



Hospice and Palliative Medicine
and Supportive Care
Flashcards

Edited by

Sriram Yennurajalingam and Eduardo Bruera

HOSPICE AND PALLIATIVE MEDICINE
AND SUPPORTIVE CARE FLASHCARDS

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PREFACE

In the United States, the subspecialty of hospice and palliative medicine has seen rapid growth since it was recognized by the American Board of Medical Specialties. During the past decade, there has been a dramatic increase in the number of palliative care programs and improved access to palliative and hospice for patients with life-limiting illness. There has also been an increase in educational opportunities as well as growth of fellowship programs to train palliative care fellows. Unfortunately, there are limited study aids available for learning and retaining essential concepts in palliative care for medical students, residents, and fellows. Prior research suggests that study aids such as “flashcards” are effective in helping students and practitioners rapidly recall essential concepts, verify the accuracy of their knowledge, boost their confidence to take the board exams, and improve clinical performance.

The purpose of this point-of-care quick reference material is to assist individuals taking care of patients requiring supportive care, hospice, and palliative care master key concepts related to clinical assessment and management. This handbook was written using clinical scenarios/vignettes with a question-and-answer format, and it will serve as a source of fast answers to all clinical questions in the field in an easy to understand format. This handbook is concise, succinct, evidenced based, and written by authors who have first-hand experience caring for patients with the diseases in question. Our team of authors also have extensive experience in training palliative care physicians to successfully pass the board exam in hospice and palliative medicine.

We believe this handbook will address most of the daily bedside clinical and administrative needs, and we hope it will help our colleagues in the delivery of excellent palliative and hospice care and supplement as study material for physicians taking the hospice and palliative medicine board examination.

We acknowledge the authors of the chapters for having committed their time and effort to our joint project. We also acknowledge the commitment to excellence by Oxford University Press and in particular Andrea Knobloch, Rebecca Suzan, and Tiffany Lu, our editors, for their excellent work in coordinating this book. Finally, we acknowledge the daily effort of health care professionals who have contributed by their daily clinical work, education, and research to the development of the extraordinary body of knowledge that we have had the privilege to synthesize in this handbook.

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HOSPICE AND PALLIATIVE MEDICINE
AND SUPPORTIVE CARE FLASHCARDS

1

**Principles of Hospice
and Palliative
Medicine and
Supportive Care**

SRIRAM YENNURAJALINGAM

Question 1.1

Mr. Joe Smith is a 67-year-old with new-onset pain in the right upper quadrant of the abdomen. Computed tomography scan of the abdomen showed multiple hepatic metastasis. α -Fetoprotein level was 1982. The clinical team made the diagnosis of metastatic hepatocellular cancer. His wife, who has been married to him for 40 years, is anxious regarding what to anticipate concerning his symptoms and wants to know what is “palliative care.”

All of the following statements are true *except*:

- A. Palliative care is an organized, highly structured system for delivering care to patients with serious life-limiting illness.
- B. The goal of palliative care is to prevent and relieve suffering and to support the best possible quality of life for patients and their families, regardless of the stage of the disease or the need for other therapies.
- C. Palliative care intends to hasten death.
- D. Prevention and relief of suffering are by early identification and impeccable assessment and treatment of pain and other problems—physical, psychosocial, and spiritual.
- E. All of the above.

Answer 1.1

The correct answer is (C)

The National Consensus Project's definition of palliative care is as follows:

The goal of palliative care is to prevent and relieve suffering and to support the best possible quality of life for patients and their families, regardless of the stage of the disease or the need for other therapies. Palliative care is both a philosophy of care and an organized, highly structured system for delivering care. Palliative care expands traditional disease-model medical treatments to include the goals of enhancing quality of life for patient and family, optimizing function, and helping with decision-making and providing opportunities for personal growth. As such, it can be delivered concurrently with life-prolonging care or as the main focus of care. Palliative care is operationalized through effective management of pain and other distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family needs, values, beliefs and culture(s) . . . Palliative care affirms life by supporting the patient and family's goals for the future, including their hopes for cure or life-prolongation, as well as their hopes for peace and dignity throughout the course of illness, the dying process and death. Palliative care aims to guide and assist the patient and family in making decisions that enable them to work toward their goals during whatever time they have remaining.

Further Reading

National Consensus Project for Quality Palliative Care. *Clinical Practice Guidelines for Quality Palliative Care*. 3rd ed. Pittsburgh, PA: Author; 2013. Retrieved August 3, 2017, from https://www.nationalcoalitionhpc.org/wp-content/uploads/2017/04/NCP_Clinical_Practice_Guidelines_3rd_Edition.pdf

Question 1.2

Dr. Williams is a newly appointed faculty member at an academic palliative care program in a National Cancer Institute designated cancer center. On Dr. Williams' first day, a surgical resident who was present during the clinical rounds with Dr. Williams' palliative care team is asked by the faculty to define the key elements of the palliative care approach that distinguish it from other specialties.

Which of the following statements is true?

- A. It is a holistic interdisciplinary approach to improve quality of life for patient and caregivers.
- B. The relationship between patient and health care professionals distinguishes palliative care from other specialties.
- C. Communication distinguishes palliative care from other specialties.
- D. The goal of palliative care is to prevent and relieve suffering and to support the best possible quality of life for patients and their families.
- E. All of the above.

Answer 1.2

The correct answer is (E)

The key elements that define the palliative care approach include (a) a focus on quality of life of the patient and the patient's caregiver(s) as a unit of care; (b) active use of clinical ethics as the method for decision-making; (c) excellent communication as a means of improving the relationship between the patient and health care professionals and care; (d) impeccable assessment and use of evidence-based treatments as a means of effective management of pain and other distressing symptoms, while incorporating psychosocial and spiritual care according to patient/family needs, values, beliefs, and culture(s); (e) establishing illness understanding based on information preference, prognostic awareness, current illness status, and treatments; and (f) addressing advance care planning, including resuscitation preferences.

Further Reading

- Gamondi C, Larkin P, Payne S. Core competencies in palliative care: An EAPC white paper on palliative care education: Part 1. *Eur J Pall Care*. 2013;20(2):86–91.
- Yoong J, Park ER, Greer JA, et al. Early palliative care in advanced lung cancer: A qualitative study. *JAMA Intern Med*. 2013;173(4):283–290.

2

Symptom Assessment

MARVIN OMAR DELGADO GUAY

Question 2.1

The experience of symptoms varies significantly in patients with life-threatening illness. Which factor(s) needs to be considered when teams evaluate these patients?

- A. Production of a symptom is the process by which nociception occurs.
- B. Production of a symptom can be significantly different in one individual compared to another.
- C. Perception is the process by which the symptom reaches the brain cortex.
- D. Expression of the distress is the only measurable part of the experience and can be a target of therapy.
- E. All of the above.
- F. None of the above.

Answer 2.1

The correct answer is (E)

There are three steps in the experience of symptoms that must be considered when evaluating patients with life-threatening illnesses: production, perception, and expression. Production can be significantly different in one individual compared to another and in different areas within the same individual. Perception is the process by which the symptom reaches the brain cortex. This can also vary significantly from one individual to another; this step cannot be measured. The expression can vary from one subject to another. Factors that might affect the expression include beliefs about the symptom experience, psychological factors (anxiety, depression, and somatization), and sociocultural factors. This is the only step of the symptom experience that can be measured and can be monitored as a response to a given therapy.

Further Reading

- Bruera E. Patient assessment in palliative cancer care. *Cancer Treat Rev.* 1996;22(Suppl A):3–12.
- Bruera E, Kim HN. Cancer pain. *JAMA.* 2003;290:2476–2479.
- Delgado-Guay MO, Bruera E. Management of pain in the older person with cancer: Part 1. *Oncology.* 2008;22:56–61.
- Kim HN, Bruera E, Jenkins R. Symptom control and palliative care. In: Cavalli F, Hansen HH, Kaye SB, eds. *Textbook of Medical Oncology.* Boca Raton, FL: Taylor & Francis; 2004:353–370.

Question 2.2

Assessment tools allow the identification of many more symptoms compared to simple unstructured evaluations. Simple assessment tools may be more appropriate for patients with advanced illnesses because these patients may be very weak and experiencing symptoms that make it difficult to complete a time-consuming and complex assessment tool.

Regarding symptoms assessment tools, all of the following are correct *except*:

- A. Assessment tools are useful not only to diagnose and evaluate the intensity of the symptoms but also to monitor the effectiveness of therapy/intervention and to evaluate the presence of side effects.
- B. Efficient symptom-assessment instruments include the Edmonton Symptom Assessment Scale (ESAS), the Memorial Symptom Assessment Scale (MSAS), the Rotterdam Symptom Checklist (RSCL), and the Symptom Distress Scale (SDS).
- C. The MSAS, a lengthier assessment tool, is mostly used for clinical purposes.
- D. The ESAS has been validated against the Hospital Anxiety and Depression Scale (HADS) for assessing the presence of depression and anxiety in advanced cancer patients. The ideal cut-off point of ESAS of 2 out of 10 is sensitive for the presence of depression and anxiety in patients in the palliative care setting.
- E. Clinical teams must be aware that some research instruments may differ from those used for clinical practice.

Answer 2.2

The correct answer is (C)

The MSAS, a lengthier assessment tool, is mostly used for research purposes. Using the MSAS, patients rate the frequency, severity, and distress associated with 32 physical and psychological symptoms. There is a short-form MSAS (MSAS-SF) that captures the patient-rated distress associated with 26 physical symptoms and the frequency of 4 psychological symptoms. The condensed MSAS (CMSAS) can be completed in 2–4 minutes and contains both quality of life and survival information; it also provides equivalent information that approximates to the original 32 items.

The ESAS is used to assess 10 common symptoms (pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath, appetite, sleep, and feeling of well-being) experienced during the past 24 hours by patients with cancer or chronic illness. The ESAS has been validated against a widely used scale, the HADS. The cut-off is 2/10 to identify depression and anxiety in patients with advanced illnesses.

Further Reading

- Bruera E, Kuehn N, Miller M.J, Selmsler P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): A simple method for the assessment of palliative care patients. *J Palliat Care*. 1991;7:6–9.
- Chang V, Hwang S, Feuerman M, Kasimis B, Thaler H. The Memorial Symptom Assessment Scale Short Form (MSAS-SF): Validity and reliability. *Cancer*. 2000;89:1163–1171.

Question 2.3

A 38-year-old male patient with advanced life-threatening illness is brought to the hospital by his family with a history of severe drowsiness, with some periods of confusion, not able to interact well with the family, and a complaint of periods of seeing animals in the walls during the past 2 days. The family reports that this was the first episode of these symptoms. The patient was feeling down during the past weeks, with not much appetite. The patient was found to be dehydrated and to have a urinary tract infection.

Which tool(s) would you use to diagnose the presence of delirium?

- A. The Memorial Delirium Assessment Scale
- B. There is no need to do a full assessment because he was already diagnosed with an infection.
- C. The Confusion Assessment Method
- D. The Mini-Mental State Examination
- E. A and C
- F. All of the above

Answer 2.3

The correct answer is (E)

The diagnosis of delirium is made on the basis of acute onset, fluctuation in course, reduced sensorium, attention deficit, and cognitive and perceptual disturbance, which occurs in the presence of an underlying organic derangement. Misdiagnoses of hypoactive delirium as depression or agitated delirium as anxiety disorder are not unusual. Different tools have been developed and validated for screening or monitoring the course of delirium, such as the Memorial Delirium Assessment Scale (MDAS), the Delirium Rating Scale, and the Confusion Assessment Method (CAM). The MDAS is a 10-item, 4-point, clinician-rated instrument (possible range, 0–30). It has been validated in inpatient palliative care settings with a sensitivity of 97% and a specificity of 95% at a cut-off score of 7.

