaches

There is a variety of pharmacologic approaches that may improve appetite. Frequently forgotten are the appetite-stimulating properties of alcohol. Particularly if the patient has enjoyed alcohol previously, it may be quite salutary to encourage an aperitif, cocktail, or other drink.

Corticosteroids have an appetite-stimulating effect, in addition to their effects on mood and energy. Consider:

- dexamethasone in doses of 2–20 mg/d is recommended because of its long half-life, permitting once-daily dosing, and relative lack of mineralocorticoid effects, though any corticosteroid will work
- megestrol acetate has been shown to stimulate appetite and promote weight gain in patients with AIDS and advanced cancer. The best dose is unclear and there appears to be large individual variation. Begin with 200 mg po q 6–8 h and titrate up or down to maintain effect
- the cannabinoids (eg, tetrahydrocannabinol [THC]) have been shown to promote weight gain in patients with AIDS and cancer. Begin with a small dose and titrate to effect and tolerability

The androgens (eg, oxandrolone, nandrolone, etc) are currently under investigation for their effects on appetite and weight. A therapeutic trial may be appropriate, especially in patients with AIDS.

Last hours of life

As patients approach the last hours of their lives, almost everyone will cease oral intake. As the patient's gag reflex and swallowing may become compromised, there may be a significant increased risk of aspiration. Patients, family members, and caregivers often find these changes distressing, and need a lot of support. Approaches to the management of feeding and nutrition at the end of life are discussed in Module 11: Withholding, Withdrawing Therapy, and Module 12: Last Hours of Living.

Fatigue/Weakness

Case vignette

T.L. is a 97-year-old woman with osteoarthritis, hypertension, and breast cancer meta-static primarily to bone. She lives independently, but complains about not having enough energy to go to the store.

In multiple series, fatigue/weakness is the most frequent distressing symptom associated with advanced illness and end-of-life care. Patients and families will frequently focus on the symptom rather than its underlying cause. Many believe that a person's strength is under his or her control, and feel that the patient is "giving up" or "not fighting."

The physician can play an instrumental role in educating the patient and family about the nature of the symptom and giving the patient "permission" to rest. The physician can help decrease the pressure from family or others exhorting the patient to be more alert, energetic, and conversant. Input from other team members may also be helpful.

Management of fatigue/weakness

Slide 44

Management of fatigue / weakness . . .

- Promote energy conservation
- Evaluate medications
- Optimize fluid, electrolyte intake
- Permission to rest
- Clarify role of underlying illness
- Educate, support patient, family
- Include other disciplines

Slide 45

. . . Management of fatigue / weakness

- Dexamethasone
 - feeling of well-being, increased energy
 - effect may wane after 4-6 weeks
 - continue until death
- Methylphenidate

General approaches

There are many general management approaches to fatigue. Help patients and families to adapt activities of daily living that promote energy conservation. Physiotherapy and occupational therapy can help with assessment, teaching, and assistive devices. Discontinue routine medications that are no longer appropriate near the end of life and may be making the fatigue worse (particularly antihypertensives, cardiac medications, diuretics, etc). Optimize fluid and electrolyte intake to maintain best possible hydration consistent with goals of care and the patient's ability to maintain intravascular hydration based on the degree of hypoalbuminemia. (See Module 7: Goals of Care, and Module 11: Withholding, Withdrawing Therapy.)

Specific approaches

While fatigue/weakness is not easily treated pharmacologically, some patients respond to a few of the following approaches. Steroids may have a beneficial effect. Dexamethasone in doses of 2 to 20 mg po daily is favored because its long half-life permits once-daily dosing and relative lack of mineralocorticoid adverse effects. Its use is frequently associated with feelings of well-being and increased energy. Dose in the morning for its activating effect. While it can be continued until death, the effect may wane after 4 to 6 weeks. As long-term adverse effects are not a factor for patients who are at the end of their lives, there is no need to taper the dose if it remains effective.

