COMMON PHYSICAL SYMPTOMS

BREATHLESSNESS (DYSPNEA)

Case Example: *MS 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.*

Definition/Description

- One of the most frightening and distressing symptoms for patients, families, and caregivers
  - Shortness of breath
  - Smothering feeling
  - Inability to get enough air
  - Suffocation
  - Sense of drowning
- Prevalence in the life-threateningly ill: 12%–74%, depending on the diagnosis and the stage of illness
- Fortunately, for the majority of patients, relief can be relatively straightforward
- Yet 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
- Respiratory rate, pO2, blood gas determinations DO NOT correlate with the feeling of breathlessness
- The only reliable measure is patient self-report
  - 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

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

Management

- Treat the underlying cause
- However, when patients report air hunger, it is frequently not possible to identify and/or correct the underlying etiology
- In patients with advanced disease, the burden of investigations and disease-modifying interventions may outweigh any potential benefit
- Symptomatic management (focus of this module)
  - Oxygen
  - Opioids
  - Anxiolytics

- Nonpharmacological interventions

Oxygen

- 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
  - Measures of hypoxemia (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
    - Goal is to make the patient feel better
    - However, clinicians should be aware that there is likely a placebo effect in non-hypoxemic 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 (e.g., from compressed air or from a fan) may relieve the sense of breathlessness
    - This is likely due to the physiological effect of stimulating the V2 branch of the fifth cranial nerve that has a centrally 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 it can be afforded

Opioids

- 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. Both central and peripheral effects possible
- In the opioid-naive patient, doses lower than those used to relieve pain may be effective
- When an effective dose has been established, convert to an extended-release preparation to simplify dosing
- 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, pharmacological tolerance is not a clinically significant problem
- In some patients, the symptom relief may be associated with 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 (i.e., double effect) or cause addiction are ***not relevant***
- When opioids are used appropriately to relieve a symptom, like the management of pain
  - Opioid treatment for dyspnea is consistent with good medical practice
  - Ethical when the intent is to relieve suffering, widely accepted dosing guidelines are followed
  - Very unlikely to be associated with abuse behaviors
- Sample opioid prescriptions
  - Mild dyspnea in patients taking no opioid analgesics
    - Hydrocodone 5 mg tab q 4h with a breakthrough dose of 5 mg q 2h prn
    - Acetaminophen 325 mg with codeine 30 mg (1 tab) q 4h with a breakthrough dose of 30 mg q 2h prn
    - For children or elderly who may require lower doses: consider hydrocodone/acetaminophen syrup 1–3 ml q 4h with a breakthrough dose equivalent to the q 4h dose offered q 2h prn
  - Severe dyspnea in the opioid-naive patient
    - Morphine (as elixir or tablets) 5–15 mg q 4h and titrate
    - Oxycodone 5–10 mg q 4h and titrate
    - Hydromorphone 0.5–2 mg q 4h and titrate
  - Comments:

        - In patients receiving an opioid on a fixed schedule, an additional dose of a short-acting opioid (e.g., morphine) equivalent to 30–50% of the amount of the baseline opioid taken over 4 hours can be tried q 1h, 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

- Breathlessness, particularly when it is acute or severe, may cause severe anxiety and panic
    - Opioid and non-drug therapies may relieve both breathlessness and resultant anxiety
    - Consequently, their use is recommended as first line pharmacological 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
- Anxiolytics are safe in combination with opioids
    - 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 1h prn until settled, then dose routinely q 4–6h to keep settled
    - diazepam 5–10 mg PO, IV q 1h until settled, then dose routinely q 6–8h prn
    - clonazepam 0.25–2.0 mg po q 12h
    - midazolam 0.5 mg IV q 15min until settled, then by continuous SC or IV infusion