Further Reading

- Breitbart W, Rosenfeld B, Roth A, et al. The Memorial Delirium Assessment Scale. *J Pain Symptom Manage.* 1997;13:128–137.
- Gagnon P, Allard P, Masse B, et al. Delirium in terminal cancer: A prospective study using daily screening, early diagnosis, and continuous monitoring. *J Pain Symptom Manage.* 2000;19:412–426.
- Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: The confusion assessment method—A new method for detection of delirium. *Ann Intern Med.* 1990;113:941–948.

Question 2.4

A 68-year-old female patient with advanced life-threatening illness who has been receiving treatment for her illness is being evaluated in your palliative care clinic. She is complaining of feeling very weak in general, not able to do her usual chores at home, not able to walk her dog as she used to do every day, and she has noticed that her appetite has decreased. She has not experiencing anhedonia or major depression symptoms. During the past few weeks, she has spent most of the day in bed or on the couch.

Which tool would help you evaluate her general performance status?

- A. The Karnofsky Performance Scale
- B. The Palliative Performance Scale
- C. The Edmonton Functional Assessment Tool
- D. A and B
- E. All of the above

Answer 2.4

The correct answer is (E)

The Karnofsky Performance Scale (KPS) and the Eastern Cooperative Oncology Group (ECOG) performance scale have been widely used in the assessment of physical function in cancer patients. Be aware that in patients with advanced and terminal illness, in the palliative care setting these instruments tend to generate clustering of scores at the extreme end of impairment. Other tools also developed for use in the palliative care setting include the Edmonton Functional Assessment Tool (EFAT) and the Palliative Performance Scale (PPS). The EFAT includes domains such as pain, mental alertness, communication, sensory function, and respiratory function, in addition to domains that more directly reflect physical function, such as balance, mobility, wheelchair mobility, activity, activities of daily living, and dependence performance status. The PPS includes domains evaluated in the KPS and assesses ambulation, activity, self-care, intake, and conscious level.

Further Reading

Anderson F, Downing GM, Hill J, et al. Palliative Performance Scale (PPS): A new tool. *J Palliat Care*. 1996;12:5–11.

Kaasa T, Loomis J, Gillis K, et al. The Edmonton Functional Assessment Tool: Preliminary development and evaluation for use in palliative care. *J Pain Symptom Manage*. 1997;13:10–19.

Yates JW, Chalmer B, McKegey FP. Evaluation of patients with advanced cancer using the Karnofsky Performance Status. *Cancer*. 1980;45:2220–2224.

Question 2.5

A 28-year-old male with advanced life-threatening illness is referred to your outpatient palliative care service with a history of difficult pain management. The patient lives with another family member. The patient always reports high pain scores, whereas his other psychological symptoms remain not significantly elevated. His doses of pain medications have continue to increase during the past few weeks. He has a history of alcohol abuse in the past. He denies any history of drug abuse. He has come to the clinic on more than two occasions with a history of lost pills. Because you recognize this patient might be having a maladaptive behavior regarding the use of pain medications, you plan to treat with an interdisciplinary team approach to better help him with this issue.

Which tool(s) will help you evaluate this patient's risk of chemical coping?

- A. The CAGE questionnaire
- B. Screener and Opioid Assessment for Patients with Pain
- C. Smoking assessment
- D. Complete psychosocial and spiritual assessment
- E. All of the above

Answer 2.5

The correct answer is (E)

It is important to recognize that patients who have a past or active history of substance abuse present a special problem for symptom management. The history of abuse reflects maladaptive coping strategies, which frequently lead to excessive expression of symptomatology. A complete psychosocial and spiritual assessment needs to be done in an interdisciplinary environment.

Alcoholism is linked with other addictive substances, including tobacco and illicit drugs. The aberrant use of these substances to help cope with life stressors is defined as chemical coping. The CAGE questionnaire is frequently used as a brief screening tool for detection of alcohol abuse. A positive screen for alcohol abuse and dependence is made with two positive answers to the four questions. The questions refer to lifetime experience. The Screener and Opioid Assessment for Patients with Pain (SOAPP) is a brief self-report measure used to identify chronic pain patients who may be at risk for problems with long-term opioid medication use.

Further Reading

Akbik H, Butler SF, Budman SH, et al. Validation and clinical application of the Screener and Opioid Assessment for Patients with Pain (SOAPP). *J Pain Symptom Manage*. 2006;32(3):287–293.

Ewing JA. Detecting alcoholism: The CAGE questionnaire. *JAMA*. 1984;252:1905–1907.

Nedeljkovic SS, Wasan A, Jamison RN. Assessment of efficacy of long term opioid therapy in pain patients with substance abuse potential. *Clin J Pain*. 2002;18(Suppl):39–51.

3

Clinical Decision-Making in Palliative Care

EDUARDO BRUERA

Question 3.1

A 65-year-old male with locally recurrent and metastatic adenocarcinoma of the colon comes to the clinic with a 2-day history of increasing abdominal pain, nausea, and vomiting. For the past 3 weeks, the patient has become progressively less active and now spends most of the time in bed. The patient has refused surgery for his colon cancer in the past, and the oncology team believes that there is no more indication for chemotherapy. The X-rays today show mechanical bowel obstruction. The clinical team must decide whether to recommend surgical consultation for the possibility of a colostomy, admission to the acute care facility for symptomatic treatment, or discharge home with hospice and symptomatic treatment.

What information is necessary to make an appropriate decision for this patient?

- A. Disease stage, previous treatment, and planned treatment
- B. Comorbidities, severity, and management
- C. Life prognosis
- D. Performance status
- E. All of the above

Answer 3.1

The correct answer is (E)

Palliative care decision-making differs from that of many other disease-oriented specialties. Palliative care clinical teams focus on personhood and family care rather than on disease management. Therefore, palliative care clinicians require a combination of disease, patient, and family information before decisions can be made. The following are important items required: (a) disease stage, previous treatment, and planned treatment; (b) comorbidities, severity, and management; (c) life prognosis; (d) performance status; (e) physical, emotional, and spiritual symptom burden; (f) patient current living arrangements; and (g) family structure and function (family may or may not be related to the patient, and the patient's perception of the role of the family in his or her present or future care needs to be recorded); (h) patient's decision-making preference (active, passive, or shared) with regard to his or her clinical team and family; (i) financial barriers to care and financial resources; and (j) spiritual support and spiritual pain. The majority of this information can be obtained after one single visit with the patient and interaction with the primary caregiver.

Further Reading

Bakitas M, Kryworuchko J, Matlock DD, Volandes AE. Palliative medicine and decision science: The critical need for a shared agenda to foster informed patient choice in serious illness. *J Palliat Med*. 2011;14(10):1109–1116.

Bernacki RE, Block SD; American College of Physicians High Value Care Task Force. Communication about serious illness care goals: A review and synthesis of best practices. *JAMA Intern Med*. 2014;174(12):1994–2003.

Question 3.2

Which one of the following statements is incorrect regarding appropriate decision-making for a palliative care intervention?

- A. Delineate potential problems and adverse effects of the clinical problem that may be influencing the patient's quality of life.
- B. Rank the discomfort associated with a specific problem within the patient's overall complex of symptoms.
- C. Balance the overall advantages and disadvantages of the intervention versus no intervention for the patient.
- D. Symptomatic management is more appropriate than identification and correction of the clinical abnormality.

Answer 3.2

The correct answer is (D)

When specific palliative care decisions need to be made, the following five steps are important:

Step 1: Delineate potential problems and adverse effects of the clinical program that may be influencing the patient's quality of life. In the case discussed in Question 3.1, these include mechanical bowel obstruction causing nausea, vomiting, and abdominal pain.

Step 2: Rank the discomfort associated with a specific problem within the patient's overall complex of symptoms. In the case of the patient discussed in Question 3.1, abdominal pain, nausea, and vomiting may be completely or partially relieved by medications or may lose priority when other problems such as delirium or dyspnea occur.

Step 3: Identify the way to correct the clinical abnormality diagnosed in Step 1 and potential problems associated with the correction of such abnormality: A painful postoperative period for a patient with a short life span. The inconvenience of an acute hospital bed for a patient who prefers to stay at home.

Step 4: Balance the overall advantages and disadvantages of the intervention versus no intervention for the patient.

Step 5: Reach consensus between the clinical team, the patient, and the family regarding the most appropriate course of action. This may require multiple discussions or even a family conference to clarify particularly complex situations.

Further Reading

Bernacki RE, Block SD; American College of Physicians High Value Care Task Force. Communication about serious illness care goals: A review and synthesis of best practices. *JAMA Intern Med.* 2014;174(12):1994–2003.

Question 3.3

A 65-year-old male with locally recurrent and metastatic adenocarcinoma of the colon comes to the clinic with a 2-day history of increasing abdominal pain, nausea, and vomiting. For the past 3 weeks, the patient has become progressively less active and now spends most of the time in bed. The patient has refused surgery for his colon cancer in the past, and the oncology team believes that there is no more indication for chemotherapy. The X-rays today show mechanical bowel obstruction.

Using the evidence-based clinical decision-making process in palliative care, the most appropriate management decision by the clinical team is which of the following?

- A. Proceed with surgery consultation for colostomy to relieve obstruction
- B. Admission to acute care for symptomatic treatment
- C. Discharge home with hospice and symptomatic treatment
- D. None of the above

Answer 3.3

The correct answer is (C)

In the case presented, if the patient and family are reluctant for the patient to be admitted to the hospital to undergo surgical evaluation and potential surgical treatment, a good potential palliative alternative might involve opioids and antiemetics as well as hydration, all administered subcutaneously at home with the family with reassessment after a few days.

Further Reading

Bakitas M, Kryworuchko J, Matlock DD, Volandes AE. Palliative medicine and decision science: The critical need for a shared agenda to foster informed patient choice in serious illness. *J Palliat Med.* 2011;14(10):1109–1116.

Bernacki RE, Block SD; American College of Physicians High Value Care Task Force. Communication about serious illness care goals: A review and synthesis of best practices. *JAMA Intern Med.* 2014;174(12):1994–2003.

Question 3.4

Excellent patient–clinician communication is critical for provision of quality palliative care. Which of the following elements are important to achieve this goal?

- A. It is important to determine decision-making preferences (active, passive, or shared) by the patient.
- B. The use of empathetic statements has to be learned and practiced.
- C. It is important to involve other team members for particularly difficult communication issues.
- D. In cases in which communication is particularly challenging and distressing for a palliative care clinician, it is completely appropriate to ask for help and even transfer the care of a patient and/or family to other members of the team.
- E. All of the above.

Answer 3.4

The correct answer is (E)

Communication with the patient and family requires palliative care clinicians to acquire sophisticated clinical skills. Didactic learning, role playing, bedside teaching, and monitored practice are all important components of communication training.

Palliative care clinicians need to be familiar with protocols for breaking bad news. In addition, they need to be familiar with the organization and conduct of family meetings. It is important to determine decision-making preferences (active, passive, or shared) by the patient regarding family and the clinical team. The use of empathetic statements has to be learned and practiced.

Mindfulness may help palliative care physicians recognize emotionally charged conversations and appropriately respond to patients and families.

Palliative care physicians need to identify private settings in which these meetings can be conducted and be aware of the importance of adopting the appropriate posture (sitting vs. standing), the use of open-ended questions to initiate the conversations, and involving other team members for particularly difficult communication issues.

In cases in which communication is particularly challenging and distressing for a palliative care clinician, it is completely appropriate to ask for help and even transfer the care of a patient and/or family to other members of the team in order to reduce the risk of burnout.