The psychostimulants may also be useful. Most experience has been gained with methylphenidate, although dextroamphetamine and pemoline have been used. Begin methylphenidate at 2.5 to 5 mg po q am and q noon and titrate to effect (usually 10–30 mg po q am and q noon, but sometimes higher). Extended-release formulations permit once-daily dosing. Methylphenidate can be used safely even in the debilitated patient. Adverse effects, including tremulousness, anorexia, tachycardia, and insomnia, should be monitored.

Fluid balance/edema

Slide 46

Fluid balance / edema . . .

- Frequently associated with advanced illness
- Hypoalbuminemia → decreased oncotic pressure
- Venous or lymphatic obstruction may contribute

Slide 47

. . . Fluid balance / edema

- Limit or avoid IV fluids
- Urine output will be low
- Drink some fluids with salt
- Fragile skin

Case vignette

O.F. is a 78-year-old mathematician with alcoholic cirrhosis of the liver with ascites and dependent edema. He complains of “tight legs and abdomen.” Blood pressure is 110/50 mm Hg and his wife notes he is not urinating very much.

This section will not cover the management of edema when the causes are easily identifiable and reversible. Difficult cases may merit interdisciplinary evaluation. This section discusses some useful points related to the management of patients with advanced disease.

In the face of hypoalbuminemia and consequent diminished oncotic pressure, patients will be unable to maintain their usual intravascular physiology. It is normal for some patients to develop relative hypotension, tachycardia, and reduced urine output. No amount of intravenous fluid and salt will return the intravascular volume to normal. Attempts to do so will create or exacerbate edema, resulting in swollen limbs, skin breakdown, ascites, pleural effusions, and pulmonary edema. Similarly, exogenous albumin infusions are ineffective and expensive and may make edema worse because of extravasation of denatured albumin into the soft tissues. Total parenteral nutrition is ineffective for different reasons (see earlier section in this module and Module 11: Withholding, Withdrawing

Therapy). These ineffective approaches will, if pursued, lead to markedly worsened physical symptoms due to edema that become more difficult to manage.

Notes on the management of patients with advanced disease and edema

The following tips and reminders can be helpful.

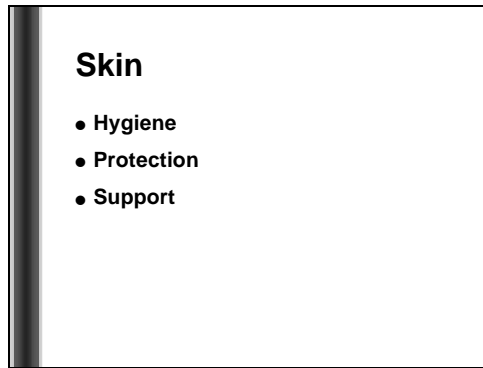
- hypoalbuminemia leads to reduced oncotic pressure, decreased intravascular volume (with relative hemoconcentration), and increased fluids in interstitial spaces (edema)
- decreased intravascular volume stimulates antidiuretic hormone secretion and increases free-water retention. This, in turn, leads to a relative hyponatremia as water exceeds salt retention
- in patients with hypoalbuminemia, a small amount of peripheral edema is indicative of “closer to normal” intravascular volumes, in contrast to the significantly decreased volumes that will be present when hypoalbuminemia is not accompanied by peripheral edema
- patients with clinical edema are not dehydrated; they have excess quantities of total body fluid and salt. With time, they may be able to reabsorb them, though not as efficiently as normal
- urine output of 300–500 ml/d or less is normal and adequate in this setting
- supplemental fluid (particularly parenteral) should be avoided. Patients should be encouraged to eat and drink as they usually do. Treat symptoms that prevent oral intake
- debilitated patients may only be drinking free water (such as in tap water, tea, coffee, juices, sodas that have no sodium chloride). Encourage them to drink some salt-containing fluids (soups, club soda, sport drinks, red vegetable juices) to help them maintain their electrolyte balance
- careful attention to mucous membranes (mouth, lips, eyes, nose, etc) can prevent sense of dryness that hypoalbuminemia and intravascular hypovolemia may bring (see Module 12: Last Hours of Living)
- edematous skin is fragile. Use other interdisciplinary team members to assess and manage it with appropriate supports and protection
- selected patients with limb edema may benefit from appropriate wrapping with compression bandages