Nonpharmacological Interventions

- When possible, coordinate treatments with the family and other caregivers
    - Work closely with the patient and family to provide understanding and support
    - 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
- Reassure and work to manage anxiety
- Behavioral approaches, e.g., relaxation, distraction, and hypnosis
- Limit the number of people in the room
- Open window, keep line of sight clear between patient and outside
- Eliminate environmental irritants (e.g., smoke)
- Reduce the room temperature (without chilling the patient), introduce humidity
- Reposition
    - Elevate the head of the bed
    - Move patient to one side or other
- Educate and support the family
- Nonpharmacological therapies may be effective without other medications
    - However, in the highly anxious patient, combination therapies are usually necessary

Family and 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

NAUSEA AND VOMITING

Case Example: *PT 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.*

Definition/Description

- Commonly associated with many advanced diseases
- 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
- Nausea
    - Subjective sensation
    - Stimulation
        - Gastrointestinal lining, chemoreceptor trigger zone, vestibular apparatus, cerebral cortex
- Vomiting
    - Neuromuscular reflex
    - Constitutes a final common pathway after stimulation of one or more of these areas

Causes

- 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, lack of understanding and unsophisticated prescribing contributes to inadequate relief and unnecessary suffering for the patient, family, and caregivers
- Pathophysiology
    - There are 2 organ systems that are particularly important in nausea and vomiting: Brain and GI tract
    - Usual process
        - 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
    - However, when mediated by the cortex, nausea and vomiting is more complex
        - Not associated with specific neurotransmitters
        - Seem to be learned responses (e.g., the anticipatory nausea associated with chemotherapy, nausea related to anxiety, etc)

Management

- Assessment
    - Which of the potential etiologies is operating?
    - What is the likely pathophysiology?
    - What would be the most appropriate intervention to prescribe?
- Different causes will require very different interventions if the symptoms are to be controlled effectively
- Focus here on general symptomatic management of nausea and vomiting
- Not frequently possible to identify or specifically correct underlying etiology

- Therapeutic trials may provide both relief and clues to underlying causes
- When causes are known, burden of disease-modifying intervention may outweigh it potential benefit
- Empirical therapy with antiemetics
    - Usually begins with a single medication
    - Target the presumed mechanism of nausea/vomiting
- Dose optimized before a second medication with a different mechanism of action is added
- Sequential combination therapy may be required

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, steroids, , inhibit secretions w. 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, e.g., esophagitis, gastritis from Candida, H pylori, herpes, CMV Systemic sepsis	 GUT CTZ	 antibacterials, antivirals, antifungals, antacids anti-DA/Hist, antibacterials, antivirals, 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

Antiemetic Types

Dopamine Antagonists

- Dopamine-mediated nausea is probably the most common form of nausea
- Frequently targeted for initial symptom management, even when the precise mechanism of nausea is not known
- These medications are phenothiazines or butyrophenone neuroleptics
- Potential to cause drowsiness and extrapyramidal symptoms, particularly in young women
- Haloperidol is less sedating
    - Haloperidol 0.5–2.0 mg PO, IV, SC q 6h, titrate
    - Prochlorperazine
        - 10–20 mg PO q 6h, or
        - 25 mg PR q 12h, or
        - 5–10 mg IV q 6h
    - Droperidol 2.5–5 mg IV q 6h
    - Thiethylperazine 10–20 mg PO q 6h
    - Promethazine
        - 12.5–25 mg IV q 4–6h, or
        - 25 mg PO, PR q 4–6h
    - Perphenazine 2–8 mg PO, IV q 6h
    - Trimethobenzamide
        - 250 mg PO q 6–8h, or
        - 200 mg PR q 6–8h

Antihistamines (Histamine Antagonists)

- 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. Types:
    - Diphenhydramine 25–50 mg PO q 6h
    - Meclizine 25–50 mg PO q 6h
    - Hydroxyzine 25–50 mg PO q 6h

Anticholinergics (Acetylcholine Antagonists)

- Opioids and anesthetics can trigger acetylcholine-mediated nausea in the vestibular apparatus
- A medication from this class may be added to other antiemetics in empirical therapy
- Scopolamine
    - 0.1–0.4 mg SC, IV q 4h, or
    - 1–3 transdermal patches q 72h, or
    - 10–80 mg/h by continuous IV or SC infusion