Further Reading

Pollak KI, Arnold RM, Jeffreys AS, et al. Oncologist communication about emotion during visits with patients with advanced cancer. *J Clin Oncol.* 2007;25:5748.

Von Gunten CF, Ferris FD, Emanuel LL. The patient–physician relationship. Ensuring competency in end-of-life care: Communication and relational skills. *JAMA.* 2000;284:3051.

4

Principles of Assessment and Pain Management and Procedures in Pain Management

FRANCISCO A. LOAICIGA
AND SURESH REDDY

Question 4.1

A 49-year-old female with uncontrolled type 2 diabetes mellitus who was recently diagnosed with pancreatic cancer with liver metastasis now presents to the outpatient palliative care clinic for symptom management. Among her complaints, she reports a bilateral lower extremity painful sensation described as “pins and needles.” The patient was previously on both gabapentin and pregabalin, but they caused her legs to swell.

What is the next best evidence-based treatment option?

- A. Acetaminophen
- B. A cyclooxygenase-1 inhibitor
- C. Duloxetine 60 mg daily
- D. Venlafaxine 37.5 mg daily

Answer 4.1

The correct answer is (C)

This patient has neuropathic pain as per her history as well as risk factors such as diabetes mellitus type 2 and metastatic cancer undergoing treatment. Among the options, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs; cyclooxygenase-1 inhibitor) have no evidence-based involvement in the treatment of this type of pain. Venlafaxine only at higher doses (≥ 150 mg daily) has demonstrated effective management of neuropathic pain. Option C, at the dose specified, has demonstrated adequate treatment of neuropathic pain in recent randomized controlled trials.

Further Reading

Dworking RH, O'Connor AB, Backonja M, et al. Pharmacologic management of neuropathic pain: Evidence based recommendations. *Pain*. 2007;132(3):237–251.

Portenoy RK. Treatment of cancer pain. *Lancet* 2011;377:2236–2247.

Question 4.2

Mr. W is a 60-year-old male with prostate cancer with metastasis to the lumbar spine who presents to the palliative care clinic for pain management. The patient is concurrently undergoing a trial of chemotherapy at this time. Per review of electronic medical records, the patient had a documented allergic reaction to morphine described as itching, morbilliform rash, hives, and angioedema in the tongue. Today, Mr. W describes his pain as severe and is not well controlled with ibuprofen, and he recently developed acute renal insufficiency secondary to regular NSAIDs. His oncologist recommended against use of acetaminophen on a regular basis. Of note, the patient admits to using marijuana for pain control and comfort (but to no avail).

Which of the following options would you recommend for managing this patient's severe pain from bone metastasis?

- A. Morphine
- B. Codeine
- C. Oxycodone
- D. Fentanyl

Answer 4.2

The correct answer is (D)

The patient has a true allergy to morphine. Unlike nausea and itching, which the patient may confuse with allergic reactions, hives and difficulty breathing are considered true allergic reactions. Morphine, codeine, and oxycodone belong to the class of opioids called phenanthrenes. In this case, a true allergic reaction to an opioid of this class renders all other members of the same family likely to have cross-reaction. Trying an opioid in another class, such as phenylpiperidines (phentanyl) or phenylethylamine (methadone), is recommended.

The chronic use of NSAIDs has proven to increase the risk of acute kidney injury and decreased renal function, which renders the medication contraindicated in some cases.

Marijuana is a known inhibitor of CYP3A4. Fentanyl is metabolized by the cytochrome P450 isoenzyme CYP3A4, and drugs that inhibit this route of metabolism can significantly increase fentanyl levels, leading to adverse effects such as sedation, confusion, and respiratory depression. As the physician, you need to educate the patient about this important medication interaction.

Further Reading

- Amabile CM, Bowman BJ. Overview of oral-modified release opioid products for the management of chronic pain. *Ann Pharmacother.* 2006;40(7–8):1327–1335.
- Lynch T, Price A. The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. *Am Fam Physician.* 2007;76(3):391–396.
- Whelton A, Hamilton CW. Nonsteroidal anti-inflammatory drugs: Effects on kidney function. *J Clin Pharmacol.* 1991;31:588–598.

Question 4.3

Roberto is a 42-year-old male being evaluated in the emergency department for uncontrolled chronic pain. His past medical history is reported as severe degenerative joint disease, chronic kidney disease stage 3, and osteoporosis. He has been receiving long-term opioid therapy with oxycodone at 20 mg taken orally every 8 hours around the clock for persisting back pain secondary to fourth lumbar vertebral compression fracture despite vertebroplasty. Per review of laboratory tests, his basic metabolic profile reveals his creatinine increased from 1.6 (baseline) to 2.8 mg/dl within the past 7 days. Roberto's wife reports that during the same period of time, he has been drowsy, has developed a jerky movement, has had no urination, and has been irritable. The bladder scan reported 400 ml of urine, and a urinary catheter is placed immediately and drains 350 ml.

In this situation, which of the following is the best next alternative opioid indicated?

- A. Hydromorphone
- B. Morphine
- C. Codeine
- D. Methadone

Answer 4.3

The correct answer is (D)

Commonly recognized adverse effects of opioid include sedation, nausea, constipation, respiratory depression, and urinary retention. Relatively recently, opioid-induced neurotoxicity (OIN) has been described.

The patient has most likely developed OIN, which includes one or more of the following: cognitive impairment, severe sedation, hallucinations, delirium, myoclonus, seizures, and hyperalgesia. In some cases, symptoms may be indistinguishable from disease progression or inadequate analgesic control and often lead to further escalation of opioid dose. Options for managing acute OIN include dose reduction, opioid rotation, hydration, and adjunctive medications.

Regarding methadone, all opioids contain active metabolites that can cause kidney disease. Methadone is the only one that does not contain active metabolites.

Further Reading

- Cherny N, Ripamonte C, Pereira J, et al. Strategies to manage the adverse effects of oral morphine: An evidence-based report. *J Clin Oncol*. 2001;19(9):2542–2554.
- Daeninck PJ, Bruera E. Opioid use in cancer pain: Is a more liberal approach enhancing toxicity? *Acta Anaesthesiol Scand*. 1999;43:924–938.
- Ersek M, Cherrier MM, Overman SS, et al. The cognitive effects of opioids. *Pain Manage Nurs*. 2004;5(2):75–93.
- Lawlor PG. The panorama of opioid-related cognitive dysfunction in patients with cancer: A critical literature appraisal. *Cancer*. 2002;94:1836–1853.
- Murtagh FE, Addington-Hall JM, Donohoe P, Higginson IJ. Symptom management in patients with established renal failure managed without dialysis. *EDTNA ERCA J*. 2006;32(2):93–98.

Question 4.4

Mrs. S is a 42-year-old female referred to the palliative care clinic for uncontrolled chronic pain. Her past medical history is significant for severe degenerative joint disease and stage 2 chronic kidney disease. She has been receiving chronic opioid therapy with oxycodone at 20 mg taken orally every 8 hours around the clock for persisting back pain secondary to lumbar spine compression fractures (L4–L5) despite vertebroplasty. Per her lab review, her basic metabolic profile shows creatinine increased from 1.6 (baseline) to 3.2 mg/dl within the past 7 days. Her husband reports that during the same period of time, she has been drowsy, has developed a jerky movement, and had no urination, and has been irritable. Bladder scan reported 500 ml of urine, and Foley is placed immediately and drains 400 ml.

Which of the following represents the most appropriate regimen if you decide to switch her pain regimen to methadone?

- A. 5 mg q8 hours
- B. 2.5 mg q12 hours
- C. 20 mg q8 hours
- D. 10 mg q4 hours

Answer 4.4

The correct answer is (A)

If one does not have to take cross-tolerance into account, the following is the best option in terms of calculating her opioid dose (methadone). The patient is receiving a total dose of 60 mg of oxycodone daily. Per review, the conversion factor from oxycodone to morphine is 1.5; therefore, the morphine equivalent daily dose (MEDD) is 90 mg in this case. The morphine to methadone conversion for doses of morphine less than 100 mg is by division of 4 (i.e., MEDD/4). Therefore, an MEDD of 90 mg divided by 4 = 22.5. Methadone at 2.5 mg every 12 hours is not correct, and the other two choices would be equal to 60 mg of methadone on day 1.

Further Reading

Bruera E, Dalal S. *The MD Anderson Supportive and Palliative Care Handbook*. Houston, TX: University of Texas; 2015.

Mercadante S. Pathophysiology of chronic pain. In: Bruera E, Higginson IJ, Ripamonti C, von Gunten C, editors. *Textbook of Palliative Medicine*. London: Edward Arnold; 2006: 359–66.

Question 4.5

Mr. Johns, a 54-year-old male with a past medical history of hypertension, hyperlipidemia, coronary artery disease, and atrial fibrillation, reports to his internal medicine clinic for a follow-up visit. He was discharged from the hospital 6 months ago with a diagnosis of stroke with residual right-sided hemiparesis. Per review of complaints, the patient is experiencing right-sided pain that has been gradually increasing for the past 2 months. The pain is described as constant, aching and burning, localized mainly in the right upper and lower extremities. Exam of the affected areas of the stroke was negative for pinprick examination, but normal touch was unpleasant and painful. Mood and temperature variation made the pain worse.

Which of the following terms most accurately describes this patient's type of pain?

- A. Peripheral neuropathic pain
- B. Central neuropathic pain
- C. Complex regional pain syndrome
- D. Vascular ischemic pain syndrome

Answer 4.5

The correct answer is (B)

Chronic postsurgical pain (CPSP) belongs to a group of chronic pain disorders that are termed central neuropathic pain disorders because the pain is due to a lesion or dysfunction of the central nervous system.

The question specifically asks for the most accurate description of the pain. Because the patient meets criteria for CPSP, option B is the most accurate answer versus option A. Also, somatic and visceral pain have their own classification.

Peripheral neuropathic pain is defined as damage to or disease affecting nerves, which may impair sensation, movement, gland or organ function, or other aspects of health, depending on the type of nerve affected.

Complex regional pain syndrome, also known as reflex sympathetic dystrophy, is a long-term condition that often worsens with time. It is characterized by severe pain and sensitivity, swelling, and changes in the skin. It may initially affect one limb and then spread throughout the body; 35% of people afflicted report symptoms throughout their whole body.

Vascular ischemic pain syndrome is related directly to lack of blood flow to an extremity or organ.

Further Reading

Hughes RAC. Clinical review: Peripheral neuropathy. *Br Med J*. 2002;324(7335):466–469.

Treede RD, Jensen TS, Campbell JN, et al. Neuropathic pain: Redefinition and a grading system for clinical and research purposes. *Neurology*. 2008;70:1630–1635.

Question 4.6

A 35-year-old female who has metastatic ovarian carcinoma presents with deep pelvic pain localized in the midline and a feeling of fullness in the abdomen; pain is vague and poorly localized. The patient is taking oxycontin 300 mg orally every 8 hours and 60 mg of oxycodone every 2 hours PRN. The patient has constipation despite the use of three laxatives on a scheduled basis. She also reports fatigue, with mild response to moderate exercise 5 days in a week for 30 minutes and methylphenidate.

Which of the following is the most appropriate nerve block for her?

- A. Hypogastric plexus block
- B. Celiac plexus block
- C. Ganglion impar block
- D. Pudendal nerve block
- E. Stellate ganglion block

Answer 4.6

The correct answer is (A)

Superior hypogastric plexus block can be a treatment approach for patients with visceral pelvic pain that failed to respond to medical management. The superior hypogastric plexus lies in the retroperitoneum and extends from the anterior aspect of L5 to the superior sacrum. Afferent fibers from the pelvic viscera pass through the plexus, which also contains sympathetic postganglionic fibers. As with celiac plexus block, only visceral pain responds to superior hypogastric plexus block; somatic pain from sacral or muscle involvement and neuropathic pain from nerve root compression or infiltration do not improve.