Last hours of life

As with nutrition, almost everyone ceases oral fluid intake as they approach the last hours of their lives. Patients, family members, and caregivers often find these changes distressing, and need a lot of support. Approaches to the management of fluids at the end of life are discussed in Module 11: Withholding, Withdrawing Therapy, and Module 12: Last Hours of Living.

Skin

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Skin

- Hygiene
- Protection
- Support

Case vignette

E.K. is a 103-year-old housewife with advanced dementia. She has been a resident of a nursing home for the past 7 years. She has become progressively bedbound. Several bedsores over bony prominences have appeared.

Skin care is often overlooked in physician education. Yet, skin breakdown and ulceration can be a source of significant morbidity for both the patient and the family. The associated pain can be significant. Exudates, particularly purulent ones, can be soiling and malodorous. Good care requires close collaboration with nurses and other caregivers, as most cases of skin breakdown are preventable. Prevention is much easier than treatment once skin breakdown occurs.

While comprehensive wound management is not the focus of this module, a few points are worth reviewing, as many require a physician's order.

Hygiene

Encourage family and caregivers to keep skin clean and dry. A variety of nursing techniques are appropriate. Absorbent surfaces, urinary catheters and rectal tubes may be of assistance if soiling is constant and/or the patient is highly debilitated.

Protection

Cover areas with appropriate dressings where prolonged urine or stool contact may occur. Cover fragile skin that is at risk for breakdown with clear, occlusive dressings. Cover pressure points with thin, hydrocolloid dressings.

Supports

Appropriate bed coverings will optimize weight distribution, reduce the risk of decubitus ulcer development, and minimize contact pain. Use draw sheets to move/turn cachectic patients. Egg crate foam pads, or other support mattresses, should be thick enough to lift the patient from the bed. One rule of thumb is to ensure that there is at least 1 inch of foam between the patient's lowest point and the surface of the bed. If foam isn't enough, air mattresses or other special air-flotation beds may be required to fully support the patient.

Pressure ulcers

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Pressure (decubitus) ulcers

- Prolonged pressure
- Inactivity
- Closely associated with mortality
- Easier to prevent than treat

Pressure ulcer management should be consistent with the overall goals of care. If overall maintenance or improvement of function is the goal, and prognosis is expected to be weeks to months, then stage and treat the ulcer with accepted management guidelines (see the AHCPR management guidelines for pressure ulcers). Avoid all iodine-containing products as they will inhibit reepithelialization.

If prognosis is limited (days to weeks) and intent is to optimize quality of life, then a conservative management strategy to minimize morbidity is appropriate. Regular cleaning with saline or Betadine is helpful. Cover ulcers with appropriate protective dressings that absorb exudates.

Odors

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Odors

- Topical and / or systemic antibiotics
 - metronidazole
 - silver sulfadiazine
- Kitty litter
- Activated charcoal
- Vinegar
- Burning candles

Odors may be very distressing to patients, families, and caregivers, and may lead to poor-quality care, as even professional caregivers avoid sickening smells. Odors are usually the result of anaerobic infections and/or poor hygiene. Treat superficial infections with topical metronidazole or silver sulfadiazine bid or tid. For soft tissue infections, add systemic metronidazole, 250 to 500 mg q 8 h to topical management.

To control odors, place open kitty litter or activated charcoal in a pan under the patient's bed, provide adequate room ventilation, place an open cup of vinegar in the room, or burn a candle. Special charcoal-impregnated dressings placed over the odorous wound may also be helpful.