Serotonin Antagonists

- 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
- Typically tried only when other medications have failed
- They should be promptly stopped if they are not effective after a short trial. Types:
    - Ondansetron 8 mg PO tid
    - Granisetron 1 mg PO q d or bid

Prokinetic Agents

- 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. Types:
    - Metoclopramide 10–20 mg PO q 6h
    - Cisapride 10–20 mg PO q 6h

Antacids

- Hyperacidity, with or without gastroesophageal reflux and/or gastric or duodenal erosions, may produce considerable
    - Nausea
    - Heartburn
    - Acidity
    - Bitter taste
- Also associated with vomiting. Types:
    - Antacids 1–2 tablespoons q 2h prn
    - H2 receptor antagonists (cimetidine, famotidine, ranitidine)
    - Proton pump inhibitors (omeprazole, lansoprazole)

Cytoprotective Agents

- Mucosal erosion secondary to NSAIDs may be associated with significant nausea. Types:
    - Misoprostol 200 mg bid–qid
    - Proton pump inhibitors (omeprazole, lansoprazole)

Other Medications

- This heterogeneous class of medications has unclear mechanisms of action, but uncontested benefits in some patients
    - Dexamethasone 6–20 mg daily
    - Tetrahydrocannabinol 2.5–5 mg po tid
    - Lorazepam 0.5–2 mg po q 4–6h
- The symptoms of bowel obstruction represent a special case
    - With complete obstruction, accumulation of intraluminal fluid from epithelial sources is principally response 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
        - Octreotide may be started by continuous IV at 10 mg/hr or intermittent subcutaneous injection 100 mg q 8-12 h
        - Titrated every 24-48 hours to relief of symptoms

CONSTIPATION

Case Example: *AR 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 mg/hour. However, she complains of persistent constipation.*

Definition/Description

- "Discomfort associated with reduced frequency of bowel movements"
- Usually associated with an increase in stool consistency that leads to difficulty in defecating
- Often neglected symptom
    - Often not carefully assessed
    - If left unmanaged, it can lead to considerable patient distress
    - Consequences of unmanaged constipation
        - Abdominal pain
        - Bloating
        - Nausea and vomiting
        - Overflow incontinence
        - Tenesmus
        - Fecal impaction
        - Bowel obstruction

Causes

- Decreased mobility, ileus, mechanical obstruction
- Metabolic abnormalities
- Spinal cord compression
- Dehydration
- Autonomic dysfunction
- Malignancy
- Medications
    - Opioids
    - Calcium-channel blockers
    - Anticholinergics

Management: General Measures

- Tailor examination, investigation, and treatment to presentation, stage, and context of the person and illness
- Correction of the underlying pathophysiological cause of constipation often not possible or appropriate for many patients at the end of life

- Establish what is "normal" -- Wide range of "normal" number of bowel movements per day or per week, consistency, color, and volume
- Regular toileting
- Have the patient toilet regularly at the same time each day
- Gastrocolic reflex
    - Take advantage of the gastrocolic reflex that occurs after eating (strongest peristalsis is in the early morning)
    - Have the patient sit upright if possible
- Medical management. Notes:
    - 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
- Stimulents
    - Prune juice 120–240 ml q d or bid
    - Senna 2 PO q hs, titrate (up to 9 or more per day)
    - Casanthranol 2 PO q hs, titrate (up to 9 or more per day)
    - Bisacodyl 5 mg PO, PR q hs, titrate
- Osmotics
    - Lactulose 30 cc PO q 4–6h, titrate (sorbitol is cheaper alternative)
    - Milk of magnesia 1–2 tablespoons 1–3 times per day or other Mg salts
    - Magnesium citrate
- Detergents
    - Stool softeners
        - Sodium docusate 1–2 po q d–bid, titrate
        - Calcium docusate 1–2 po q d–bid, titrate
    - Phospho-soda enema prn
- Lubricants
    - Mineral and peanut oil
    - Glycerin suppositories
- Large-volume enemas
    - Warm water - distends colon to soften stool and induce peristalsis
    - Soap suds - irritates colon to induce peristalsis
- Prokinetic Agents
    - Metoclopramide 10–20 mg PO q 6h
    - Cisapride 10–20 mg PO q 6h