Several prospective case series indicate good to excellent pain relief in more than 70% of patients, reduced opioid consumption, and a favorable adverse event profile.

Celiac plexus helps pain originating from lower esophagus to mid transverse colon. Ganglion impar helps pain originating in the rectal area, whereas stellate ganglion block covers regions of the face and upper extremities.

Further Reading

Amr YM, Makharita MY. Neurolytic sympathectomy in the management of cancer pain-time effect: A prospective, randomized multicenter study. *J Pain Symptom Manage.* 2014;48:944.

de Leon-Casasola OA, Kent E, Lema MJ. Neurolytic superior hypogastric plexus block for chronic pelvic pain associated with cancer. *Pain.* 1993;54:145.

Plancarte R, de Leon-Casasola OA, El-Helaly M, Allende S, Lema MJ. Neurolytic superior hypogastric plexus block for chronic pelvic pain associated with cancer. *Reg Anesth.* 1997;22:562–568.

Question 4.7

A 75-year-old patient developed herpes zoster on the right forehead 4 weeks ago. Pain is severe, controlled mildly by a combination of fentanyl patch 25 µg/hr and gabapentin 100 mg tid.

Which of the following procedures may be appropriate for this patient?

- A. Trigeminal nerve block
- B. Facial nerve block
- C. Stellate ganglion block
- D. Gasserian ganglion block

Answer 4.7

The correct answer is (C)

Intense sympathetic stimulation and activation of adrenergic receptors may play a role in both acute zoster pain and chronic postherpetic neuralgia. Acute inflammatory response may be associated with intense sympathetic stimulation leading to a decrease in neuronal blood flow and neuronal ischemia. Hence, a sympathetic block will increase blood flow and relieve pain. Trigeminal nerve, facial nerve, and gasserian ganglion block are not sympathetic nerves.

Further Reading

Wu CL, Marsh A, Dworkin RH. The role of sympathetic nerve blocks in herpes zoster and postherpetic neuralgia. *Pain*. 2000;87(2):121–129.

Question 4.8

A 65-year-old female with a history of metastatic colon cancer, with metastasis to lung, liver, and right adrenal gland, presents with severe abdominal pain with radiation to the right back. She had nausea and vomiting for the past 5 days and appears to be dehydrated. Abdominal X-ray revealed stool in all four quadrants. The patient was admitted and treated for dehydration and constipation. Pain persisted, and the patient experienced sedation and myoclonus from intravenous hydromorphone.

Which one-time procedure should be initiated for this patient?

- A. Intrathecal morphine
- B. Lumbar sympathetic block
- C. Splanchnic block
- D. Hypogastric plexus block
- E. Psoas compartment block

Answer 4.8

The correct answer is (C)

Pain in this case is visceral, and its origin is the liver with corresponding back radiation. Pain may also occur from the adrenal gland. In either condition, a celiac plexus or a splanchnic nerve block is appropriate. The celiac plexus lies in front of the aorta at the L1 level, whereas the splanchnic nerve is higher up at the anterolateral part of the T12 vertebra. Both are sympathetic nerves/plexus that carry fibers from the upper abdominal viscera to the mid transverse colon. In this case, intrathecal therapy is an option but for long-term use. Lumbar sympathetic block is usually indicated for sympathetic pain in the lower extremities. Psoas compartment block is also done for pain in the lower extremities, covering dermatomes of L1–L3.

Further Reading

de Leon-Casasola OA. Critical evaluation of chemical neurolysis of the sympathetic axis for cancer pain. *Cancer Control*. 2000;7(2):142–148.

Question 4.9

A 39-year-old female with a history of gastrointestinal stromal tumor presents to the palliative care clinic with chronic neck pain of 2 years' duration. Trials of NSAIDs, massage, and stretching helped her occasionally, but pain relief was only temporary. On examination, there are a number of painful sites in the trapezius muscle, right more than left.

Which of the following procedures would likely most benefit the patient?

- A. Epidural injection
- B. Facet joint injection
- C. Trigger point injection
- D. Selective root block
- E. Cervical plexus block

Answer 4.9

The correct answer is (C)

Trigger points are discrete, focal, hyperirritable spots located in a taut band of skeletal muscle:

- They produce pain locally and in a referred pattern and often accompany chronic musculoskeletal disorders.
- Acute trauma or repetitive microtrauma may lead to the development of stress on muscle fibers and the formation of trigger points.
- Referred pain is an important characteristic of a trigger point.

Further Reading

Simons D, Travell J, Simons L. *Travell & Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual*. 2nd ed. Baltimore, MD: Williams & Wilkins; 1999.

Wong CSM, Wong SHS. A new look at trigger point injections. *Anesthesiol Res Pract*. 2012;2012:492452.

Question 4.10

Mrs. Smith is a 36-year-old female with a history of sarcoma, large pelvic mass compressing the lower lumbar and upper sacral nerves. She has been previously treated with morphine, oxycodone, hydromorphone; as well as gabapentin, pregabalin, and trileptal, but she did not tolerate them and developed severe drowsiness and ataxia with most drugs. Subsequently, she had trials of epidural injection and intrathecal morphine with no success. The patient was admitted to the emergency room for severe pelvic and lower extremity pain. She was started on a hydromorphone patient-controlled analgesia (PCA) that rapidly escalated in the past 48 hours to 4 mg/hr and 6 mg RN boluses as needed (used 12 boluses in 24 hours), with development of mild myoclonus. The patient is in severe distress and apparently told a family member that she will hurt herself if the pain is not well controlled. The patient did not sleep for the past 3 nights.

Which of the following interventions may be appropriate in this situation?

- A. Increasing dose of hydromorphone continuous (basal) and bolus
- B. Trial of ketamine
- C. IV lidocaine infusion
- D. Add parenteral ketorolac

Answer 4.10

The correct answer is (B)

This patient has not achieved adequate pain control with multiple pain regimens and is now presenting with signs of OIN, so increasing hydromorphone basal bolus (option A) would be inappropriate. Ketamine represents an option for neoplastic pain that no longer responds to conventional opioid treatment. Although IV lidocaine infusion (option C) is an option, there is not much evidence to consider it above ketamine. Parenteral ketorolac (option D) also appears to be promising, but currently evidence for its use is lacking compared to ketamine.

Further Reading

Benedetti C, Buttlar SH. Systemic analgesics. In: Bonica JJ, ed. *The Management of Pain*. 2nd ed. Philadelphia, PA: Lea & Febiger; 1990:1640–1675.

Morgan C. *Clinical Anesthesiology*. 5th ed. New York, NY: McGraw-Hill; 2005:125–130.

Petersen P, Kastrop J, Zeeberg I, Boysen G. Pain in peripheral nerve disease. *Neurol Res*. 1986;8(3):189–190.

Question 4.11

A 67-year-old male with metastatic bladder cancer with a 6-cm mass in the bladder was recently treated with cisplatin-based combination chemotherapy and now presents to the emergency room with a 2-day history of profuse hematuria/passing clots, dysuria, and urinary frequency. Vital signs suggest mild hypotension, and urine analysis is negative for urinary tract infection. The patient is in severe distress, reporting severe pain on voiding.

Which of the following options is the most appropriate in this situation?

- A. IV hydration
- B. Antibiotic therapy
- C. Radiotherapy
- D. Aminocaproic acid

Answer 4.11

The correct answer is (C)

Palliative radiotherapy may benefit those with symptoms of hematuria, dysuria, urinary frequency, or nocturia caused by advanced bladder cancer.

Antibiotic therapy would be incorrect because urine analysis is negative, and the patient has no signs of urinary tract infection.

Aminocaproic acid has been used in the treatment of fibrinolytic bleeding and also for hyphema, but it is contraindicated in upper genitourinary bleeding due to the risk of glomerular capillary thrombosis in the renal pelvis.

Intravenous hydration will provide resuscitative measures in this case but unfortunately will not resolve the problem.

Further Reading

Bladder cancer: Diagnosis and management of bladder cancer (NICE Clinical Guidelines). National Institute for Health and Care Excellence website. <https://www.nice.org.uk/guidance/ng2>. Published February 2015.

Question 4.12

Which of the following statements best describes allodynia?

- A. Increased response to a painful stimulus
- B. Painful response to a normally innocuous stimulus
- C. Painful response to repeated stimulus
- D. Spontaneous unpleasant sensation, without stimulus

Answer 4.12

The correct answer is (B)

Allodynia refers to central pain sensitization (increased response of neurons) following painful, often repetitive stimulation. Allodynia can lead to the triggering of a pain response from stimuli that do not normally provoke pain. Temperature or physical stimuli can provoke allodynia, which may feel like a burning sensation, and it often occurs after injury to a site. Allodynia is different from hyperalgesia in that hyperalgesia is an extreme, exaggerated reaction to a stimulus, which is normally mildly painful.

Hyperpathia (option C) is a clinical symptom of certain neurological disorders wherein nociceptive stimuli evoke exaggerated levels of pain. This should not be confused with allodynia, in which normally nonpainful stimuli evoke pain.

Dysesthesia (option D) is an unpleasant abnormal sense of touch. Option A is one of the multiple definitions of pain.

Further Reading

- Jensen, T. S. (1996). Mechanisms of neuropathic pain. In: Campbell JN, ed. *Pain: An updated review*. Seattle, WA: IASP Press; 1996:77–86.
- Merskey H, Bogduk N, eds. *Classification of Chronic Pain*. Seattle, WA: IASP Task Force on Taxonomy; 1994.

Question 4.13

Mr. Joseph is a 32-year-old male with a past medical history of metastatic pancreatic cancer diagnosed 4 months ago. The patient is admitted to the hospital for uncontrolled abdominal pain, inattention, acute changes in mental status, disorganized speech, and intermittent jerky movements in bilateral upper extremities. He is currently taking fentanyl patch 200 $\mu\text{g/hr}$ and hydromorphone 8 mg oral every 2 hours on an as needed basis (requiring six doses overnight). You decide to switch the patient to PCA hydromorphone.

What is the PCA starting dose?

- A. 0.7 mg/hr of hydromorphone and 2 mg every hour as needed for breakthrough pain
- B. 0.1 mg/hr of hydromorphone and 1 mg every hour as needed for breakthrough pain
- C. 1.1 mg/hr of hydromorphone and 2 mg every hour as needed for breakthrough pain
- D. 2.6 mg/hr of hydromorphone and 4 mg every hour as needed for breakthrough pain

Answer 4.13

The correct answer is (C)

The first step in the calculation of the dose of IV hydromorphone is to calculate the daily oral morphine dose (MEDD) based on the previous use of opioids. Per conversion table, a 200 $\mu\text{g/hr}$ patch of fentanyl is equal to 400 mg oral morphine or 40 mg of IV hydromorphone (400 mg MEDD divided by 5 = 80 mg of oral hydromorphone; to obtain IV daily dose of hydromorphone, divide 80 mg by 2 = 40 mg). Reduce by 30% for incomplete tolerance, which will be 28 mg IV of hydromorphone over 24 hours; in terms of PCA, it will be 0.9 mg per hour of hydromorphone (22 mg divided by 24 hours).

Then to calculate the breakthrough, calculate 15%–20% of 15 mg, yielding a starting dose of 2 mg Q1 hour as needed for breakthrough pain.

Further Reading

Breitbart W, Chandler S, Egel B, et al. An alternative algorithm for dosing transdermal fentanyl for cancer-related pain. *Oncology*. 2000;14:695–705.