Insomnia

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Insomnia

- Assessment of sleep
- Other unrelieved symptoms
- Use family to help assess

Case vignette

G.E. is a 92-year-old seamstress with progressive dementia. Her daughter, who lives with her but works during the day, indicates the patient isn't sleeping well. The caregiver during the day indicates she spends most of the day in a chair in front of the television, and naps frequently.

Many patients (and their families) complain that they cannot sleep. Management begins with an assessment of usual and current sleep patterns. Do they have difficulty falling asleep or are they waking? Are they awakened by nightmares? Are they experiencing early morning awakening or nighttime restlessness? What do they think about when they are awake? Are they afraid? Are they experiencing day-night reversal of sleep patterns? What are the associated symptoms (eg, anxiety, pain, nausea and vomiting, breathlessness, medication effects), psychosocial or spiritual issues, or practical concerns that may be interfering with sleep? Family and other team members will often be needed to find answers.

Management of insomnia

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Management of insomnia . . .

- Regular sleep schedule, avoid staying in bed
- Avoid caffeine, assess alcohol intake
- Cognitive / physical stimulation
- Avoid overstimulation
- Control pain during the night
- Relaxation, imagery

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. . . Management of insomnia

- Antihistamines
- Benzodiazepines
- Neuroleptics
- Sedating antidepressant (trazodone)
- Careful titration
- Attention to adverse effects

General approaches

To manage insomnia, general measures will need to be instituted that support good sleep patterns. Establish and maintain a regular sleep schedule. If possible, avoid staying in bed when awake. Avoid caffeine (including analgesics with caffeine), particularly late in the day. Assess alcohol use. Many patients use alcohol as a soporific or “toddy” at bedtime. Yet, alcohol makes a poor sleeping medicine, as it can cause a paradoxical awakening several hours after falling asleep. Plan for cognitive and physical stimulation during the day. Avoid overstimulation in the period before going to sleep. Control bothersome

symptoms and use long-acting medication to control pain during the night. Interventions such as relaxation and imagery may be helpful.

Specific approaches

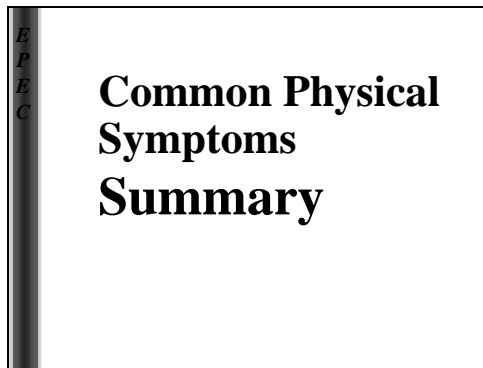
A number of pharmacologic measures may be adjuncts to the general measures indicated above. Antihistamines are frequently used. Examples include diphenhydramine, 25 to 50 mg po q hs, and meclizine, 25 to 50 mg po q hs. However, tolerance may develop quickly, and some patients find the anticholinergic adverse effects troubling. Benzodiazepines (eg, lorazepam, 0.5–2 mg po q hs) are frequently used. However, dementia and delirium may be worsened, particularly in the frail or elderly. Imidazopyridines (eg, zolpidem, 5–10 mg po q hs) may have fewer adverse effects.

Neuroleptic medications may be required, particularly if day-night reversal or delirium is present. (Management of delirium is covered in more detail in Module 6: Depression, Anxiety, Delirium). Risperidone or haloperidol, 1 mg q hs (less sedating), or chlorpromazine, 10–25 mg q hs (more sedating), may be useful.

Debilited and frail patients require careful titration and attention to undesired effects of medications. Commonly used medications may be associated with excessive daytime sedation. Trazodone, 25 mg po q hs (titrating to up to 200 mg q hs) may be particularly useful in the frail and/or elderly.

Summary

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Symptom control requires the physician to combine scientific knowledge of pathophysiology, pharmacotherapeutics, and human behavior with communication skills and clinical judgment. It is challenging and rewarding to help patients feel better in spite of progressive disease. Careful attention to symptom control may lead to better tolerance of disease-modifying therapies, and may even help prolong life. Continued symptom control as patients approach the end of their lives will give them the opportunity to realize the final goals they are striving for.