Constipation from Opioids

- Occurs with all opioids
- Prophylactic measures
    - Consider prophylactic measures
    - Easier to prevent than treat
    - Reasonable in the elderly, debilitated patient who may have other coexisting causes of constipation
    - 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 radiologist that you are looking for the volume of stool present, not just signs of obstruction
- Pharmacological tolerance developed slowly, or not at all
- Dietary interventions alone are usually not sufficient
- Combination stimulant/softeners are useful first-line medications
    - Casanthranol + docusate sodium
    - Senna + docusate sodium
- Avoid bulk-forming agents in debilitated patients
- Prokinetic agents helpful in management

- While opioids cause constipation, they are not the only medication to do so
    - Calcium-channel blockers
    - Any medication with anticholinergic adverse effects (such as tricyclic antidepressants)

DIARRHEA

Clinical Example: *SD 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 12–15 times per day is exhausting.*

Definition/Description

- Stools that are looser than normal and that may be increased in numbers. If persistent, diarrhea can lead to:
    - Dehydration
    - Malabsorption
    - Fatigue
    - Hemorrhoids
    - Perianal skin breakdown

Causes

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

General Management

- Establish normal bowel pattern (wide variation)
- Avoid gas-forming foods, particularly lactose
- Increase bulk (e.g., psyllium, bran, pectin)

Specific Management

- Transient, mild
    - Attapulgite 30ml or 2 tabs prn
    - Bismuth salts 15–30 cc bid–qid
- Persistent
    - loperamide 2–4 mg PO q 6h, or higher
    - Diphenoxylate/atropine 2.5–5.0 mg PO q 6h or higher
    - Tincture of opium 0.7 cc PO q 4h and titrate
- For persistent, severe secretory diarrhea
    - octreotide 50 mg SC q 8–12h, then titrate up to 500 mg q 8h SC, or higher, or 10–80 mg q 1h by continuous SC, IV infusion
    - parenteral fluid support, as needed, and appropriate

ANOREXIA/CACHEXIA

Clinical Example: *MC 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.*

Definition/Description

- Anorexia (loss of appetite)
- Cachexia (loss of weight)
- Frequently accompanied by generalized fatigue (asthenia)
- Occur in many illnesses, particularly in advanced disease process
- Wasting syndromes often seen with malignancies, heart and pulmonary disease, renal, and hepatic failure, and chronic infections, including AIDS

Causes

- Specific etiology of these symptoms is not well understood
- Significant cause of distress to patients and, even more so, to families and caregivers
    - 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
    - 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

Assessment

- 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

General Management of Anorexia/Cachexia

- Assess, manage comorbid conditions
    - Anxiety
    - Nausea
    - Dehydration
    - Constipation
    - Oral or systemic infections
- Educate, support 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 with these symptoms, but the family is distressed
- Favorite foods/nutritional supplements
    - 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 Management of Anorexia/Cachexia

- Alcohol
    - 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
    - dexamethasone in doses of 2–20 mg/day 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 6–8h and titrate up or down to maintain effect
    - the cannabinoids (e.g., 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
- Androgens
    - The androgens (e.g., oxandrolone, nandrolone, etc) are currently under investigation for their effects on appetite and weight
    - A therapeutic trial may be appropriate, especially in patients with HIV/AIDS

Comments on the 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

FATIGUE/WEAKNESS

Clinical Example: *TL is a 97 year old woman with osteoarthritis, hypertension, and breast cancer metastatic primarily to bone. She lives independently, but complains about not having enough energy to go to the store.*

Definition/Description

- Fatigue/weakness is one of the most frequent distressing symptoms
- 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
    - Feel that the patient is "giving up" or "not fighting"
- Education of patient and family crucial
    - Giving the patient "permission" to rest
    - Decrease the pressure from family or others exhorting the patient to be more alert, energetic and conversant