Bruera E, Dalal S. *The MD Anderson Supportive and Palliative Care Handbook*. Houston, TX: University of Texas; 2015.

Question 4.14

A 44-year-old female with recurrent breast cancer presents with worsening of her back pain. Her current regimen is morphine extended-release 120 mg PO q12 hours and morphine immediate-release 45 mg PO q2 hours PRN for breakthrough pain. She received eight doses of 45 mg within the past 24 hours. Of note, the patient has chronic kidney disease stage 3, blood urea nitrogen level of 62 mg/dl, and creatinine level of 3.1 mg/dl. The patient presents with altered mental status. She also has a history of peripheral neuropathic pain, and she takes pregabalin 300 mg daily. Opioid rotation is indicated in this setting.

Which of the following options would be an appropriate regimen for this patient?

- A. Methadone 45 mg PO q12 hours
- B. Methadone 30 mg PO q12 hours
- C. Methadone 17 mg PO q12 hours
- D. Methadone 5 mg PO q12 hours

Answer 4.14

The correct answer is (C)

The MEDD for this patient is 700 mg. You need to take into consideration the incomplete tolerance by reducing the MEDD by 50%, which will lead to a new dose of 350 mg daily. Then, you need to convert this to methadone. Calculate by dividing 350 mg by 10 to get the equianalgesic dose; however, you will probably want to give the medication twice a day, so divide that total (35 mg) by 2, which equals approximately 17 mg q12 hours. Breakthrough medication is the standard of care in pain management; in this case, morphine is a good option. You can calculate by using 15%–20% of the MEDD—in this case, 50–70 mg of morphine q3 hours as needed.

Further Reading

Bruera E, Dalal S. *The MD Anderson Supportive and Palliative Care Handbook*. Houston, TX: University of Texas; 2015.

Ripamonti C, Groff L, Brunelli C, et al. Switching from morphine to oral methadone in treating cancer pain: What is the equianalgesic dose ratio? *J Clin Oncol*. 1998;16:3216–3221.

Question 4.15

A 48-year-old female was diagnosed with metastatic cervical carcinoma involving the lungs and pelvic lymph nodes. Her disease was deemed inoperable. She initially responds to six cycles of cisplatin-based chemotherapy but has now started on paclitaxel due to disease progression. She presents to the palliative care clinic with new-onset progressive bilateral numbness in her hands and feet with the new chemotherapy. She describes her pain as burning, 7/10, that intensifies at night and interferes with her sleep quality and is not related to movement. Neurological examination shows no motor deficit, with decreased light touch in distal lower limbs.

All of the following are considered appropriate treatment options *except*:

- A. Gabapentin
- B. Ibuprofen
- C. Duloxetine
- D. Tramadol

Answer 4.15

The correct answer is (B)

Peripheral neuropathy is a common sequelae of cytotoxic therapy. It can be disabling and usually requires pharmacotherapy. Various agents, such as gabapentin, duloxetine, and opioids such as tramadol are reasonable options to control the neuropathic pain.

Further Reading

Ewertz M, Qvortrup C, Eckhoff L. Chemotherapy-induced peripheral neuropathy in patients treated with taxanes and platinum derivatives. *Acta Oncol.* 2015;54(5):587–691. doi:10.3109/0284186X.2014.995775

Moulin D, Boulanger A, Clark A, et al. Pharmacological management of chronic neuropathic pain: Revised consensus statement from the Canadian Pain Society. *Pain Res Manage.* 2014;19(6):328–335.

Question 4.16

Mrs. Rogers is a 55-year-old female with breast cancer metastatic to the bones. Her physician prescribed a long-acting opioid regimen that comprises extended-release morphine at 30 mg administered orally every 8 hours around the clock. Mrs. Rogers noticed that although extended-release morphine alleviates her pain most of the day, she still experiences breakthrough back pain a couple of times a day that increases to an intensity of 7/10. She visits your palliative care clinic and requests medication changes to address the breakthrough back pain.

Breakthrough dosage of the rescue opioid is usually based on which of the following?

- A. Time to peak effect
- B. Half-life
- C. Duration of action
- D. Absorption rate
- E. Elimination rate

Answer 4.16

The correct answer is (A)

Breakthrough pain is a transitory pain that occurs despite the use of long-term, around-the-clock opioids to control chronic pain. Morphine and other short-acting opioids, such as oxycodone and hydromorphone, have frequently been used for the management of breakthrough pain. One of the important aspects to consider while dosing is the pharmacokinetic profile of these agents. For example, for morphine, time to achieve maximal plasma concentration (t_{\max}) is 1.1 hours, and onset of analgesia is approximately 30 minutes. This information correlates well with onset and severity of breakthrough pain. Half-life ($t_{1/2}$; 2 hours for oral morphine), absorption rate, bioavailability (20%–40%), and elimination are less important. Adjustment of around-the-clock opioids is another option to manage the pain.

Further Reading

Mercadante S, Villari P, Ferrera P, Mangion S, Casuccio A. The use of opioids for breakthrough pain in acute palliative care unit by using doses proportional to opioid basal regimen. *Clin J Pain.* 2010;26:306–309.

Question 4.17

All of the following drugs, commonly used in the palliative setting, have been associated with QT interval prolongation and risk of torsades de pointes *except*:

- A. Methadone
- B. Morphine
- C. Ondansetron
- D. Haloperidol

Answer 4.17

The correct answer is (B)

Drug–drug interactions are an important consideration when prescribing medications to alleviate symptoms. Because palliative care patients are being referred earlier, it is even more important to know the medication interactions because they may impact disease-specific treatment. Use of methadone especially with the use of ondansetron, haloperidol, and various targeted therapies in the oncology setting can potentially result in QT prolongation. However, there have been no reports of QT prolongation due to morphine.

Further Reading

- LeBlanc TW, McNeil MJ, Kamal AH, Currow DC, Abernethy AP. Polypharmacy in patients with advanced cancer and the role of medication discontinuation. *Lancet Oncol*. 2015;16(7):e333–e341.
- Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med*. 2004;350(10):1013–1022.

Question 4.18

Mr. Smith is a 62-year-old male with non-small cell lung cancer (NSCLC) and metastasis to the spine. He is currently receiving PD1 immunotherapy for the treatment of his cancer. He had an allergic reaction to morphine in the past that included rash, hives, itching, and some swelling of his tongue. He has back pain that is not resolved by taking ibuprofen. His oncologist has recommended that acetaminophen not be used on a regular basis.

Which of the following would you recommend for managing his severe pain from bone metastasis?

- A. Morphine
- B. Codeine
- C. Oxycodone
- D. Methadone

Answer 4.18

The correct answer is (D)

Unlike nausea and itching, which patients confuse as allergic reactions, hives and difficulty breathing are true allergic reactions. Morphine, codeine, hydrocodone, hydromorphone, oxycodone, and oxymorphone belong to a class of opioids called phenanthrenes. In the instance of allergic reaction to an opioid in this class, trying an opioid in another class, such as phenylpiperidines (e.g., fentanyl) or phenylheptylamines (e.g., methadone), is recommended.

Further Reading

Amabile CM, Bowman BJ. Overview of oral modified-release opioid products for the management of chronic pain. *Ann Pharmacother.* 2006;40(7–8):1327–1335.

Question 4.19

Mrs. Smith is a 56-year-old female with cervical cancer and retroperitoneal lymph node involvement. She takes extended-release oxycodone at 40 mg orally every 12 hours and immediate-release oxycodone at 10 mg orally every 4 hours as needed. She has taken four doses per day of immediate-release oxycodone consistently for the past week but still reports poor pain control.

What is the ideal next step in optimizing the patient's pain control?

- A. Increase extended-release oxycodone to 40 mg administered orally every 8 hours around the clock
- B. Change to oxycontin at 20 mg administered orally every 12 hours
- C. Change to transdermal fentanyl at 50 μ g every 72 hours
- D. Change to methadone at 50 mg every 12 hours

Answer 4.19

The correct answer is (A)

Due to uncontrolled pain, the best strategy would be adjustment of extended-release prescription dose by 33%–50%. If the patient had presented with side effects such as delirium or myoclonus, opioid rotation could be considered. In this vignette, however, there is no mention of uncontrolled side effects. The patient's current long-acting opioid dosage is 120 mg of oral morphine per day. An increase to 180 mg (50% increase) of oral morphine per day would be appropriate in this circumstance.

Further Reading

Mercadante S. Opioid titration in cancer pain: A critical review. *Eur J Pain*. 2007;11(8):823–830.

Question 4.20

Mrs. Rogers is a 55-year-old female with breast cancer metastatic to the bones. Her physician prescribed a long-acting opioid regimen that comprises extended-release morphine at 30 mg administered orally every 8 hours around the clock. Mrs. Rogers noticed that although extended-release oxycodone alleviates her pain most of the day, she still experiences breakthrough back pain a couple of times a day that increases to an intensity of 7/10. She visits her physician in the clinic and requests medication changes to address the breakthrough back pain.

What changes should her physician prescribe?

- A. Switch to extended-release oxycodone at 40 mg taken every 12 hours
- B. Increase to extended-release morphine at 60 mg taken every 12 hours
- C. Add immediate-release morphine at 15 mg taken every 4 hours as needed
- D. Add immediate-release oxycodone at 20 mg taken every 4 hours as needed

Answer 4.20

The correct answer is (C)

Mrs. Rogers is experiencing breakthrough cancer pain. Breakthrough pain is treated with a short-acting opioid usually at a ratio of 10%–20% of the MEDD taken every 4 hours as needed. The patient is currently taking 90 mg of morphine per day; 10%–20% of that would be 9–18 mg of immediate-release morphine every 4 hours as needed.

Further Reading

Hanks GW, Conno F, Cherny N, et al. Morphine and alternative opioids in cancer pain: The EAPC recommendations. *Br J Cancer*. 2001;84(5):587–593.

Question 4.21

Mr. James is a 50-year-old male with NSCLC of the right upper lobe. He has right-sided chest pain for which he takes morphine extended-release 60 mg three times daily, and he takes 15 mg of immediate-release morphine at least four times daily for breakthrough pain. His opioid regimen was increased twice during the past 3 weeks, and he still experiences uncontrolled pain. The plan is to rotate him to extended-release hydromorphone.

Which of the following would you prescribe at this time?

- A. Hydromorphone extended-release 8 mg once daily with 8 mg immediate-release taken every 4 hours as needed for breakthrough pain
- B. Hydromorphone extended-release 16 mg once daily with 4 mg immediate-release taken every 4 hours as needed for breakthrough pain
- C. Hydromorphone extended-release 40 mg once daily with 8 mg immediate-release taken every 4 hours as needed for breakthrough pain
- D. Hydromorphone extended-release 24 mg once daily with 4 mg immediate-release taken every 4 hours as needed for breakthrough pain
- E. Hydromorphone extended-release 32 mg once daily with 16 mg immediate-release taken every 4 hours as needed for breakthrough pain

Answer 4.21

The correct answer is (D)

Uncontrolled pain is one of the most important reasons for opioid switching or opioid rotation. The first step in determining the starting dose of extended-release hydromorphone is to calculate the daily morphine dose, which in this case is 240 mg. A daily dose of extended-release hydromorphone 24 mg was estimated after using a conversion factor of 5 ($240/5 = 48$) and conservative 50% reduction for cross-tolerance ($48/2 = 24$). A 4 mg of hydromorphone breakthrough dose is calculated based on 10%–20% of the total daily dose.

Further Reading

Mercadante S. Opioid titration in cancer pain: A critical review. *Eur J Pain.* 2007;11(8):823–830.