Resources

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Appendix

Treatment of selected underlying causes of breathlessness

Bronchospasm

Although wheezes and/or rhonchi may be present, always look for intercostal retraction on examination (evidence of bronchoconstriction, increased inspiratory pressures). If bronchospasm is suspected, a clinical trial of bronchospasmolytics may be indicated (though the potential of β -adrenergic agents, eg, albuterol, to cause adverse cardiac effects in patients with cardiac compromise must be carefully considered). Frail patients may have difficulties using puffers, even with aerochambers. Nebulized aerosols may be more effective. If adequate doses are ineffective, discontinue therapy to minimize the number of medications, risk of adverse effects, and cost. Possible medications include:

- steroids to reduce swelling and inflammation
 - dexamethasone, 2–20 mg po, IV, SC q d (long half-life permits once-daily dosing; minimal glucocorticoid effects and edema)
- albuterol, 2–3 puffs q 4–8 h (with aerochamber), or albuterol 0.5%, 2.5–5.0 mg diluted to 4.0 mL with saline by nebulizer q 4 h
- ipratropium bromide, 2–3 puffs q 4–8 h prn or 0.125 mg q 4 h via nebulizer
- theophylline and adrenergic agents may cause tremor and anxiety that will exacerbate dyspnea

Thick secretions

Thick secretions can accumulate around tracheostomy appliances and in airways of patients with obstruction or bronchospasm or those who are weak/frail. To minimize secretion buildup, maintain best possible hydration of the patient, keep mucous membranes moist, and increase humidity of inspired air (be careful not to increase risk of respiratory infections). If the cough reflex is strong, loosen secretions with nebulized saline and guaifenesin. If the cough reflex is weak, to dry secretions consider:

- scopolamine, 0.1–0.4 mg SC, IV q 4 h or 1–3 transdermal patches q 72 h or 10–80 µg/h by continuous IV or SC infusion
- glycopyrrolate, 0.4–1.0 mg q d by SC infusion or 0.2 mg SC, IV q 4–6 h prn
- hyoscyamine, 0.125 mg po or sl q 8 h

Pleural effusion

Pleural effusions can reduce lung volume considerably and cause great distress. Thoracentesis may be effective if fluids are not loculated. If the effusion continues to recur and thoracentesis is ineffective, consider talc, tetracycline, or bleomycin pleurodesis or Tenckhoff catheter insertion to facilitate repeat drainage (drainage can be done at home by visiting nurse).

Anemia

Selected patients who are anemic and breathless may benefit from a blood transfusion. Consider a clinical trial. Transfuse to a hemoglobin level greater than 10 g/dL and evaluate over several days. There may be an initial placebo effect. If the patient experiences a sustained increase in his or her energy and/or reduced breathlessness, consider following the hematocrit and transfuse as needed. If there is no benefit, do not follow the hematocrit or repeat transfusion.

If the patient has a life expectancy of months or more, consider epoetin alfa 10,000 IU SC 3 times per week (onset of effect takes 4 weeks). Double the dose if the hemoglobin does not increase by more than 1 g/dL within 4 weeks.

Airway obstruction

Airway obstruction can cause considerable distress. High-pitched inspiratory stridor is often audible at a distance. Make sure tracheostomy appliances are cleaned regularly. If the patient is still eating and aspiration is likely, puree solids, thicken liquids with cornstarch or other thickeners, and instruct family members and caregivers on positioning during feeding and suctioning. Surgical management or radiation therapy may be appropriate. Possible medications include:

- steroids to reduce swelling and inflammation
 - dexamethasone, 2–20 mg po, IV, SC q d (long half-life permits once-daily dosing; minimal mineralocorticoid effect or edema)
- manage thick secretions
- racemic epinephrine by inhaler
- oxygen mixed with helium