General Management

- Adapt activities of daily living
    - Promote energy conservation
    - Physiotherapy and occupational therapy can help with assessment, teaching, and assistive devices
- Evaluate medications
    - Discontinue routine medications that are no longer appropriate near the end of life
    - May be making the fatigue worse
    - Particularly antihypertensives, cardiac medications, diuretics, etc
- Optimize fluid, electrolyte intake
    - Best possible hydration
    - Consistent with goals of care and the patient's ability to maintain intravascular hydration
    - Based on the degree of hypoalbuminemia
- Permission to rest
- Clarify role of underlying illness
- Educate, support patient, family

Specific Management

- 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
        - Doses of 2–20 mg PO daily is favored because of its long half-life (permitting once-daily dosing) and relative lack of mineralocorticoid adverse effects
        - Dose in the morning for its activating effect
        - Associated with feeling of well-being, increased energy
        - 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 not need to taper the dose if it remains effective
- Psychostimulants may also be useful
    - Most experience has been gained with methylphenidate
        - Also, dextroamphetamine and pemoline have been used
        - Begin methylphenidate at 2.5–5 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

Clinical Example: *OF 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 isn't urinating very much.*

Definition/Description

- Frequently associated with advanced illness
- Focus in this section is on management of patients with advanced disease
- This does not cover the management of edema when the causes are easily identifiable and reversible
- Difficult cases may merit interdisciplinary evaluation

Causes

- Hypoalbuminemia leads to reduced oncotic pressure, decreased intravascular volume (with relative hemoconcentration), and increased fluids in interstitial spaces (edema)
    - In the face of hypoalbuminemia and consequent diminished oncotic pressure, patients will be unable to maintain their usual intravascular physiology
    - 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
    - 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
        - These ineffective approaches will, if pursued, lead to markedly worsened physicalsymptoms due to edema that become more difficult to manage
        - 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
        - Venous or lymphatic obstruction may contribute

Management

- Limit or avoid IV fluids
- Urine output will be low -- urine output of 300–500 ml/day or less is normal and adequate in this setting
- Drink some fluids with salt
    - 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
- Fragile skin
    - 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
- 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).

Comments on Last Hours of Living

- As with nutrition, almost everyone ceases oral 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

SKIN

Clinical Example: *EK 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.*

Definition/Description

- 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 family
    - The associated pain can be significant
    - Exudates, particularly purulent ones, can be soiling and malodorous

Management

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

ODORS

Definition/Description

- Odors may be very distressing to patients, families, and caregivers
- 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

Management

- Topical and/or systemic antibiotics
    - Treat superficial infections with topical metronidazole or silver sulfadiazine bid–tid
    - For soft tissue infections, add systemic metronidazole 250–500 mg q 8h to topical management
- Nonpharmacologic approaches
    - To control odors in room:
        - 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
        - Burn a candle

INSOMNIA

Clinical Example: *GE 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.*

Definition/Description -- Many patients (and their families) complain that they cannot sleep

Assessment

- 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 (e.g., 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

General Management

- Encourage patient:
    - Maintain a regular sleep schedule
    - If possible, avoid staying in bed when awake
    - Avoid caffeine, including analgesics with caffeine, especially late in the day
- Assess alcohol
    - Many patients use alcohol as a soporific or "toddy" at bedtime
    - Can cause a paradoxical awakening several hours after falling asleep
- Plan for cognitive/physical stimulation during the day
- Suggest that the patient avoid overstimulation in the period before going to sleep
- Control pain during the night with long-acting medication
- Relaxation and imagery interventions may be helpful
    - Maintain a regular sleep schedule
    - If possible, avoid staying in bed when awake
    - Avoid caffeine, including analgesics with caffeine, especially late in the day

Specific Management

- Pharmacological measures may be adjuncts to the general measures indicated above
- Antihistamines are frequently used
    - Examples include:
        - diphenhydramine 25–50 mg po q hs
        - meclizine 25–50 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
    - Risperidone or haloperidol 1 mg q hs (less sedating)
    - chlorpromazine 10–25 mg q hs (more sedating)
- Debilitated 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

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