Question 4.22

The treatment of stenosing tenosynovitis includes all of the following *except*:

- A. Trial of NSAIDs such as ibuprofen
- B. Rest, ice or heat, splint, and stretching exercises
- C. Steroid injection
- D. Percutaneous release
- E. Botox injection

Answer 4.22

The correct answer is (E)

All the treatment modalities mentioned except option E are part of the treatment of stenosing tenosynovitis (trigger finger). The approach depends on the severity and duration. If the patient is moderately distressed and the symptoms just started, a trial of NSAIDs such as ibuprofen with rest, ice or heat, splint, and stretching exercises is the recommended option. If conservative measures fail to control the symptoms, a trial of steroid injection is also recommended. In refractory cases, surgical intervention may be necessary.

Further Reading

Ferri FF. *Ferri's Clinical Advisor 2015: 5 Books in 1*. Philadelphia, PA: Mosby Elsevier; 2015.

Frontera WR, Silver JK, Rizzo TD Jr. *Essentials of Physical Medicine and Rehabilitation: Musculoskeletal Disorders, Pain, and Rehabilitation*. 2nd ed. Philadelphia, PA: Saunders; 2008.

Question 4.23

Which of the following statements is correct?

- A. The rewarding effects of drugs with risk of abuse, development of incentive salience, and development of drug-seeking habits in the binge/intoxication stage involve changes in dopamine and opioid peptides in the basal ganglia.
- B. Molecular genetic studies have identified transduction and transcription factors that act in neurocircuitry associated with the development and maintenance of addiction that might mediate initial vulnerability, maintenance, and relapse associated with addiction.
- C. Addiction is a chronic disease that involves day-to-day management rather than one rehabilitation session.
- D. Only A and B.
- E. None of the above.

Answer 4.23

The correct answer is (D)

Drug addiction represents a dramatic dysregulation of motivational circuits that is caused by a combination of exaggerated incentive salience and habit formation, reward deficits, stress surfeits, and compromised executive function in three stages. The rewarding effects of drugs of abuse, development of incentive salience, and development of drug-seeking habits in the binge/intoxication stage involve changes in dopamine and opioid peptides in the limbic system. The increases in negative emotional states and dysphoric and stress-like responses in the withdrawal/negative affect stage involve decreases in the function of the dopamine component of the reward system and recruitment of brain stress neurotransmitters, such as corticotrophin-releasing factor and dynorphin, in the neurocircuitry of the extended amygdala. The craving and deficits in executive function in the so-called preoccupation/anticipation stage involve the dysregulation of key afferent projections from the prefrontal cortex and insula, including glutamate, to the basal ganglia and extended amygdala. Molecular genetic studies have identified transduction and transcription factors that act in neurocircuitry associated with the development and maintenance of addiction that might mediate initial vulnerability, maintenance, and relapse associated with addiction.

Further Reading

- Koob GF, Volkow ND. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry*. 2016;3(8):760–773.
- Saitz R. Candidate performance measures for screening for, assessing, and treating unhealthy substance use in hospitals: Advocacy or evidence-based practice? *Ann Intern Med*. 2010;153:40–43.

Question 4.24

A 32-year-old female with abdominal pain secondary to widely metastatic colon cancer has been in the palliative care unit for the past 3 days for uncontrolled abdominal pain. As of today, she is taking morphine sulfate immediate release 15 mg q4 hours as needed for pain. She used 90 mg in the past 24 hours without side effects. Today, she is being discharged home.

What would be her discharge regimen?

- A. Morphine sustained release 45 mg q12 hours and 15 mg q1 hour as needed for breakthrough pain
- B. Morphine sustained release 90 mg q12 hours and 15 mg q1 hour as needed for breakthrough pain
- C. Increase morphine immediate release to 30 mg q4 hours PRN
- D. Switch to oxycontin 30 mg q12 hours and 5 mg oxycodone q12 hours PRN
- E. Morphine 45 mg q12 hours and hydromorphone 2 mg q4 hours PRN

Answer 4.24

The correct answer is (A)

Option B would almost double the baseline dose of morphine, which is not correct. Option C is incorrect because PRN regimen is inconvenient for the patient in an unsupervised environment. Also, not adding breakthrough would leave the patient uncovered for incidental pain. Using a different opioid in the setting of good pain control with another one would not be recommended (option D), even for breakthrough pain (option E).

For the calculation of the daily dose and frequency, first the total dose of short-acting morphine in 24 hours is divided by 2 for a twice-a-day dosing. Because you already know that the patient used 90 mg in 24 hours, the morphine extended-release dose will be 45 mg q12 hours. The patient will need breakthrough pain management at home as well. To determine the required needs of breakthrough, calculate 15%–20% of the 24-hour morphine need, which is 15 mg q1 hour as needed.

Further Reading

Bruera E, Dalal S. *The MD Anderson Supportive and Palliative Care Handbook*. Houston, TX: University of Texas; 2015.

Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep*. 2016;65(1):1–49.

Question 4.25

During your routine daily rounds as an attending physician in a tertiary palliative care unit, you decide to rotate a patient's opioids to methadone due to opioid-induced neurotoxicity. After reviewing the patient's medication profile, the pharmacist on your team mentions to you during the rounds that the patient is at risk for QTc prolongation.

Which of the following is an accurate statement regarding QTc prolongation?

- A. Methadone does not increase the risk of QTc interval prolongation.
- B. Borderline QTc in males is 431–450 msec, and in females it is 451–470 msec.
- C. QTc prolongation due to methadone is dose dependent.
- D. Methadone, if given with benzodiazepines, will prolong the QTc interval.
- E. Electrocardiography (ECG) should be performed every week to check methadone QTc.

Answer 4.25

The correct answer is (B)

Methadone does increase the risk of QTc prolongation (option A). QTc prolongation related to methadone is not dose dependent (option C). Depending on a patient's life expectancy and goals of care, ECG monitoring may not be warranted for the palliative care of the patient (option E). Benzodiazepines may increase the levels of methadone in blood via CYP metabolism, but there is no evidence of a role in increasing QTc interval (option D).

Further Reading

Moss AJ. QTc prolongation and sudden cardiac death: The association is in the detail. *J Am Coll Cardiol*. 2006;47:368–369.

Reddy S, Hui D, El Osta B, et al. The effect of oral methadone on the QTc interval in advanced cancer patients: A prospective pilot study. *J Palliative Med*. 2010;13:33–38.

Straus SM, Kors JA, De Bruin ML, et al. Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. *J Am Coll Cardiol*. 2006;47:362–367.

Question 4.26

As the palliative care consultant in the pediatric intensive care unit, you are evaluating pain in a 4-year-old male admitted for complications related to his Wilms tumor. The patient has a clenched jaw and is tense and restless, squirming, and crying steadily. He is reassured by occasional touching.

According to the Face, Legs, Activity, Cry, Consolability (FLACC) scale pain scoring system, what is the pain score for this patient?

- A. 6
- B. 8
- C. 7
- D. 9

Answer 4.26

The correct answer is (C)

The FLACC scale is an instrument used to assess pain for children between the ages of 2 months and 7 years or individuals who are unable to communicate their pain. The scale is scored in a range of 0–10, with 0 representing no pain. The scale has five criteria, which are each assigned a score of 0, 1, or 2.

In this case, the score is 7: clenched jaw (2), tense and restless (1), squirming (1), crying steadily (2), and reassured by occasional touching (1).

Further Reading

FLACC scale (extracted from The FLACC: A behavioral scale for scoring postoperative pain in young children, by S Merkel and others, 1997, *Pediatr Nurse*. 23(3):293–297).

Voepel-Lewis T, Zanolli J, Dammeyer JA, Merkel S. Reliability and validity of the Face, Legs, Activity, Cry, Consolability Behavioral tool in assessing acute pain in critically ill patients. *Am J Crit Care*. 2010;19(1):55–61. doi:10.4037/ajcc2010624. PMID 20045849

Question 4.27

As the palliative care consultant in the pediatric intensive care unit, you are evaluating pain in a 6-year-old male admitted for complications related to his osteosarcoma. The patient has an occasional grimace and is uneasy, jerking, crying, moaning, and difficult to console or comfort. According to the FLACC scale pain scoring system, what pain score will you assign to this patient?

- A. 8
- B. 7
- C. 9
- D. 10

Answer 4.27

The correct answer is (A)

The FLACC scale is an instrument used to assess pain for children between the ages of 2 months and 7 years or individuals who are unable to communicate their pain. The scale is scored in a range of 0–10, with 0 representing no pain. The scale has five criteria, which are each assigned a score of 0, 1, or 2.

In this case, the score is 8: occasional grimace (1), uneasy (1), jerking (2), crying (2), moaning, and difficult to console or comfort (2).

Further Reading

FLACC scale (extracted from The FLACC: A behavioral scale for scoring postoperative pain in young children, by S Merkel and others, 1997, *Pediatr Nurse*. 23(3):293–297).

Voepel-Lewis T, Zanoliti J, Dammeyer JA, Merkel S. Reliability and validity of the Face, Legs, Activity, Cry, Consolability Behavioral tool in assessing acute pain in critically ill patients. *Am J Crit Care*. 2010;19(1):55–61. doi:10.4037/ajcc2010624. PMID 20045849

Question 4.28

Mrs. Carpenter is a 75-year-old female with advanced dementia. She is nonverbal and scored 7 on the assessment of advanced dementia.

Which of the following indicates 7 on the Pain Assessment in Advanced Dementia (PAINAD) scale scoring system?

- A. Occasional labored breathing; occasional moan or groan; frown facial expression; fists clenched; unable to console, distract, or reassure
- B. Noisy labored breathing, loud moaning, facial grimacing, relaxed, no need to console
- C. Occasional labored breathing, occasional moan or groan, frown facial expression, tense looking, distracted
- D. Noisy labored breathing; crying; facial grimacing; rigid; unable to console, distract, or reassure

Answer 4.28

The correct answer is (A)

For option A, the score is 7. For option B, the score is 6, for option C it is 5, and for option D the patient would have a score of 10.

The PAINAD score is used for the assessment of pain in patients with advanced dementia. The total score ranges from 0 to 10 points. The following is a possible interpretation of the scores: 1–3 = mild pain, 4–6 = moderate pain, and 7–10 = severe pain.

Further Reading

Warden V, Hurley AC, Volicer L. Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) scale. *J Am Med Dir Assoc.* 2003;4(1):9–15.

Question 4.29

Which of the following statements regarding salmon calcitonin is true in relation to its role in hypercalcemia?

- A. Unlike other hypocalcemic agents, it is effective within 2 hours after first dosing.
- B. This pharmacologic agent shows peak effect at 24–48 hours and has a duration of action of 4–7 days in most cases.
- C. Its effectiveness may diminish after 4–7 days despite continuous administration (the so-called “escape phenomenon”).
- D. Options A–C are correct.
- E. Salmon calcitonin is toxic and should not be used in the treatment of hypercalcemia.

Answer 4.29

The correct answer is (D)

Salmon calcitonin has been used for the management of acute hypercalcemia. Unlike other hypocalcemic agents, it is effective within 2 hours after first dosing. This pharmacologic agent shows peak effect at 24–48 hours and has a duration of action of 4–7 days in most cases. Its effectiveness may diminish thereafter, despite continuous administration (the so-called “escape phenomenon”). Salmon calcitonin has been shown to be effective in the management of acute hypercalcemia due to a variety of causes, and because of its low toxicity profile, it may be administered to patients with congestive heart failure or azotemia. Salmon calcitonin is also an analgesic agent in patients with pain associated with bone metastases, and it may be used in conjunction with other hypocalcemic agents, such as mithramycin, the bisphosphonates, or gallium nitrate, to prolong the clinical response to more than 1 week. Salmon calcitonin is therefore effective and safe in the management of acute hypercalcemia.

Further Reading

Copp HA, Cameron EC, Cheney BA, Davidson AG, Henze, KG.

Evidence for calcitonin—A new hormone from the parathyroid that lowers blood calcium. *Endocrinology*. 1962;70:638–649.

Wisneski LA. Salmon calcitonin in the acute management of hypercalcemia. *Calcif Tissue Int*. 1990;46:S26. doi:10.1007/BF02553290

Question 4.30

Mr. Rao is a 37-year-old male with a past history of metastatic colon cancer refractory to multiple therapies. The patient has been managed for pain at an outside facility. At your inpatient consultation visit, you find that his pain is not controlled with a MEDD of 1050 mg; he rates the severity of his pain as 10/10 and is immediately switched to IV Dilaudid PCA and transferred to the palliative care unit per the patient's decision. In the unit, the nursing staff perception is that the patient is always comfortable, but the moment somebody walks into the room, the patient starts showing symptoms of excruciating pain, such as moaning and moving within the bed holding his abdomen and asking for IV breakthrough medication.

How would you assess and treat this patient's pain?

- A. The Screener and Opioid Assessment for Patients with Pain (SOAPP) questionnaire
- B. Motivational interviewing
- C. Restricted quantities of breakthrough opioids
- D. Rule out any psychiatric condition
- E. All of the above

Answer 4.30

The correct answer is (E)

Chemical coping is a working definition that describes patients' intake of opioids on a scale that spans the range from normal (no addictive opioid use for pain) to opioid addiction. Most patients will fall somewhere between the two extremes in using opioid analgesics to cope with their psychological or spiritual distress. As part of the initial evaluation of patients with cancer-related pain, a brief screening tool such as the CAGE questionnaire should be used to identify patients who may be at risk for chemical coping. Identifying patients at risk will allow clinicians to avoid unnecessary opioid toxicity, control pain, and improve quality of life. A structured approach for managing opioid use should be adopted, including standardized documentation, opioid treatment agreements, urine drug screens, frequent visits, and restricted quantities of breakthrough opioids. All patients at risk should receive brief motivational interviewing with an objective, nonjudgmental, and empathic style that includes personalized feedback, particularly about markers of risk or harm. For chemical copers approaching the addiction end of the spectrum, with evidence of compulsive use and destructive behavior, referral should be made to substance abuse specialists. The SOAPP is a 14-item self-administered screening instrument originally used to assess risk for aberrant opioid use in patients with chronic noncancer pain.

Further Reading

Del Fabbro E. Assessment and management of chemical coping in patients with cancer. *J Clin Oncol*. 2014;32(16):1734–1738.

Question 4.31

Regarding chemical coping, which of the following statement(s) is true?

- A. It is defined as the intake by patients with cancer of opioids on a scale spanning the range from normal (no addictive opioid use for pain) to total addiction and its accompanying compulsive, destructive behavior.
- B. "All addicts are chemical copers but not all chemical copers are addicts."
- C. Mild chemical copers may not experience any major adverse effects, whereas those approaching the addiction end of the spectrum are at risk for increased morbidity and mortality.
- D. All of the above.
- E. Only A and C.

Answer 4.31

The correct answer is (D)

Chemical coping is defined as the intake by patients with cancer of opioids on a scale spanning the range from normal non-addictive opioid use for pain to total addiction and its accompanying compulsive, destructive behavior. Most patients will fall somewhere between the two extremes, using their medications in nonprescribed ways to cope with their stress. The relationship between addiction and chemical coping is summarized by Kirsh et al. as follows: “All addicts are chemical copers but not all chemical copers are addicts.” Mild chemical copers may not experience any major adverse effects, whereas those approaching the addiction end of the spectrum are at risk for increased morbidity and mortality. Thus, there is a broad spectrum of chemical coping, and the degree to which patients use their medications in a maladaptive manner will determine their susceptibility to drug toxicity and harm. Chemical coping and addiction should be distinguished from physical tolerance and withdrawal syndrome when opioids are abruptly discontinued. Addiction is characterized by changes in brain structure and function that accompany chronic exposure to drugs of abuse.

Further Reading

- Bruera E, Moyano J, Seifert L, et al. The frequency of alcoholism among patients with pain due to terminal cancer. *J Pain Symptom Manage.* 1995;10:599–603.
- Kirsh KL, Jass C, Bennett DS, et al. Initial development of a survey tool to detect issues of chemical coping in chronic pain patients. *Palliat Support Care.* 2007;5:219–226.
- Robison AJ, Nestler EJ. Transcriptional and epigenetic mechanisms of addiction. *Nat Rev Neurosci.* 2011;12:623–637.

Question 4.32

In reference to the use of a high-concentration capsaicin dermal patch (NGX-4010), which of the following statements is true?

- A. A single high-concentration dermal patch (NGX-4010) application was safe and provided at least 12 weeks of pain reduction in patients with HIV-associated distal sensory polyneuropathy.
- B. A single high-concentration dermal patch (NGX-4010) application was safe and provided at least 6 weeks of pain reduction in patients with HIV-associated distal sensory polyneuropathy.
- C. No evidence has been found between the use of the high-concentration capsaicin dermal patch (NGX-4010) and the treatment of distal sensory HIV-related polyneuropathy.
- D. A single high-concentration dermal patch (NGX-4010) application was safe and provided at least 1 week of pain reduction in patients with HIV-associated distal sensory polyneuropathy.
- E. A and D are correct.

Answer 4.32

The correct answer is (A)

A double-blind multicenter study by Simpson et al. found that a single NGX-4010 application was safe and provided at least 12 weeks of pain reduction in patients with HIV-associated distal sensory polyneuropathy.

Further Reading

Simpson, DM, Brown S, Tobias J; the NGX-4010 C107 Study Group. Controlled trial of high-concentration capsaicin patch for treatment of painful HIV neuropathy *Neurology*. 2008;70(24):2305–2313.

Question 4.33

Mr. Ming, a 75-year-old who is a retired computer hacker with a history of squamous cell cancer of the tonsil now in remission, presents to your outpatient clinic complaining of sleep problems with irritability and loss of appetite for the past 6 months. He has frequent headaches, dizziness, and a sensation of tightness in the chest. Three weeks prior to this visit, he had several episodes of chest pain. The patient reports that he went to the local hospital, where he was admitted for a medical evaluation. Results of all investigations, including tests for coronary artery disease, were normal. He was referred for psychiatric consultation. Despite sensitive probing by the psychiatrist, Mr. Ming denies symptoms of anxiety and depression. He has no history of psychiatric or physical illness.

Of the following options, which one is the most probable diagnosis?

- A. Somatization disorder
- B. Hypochondriasis
- C. Pain disorder
- D. Somatic symptom disorder

Answer 4.33

The correct answer is (D)

Somatic symptom disorder (SSD) is characterized by somatic symptoms that are either very distressing or result in significant disruption of functioning, as well as excessive and disproportionate thoughts, feelings, and behaviors regarding those symptoms. To be diagnosed with SSD, the individual must be persistently symptomatic for at least 6 months.

Symptoms: Cardiac, musculoskeletal, urological, gastrointestinal, or neurological.

Diagnosis: There may be multiple symptoms, often occurring in different organ systems.

Management: Providers need to be careful in communicating the diagnosis because the patient–doctor relationship may be threatened. The BATHE technique provides a framework for exploration of psychosocial stressors in less than 5 minutes:

- *Background:* “What is going on in your life?”
- *Affect:* “How do you feel about it?”
- *Trouble:* “What troubles you the most about that situation?”
- *Handle:* “What helps you handle that?”
- *Empathy:* “This is a tough situation to be in. Your reaction makes sense to me.”

Psychotherapy has been shown to reduce the intensity and frequency of complaints.

Regarding antidepressants, one study showed the successful use of duloxetine.

Somatization disorder (option A), hypochondriasis (option B), and pain disorder (option C) belong to the same group as SSD per the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*.

Further Reading

Leiblum SR, Schnall E, Seehuus M, et al. To BATHE or not to

BATHE: Patient satisfaction with visits to their family physician. *Fam Med*. 2008;40(6):407–411.

Question 4.34

Mrs. Baker is a 45-year-old female with a history of early breast cancer diagnosed in her 20s now in remission for the past 16 years. She presents to your clinic with a complaint of a 2-year history of widespread musculoskeletal pain in the bilateral shoulder girdle, bilateral upper arms, bilateral buttocks, and lower back area. She also has been complaining of severe fatigue, especially after waking up from her sleep and in the mid-afternoon; intermittent headaches; and paresthesias in bilateral upper and lower extremities that are described as pervasive and interfering with daily activities. Extensive testing throughout the years, including multiple site computed tomography (CT) scans and magnetic resonance imaging (MRI) scans, has been negative. She has also had negative blood work, such as complete blood count, erythrocyte sedimentation rate, C-reactive protein, and rheumatoid factor. The patient was eventually diagnosed with fibromyalgia.

This patient satisfies the diagnostic criteria for fibromyalgia if which of the following conditions are met?

- A. Widespread Pain Index (WPI) ≥ 7 and Symptom Severity (SS) scale score ≥ 5 or WPI 3–6 and SS scale score ≥ 9 . Symptoms have been present at a similar level for at least 3 months. The patient does not have a disorder that would otherwise explain the pain.
- B. WPI ≥ 6 and SS scale score ≥ 4 or WPI 2–5 and SS scale score ≥ 8 . Symptoms have been present at a similar level for at least 6 months. The patient does not have a disorder that would otherwise explain the pain.
- C. WPI ≥ 8 and SS scale score ≥ 6 or WPI 4–7 and SS scale score ≥ 10 . Symptoms have been present at a similar level for at least 12 months. The patient does not have a disorder that would otherwise explain the pain.
- D. None of the options are correct.

Answer 4.34

The correct answer is (A)

The clinical scenario presented in Question 4.34 represents a depiction of a typical presentation of a fibromyalgia patient. The question is asking for the criteria used for diagnosis of this pathology. The 1990 American College of Rheumatology (ACR) classification criteria had greater than 85% sensitivity and specificity for differentiating fibromyalgia from other rheumatic disease; pain perception was making the point of tenderness localization an arbitrary decision instead of an objective finding. The 2010 ACR preliminary diagnostic criteria advocate for not using the points of tenderness but do provide a scale for measurement of the severity of symptoms that are characteristic of fibromyalgia.

Further Reading

- Aggarwal R, Ringold S, Khanna D, et al. Distinctions between diagnostic and classification criteria? *Arthritis Care Res.* 2015;67:891–897.
- Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: Report of the Multicenter Criteria Committee. *Arthritis Rheum.* 1990;33:160–172.

Question 4.35

Mrs. Rosas is a 67-year-old female from Guatemala with a surgical history of microdiscectomy and spinal fusion 3 months ago without major complications, except for residual lumbar back pain. She recently moved to the United States and came to your clinic seeking treatment for her chronic back pain. After a careful physical examination, you note that her pain is localized in the paraspinal lumbar area. In addition, imaging (lumbar spine X-ray and lumbar spine MRI) performed during a recent emergency room visit for acute or chronic back pain was negative for acute changes. You diagnose the patient with failed back syndrome.

Which of the following treatment modalities has not proven to be first-line treatment for failed back syndrome?

- A. Vigorous physical therapy and behavioral therapy
- B. Anticonvulsants for neuropathic pain (if present)
- C. NSAIDs for somatic pain (if present)
- D. Repeat surgery within 3 months to prevent permanent damage

Answer 4.35

The correct answer is (D)

Failed back syndrome (FBS) is a term embracing a constellation of conditions that describes persistent or recurring low back pain, with or without sciatica, following one or more spine surgeries.

This patient is suffering from myofascial pain development, a common complication of back surgery leading to FBS. During surgery, dissection and prolonged retraction of the paraspinal musculature results in denervation and atrophy with subsequent pain development. This patient may benefit from pertinent physical therapy, pain management with NSAIDs, or use of anticonvulsants such as gabapentin in the case of neuropathic pain symptoms. Surgical interventions without previous appropriate characterization of the pain can exacerbate the ongoing baseline pain. The literature recommends against multiple unnecessary surgical interventions in these patients (Option D).

Options A–C are part of the treatment of FBS.

Further Reading

Deyo RA. Back surgery—Who needs it? *N Engl J Med.* 2007;356:2239–2243.

Deyo RA, Mirza SK. Trends and variations in the use of spine surgery. *Clin Orthop Relat Res.* 2006;443:139–146.

Question 4.36

Mrs. Smith is a 67-year-old female with a history of hepatocellular carcinoma s/p transarterial chemo-embolization and was subsequently maintained on sorafenib due to persistent residual tumor. She had chronic abdominal pain related to the malignancy, as well as degenerative joint disease of the spine. She had a past history of alcohol and IV drug abuse and was actively smoking tobacco. She was referred to the palliative care clinic for management of her chronic malignant pain and was initially started on hydrocodone/APAP 10/325 mg 1 tablet every 3 hours as needed for pain. She started running out of her prescribed medications prematurely and received early refills.

The treating physician switched opioid to morphine due to uncontrolled pain. However, during follow-up visits, pain was still not controlled, prompting the physician to order a random urine drug test (UDT) after 4 months of outpatient palliative care visits. The test was positive for an unprescribed opioid (hydrocodone) and an illicit drug (tetrahydrocannabinol), but it was negative for the prescribed opioid (morphine).

All of the following statements are true with regard to UDT in the setting of the palliative care clinic, and its interpretation, *except*:

- A. The effective use of UDT requires a good understanding of the physiology, pharmacology, and toxicology of opioids.
- B. The confirmatory tests, which utilize gas or liquid chromatography/mass spectrometry techniques, are able to detect specific drugs but may be more expensive and have a longer turnaround time.
- C. The complexity of the opioid metabolic pathways sometimes makes the interpretation of UDT quite challenging, irrespective of the type of test used.
- D. If a patient is taking one opioid, I should expect only one metabolite in the UDT results. Two or more metabolites always will bring grounds for suspicion of aberrant drug use.

Answer 4.36

The correct answer is (D)

Options A–C are correct statements. The teaching point of the question is to remember that the metabolism of some opioids sometimes results in more than one metabolite, and this may lead to mistakes in the approach of the patient.

For example, patients receiving hydrocodone might have both hydromorphone and hydrocodone in their urine, and this might lead to conflict if the clinician erroneously interprets this as the presence of an abnormal opioid.

Further Reading

Arthur JA, Haider A, Edwards T, et al. Aberrant opioid use and urine drug testing in outpatient palliative care. *J Palliat Med.* 2016,19(7):778–782. doi:10.1089/jpm.2015.0335

Question 4.37

Mr. Thomas is a 69-year-old male with gastric cancer metastatic to spine and peritoneum currently undergoing chemotherapy with folinic acid, fluorouracil, and oxaliplatin (FOLFOX). He has chronic abdominal pain and lumbar spine pain due to peritoneal invasion, and he has L4–L5 metastatic lesions (s/p vertebroplasty) due to a pathologic fracture. The patient has a history of social alcohol use (once a month), denies IV drug use, and quit smoking tobacco 3 months ago. The patient was initially started on hydrocodone/APAP 5/325 mg every 8 hours as needed for pain. It was noticed that the patient started running out of meds early and started scheduling his follow-up appointments 1 or 2 days earlier each month.

Due to high suspicion for aberrant opioid use, the hospice and palliative care team ordered a UDT. The test was positive for hydrocodone, negative for morphine, and positive for tetrahydrocannabinol.

All of the following statements are true regarding aberrant opioid use *except*:

- A. Just like in the general population, oncology and palliative care patients may also have preexisting issues with drug and substance abuse and are therefore similarly predisposed to aberrant prescription drug use.
- B. Although opioid risk assessment tools are useful screening tools that may reveal the possibility of maladaptive behavior, they are based on patient self-report, which limits their usefulness.
- C. Patients with a negative CAGE-AID and SOAPP screenings should not be screened with random UDT because it increases the risk of misinterpretation of the results and may undermine the patient–doctor relationship.
- D. Aberrant drug use is a major problem in the palliative care setting, and valid screening tools have been implemented to diagnose it.

Answer 4.37

The correct answer is (C)

Options A, B, and D are correct statements. The palliative care population has the same risk for aberrant drug use as the rest of the general population. The opioid risk assessment tools are subject to self-report, and this is a limitation to their validity, so other factors always need to be taken into consideration in the evaluation of aberrant drug use. Option C is an inaccurate statement. The physician should always consider aberrant opioid use in a patient with abnormal behavior, regardless of the screening tool results.

Further Reading

Arthur JA, Haider A, Edwards T, et al. Aberrant opioid use and urine drug testing in outpatient palliative care. *J Palliat Med.* 2016,19(7):778–782. doi:10.1089/jpm.2015.0335

Question 4.38

Mr. Johnson is a 52-year-old male with a past medical history of localized prostate cancer diagnosed 3 years ago. The patient has been treated for nociceptive, somatic-type cancer-related pain in the lower abdomen and back with morphine extended-release 15 mg q12 hours and morphine 7.5 mg q4 hours as needed for breakthrough pain. During the current office visit, the patient reports a history of severe unilateral orbital headaches. These headaches usually last 15–20 minutes, during which he has ipsilateral watery and “puffy” eyes and sometimes ipsilateral runny nose. The attacks happen every other day, and sometimes he has up to three attacks per day. The patient reports he had similar symptoms 1 year ago that lasted 3 weeks, but they went away eventually with an over-the-counter medication. Recent head imaging with CT and MRI done by oncology was negative for metastatic lesions. The patient wonders if you can start a medication that can control his distressing pain, which has been persistent for the past 6 months.

Which of the following treatments can be effective in managing this type of headache?

- A. Increase the dose of morphine
- B. Rotate opioids because this could be a sign of opioid-induced neurotoxicity
- C. Start a trial of sumatriptan 6 mg subcutaneous injection (up to 12 mg daily) and gabapentin 100 mg three times a day
- D. Use oxygen 1 l/min by non-rebreather mask for 15–20 minutes

Answer 4.38

The correct answer is (C)

This patient has a typical presentation of cluster headaches. Options A and B are incorrect because the use of opioid in the treatment of cluster headaches is inappropriate and may lead to unnecessary opioid toxicity.

Option D is incorrect because the appropriate abortive oxygen dose of cluster headaches is oxygen 7–15 l/min by non-rebreather mask for 15–20 minutes, or high-flow oxygen.

Option C represents a good treatment alternative for cluster headache in this case because sumatriptan can act as an abortive medication as needed, and chronic use of gabapentin can prevent recurrence.

Further Reading

Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edition. *Cephalgia*. 2004;24(Suppl 1):1–160.

McConaghy J. Headache in primary care. *Primary Care*. 2007;34:83–97.

Question 4.39

A 55-year-old female has a past medical history of diabetes mellitus, hypothyroidism, rheumatoid arthritis, and metastatic squamous cell carcinoma of the lung. The patient's medication regimen includes metformin, hydroxychloroquine, levothyroxine, and morphine extended-release 20 mg q12 hours and morphine immediate-release 15 mg q4 hours as needed. The patient presents to the clinic with history of 3 days of left knee excruciating tenderness, mild edema, and erythema.

Which of the following is the best treatment option for this patient's pain?

- A. Increase the dose of morphine dose
- B. Trial of steroids
- C. Heat and cold compresses twice a day for 7 days
- D. Rotate opioids because this is a sign of neurotoxicity

Answer 4.39

The correct answer is (B)

This patient is suffering from a rheumatoid arthritis (RA) flare episode. Option A is not correct because the RA pain is related to an immunologic mechanism, which is not treated with opioids. Heat and cold compresses (option C) do not have a role in the treatment of RA flares. Rotating opioids (option D) is also inappropriate.

Further Reading

Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. *Lancet*. 2010;376(9746):1094–1108.

Question 4.40

A 37-year-old female with a history of early breast cancer s/p treatment now with no evidence of disease for the past 8 years. She recently delivered a healthy baby after an uncomplicated pregnancy. She now complains of a constant throbbing headache that started right after her epidural injection. It has been 3 days since the headache started. It has not responded to sumatriptan or caffeine.

Which of the following is the best approach to treat this procedure-related complication?

- A. Increase the dose of oral caffeine.
- B. Epidural blood patch.
- C. Sumatriptan is not a treatment option for this complication.
- D. Both A and B.
- E. All the options are correct.

Answer 4.40

The correct answer is (B)

This patient has post-dural puncture headache, one of the possible complications related to epidural injection. Intravenous caffeine is an effective therapy for post-dural puncture headache, but oral caffeine (option A) is not. Epidural blood patch (option B) as a technique has a success rate of 70%–98% if carried out more than 24 hours after the dural puncture. Sumatriptan (option C) is a 5-HT_{1D} receptor agonist that promotes cerebral vasoconstriction in a similar manner as caffeine, and it is one of the treatment options for post-dural puncture headache.

Further Reading

- Bart AJ, Wheeler AS. Comparison of epidural saline placement and epidural blood placement in the treatment of post-lumbar-puncture headache. *Anesthesiology*. 1978;48:221–223.
- Baysinger CL, Menk EJ, Harte E, Middaugh R. The successful treatment of dural puncture headache after failed epidural blood patch. *Anesth Analg*. 1986;65:1242–1244.

Question 4.41

The Edmonton Symptom Assessment System (ESAS) is a widely used self-report symptom intensity tool for assessing 10 common symptoms in palliative care, with ratings ranging from 0 (none, best) to 10 (worst).

Regarding how to apply the ESAS, which of the following is an incorrect statement?

- A. It is recommended that the patient complete the ESAS with guidance from a health care professional, especially on the first occasion.
- B. The patient should be instructed to rate the severity of each symptom on a 0 to 10 scale, where 0 represents absence of the symptom and 10 represents the worst possible severity. The number should be circled on the scale.
- C. The patient should be instructed to rate each symptom according to how he or she feels now. The health care professional may choose to ask additional questions about the severity of symptoms at other time points—for example, symptom severity at best and at worst during the past 24 hours.
- D. It is recommended that the patient complete the ESAS with guidance from a health care professional, all the time, to decrease errors.

Answer 4.41

The correct answer is (D)

Option D is an incorrect statement; the ESAS form has been validated, and a prior multicenter study demonstrated that patients perceived the ESAS as significantly easier to understand. There is no need to have a health care provider in the room for the length of the evaluation. Options A–C are correct statements in regard to the ESAS form.

Further Reading

Bruera E, Macdonald S. Audit methods: The Edmonton Symptom Assessment. In: Higginson I, ed. *Clinical Audit in Palliative Care*. Oxford, UK: Radcliffe Medical Press; 1993:61–77.

Watanabe SM, Nekolaichuk CL, Beaumont C. The Edmonton Symptom Assessment System, a proposed tool for distress screening in cancer patients: Development and refinement. *Psycho-Oncology*. 2012;21(9):977–985. doi:10.1002/pon.1996 Review.

Question 4.42

Regarding chronic pain management, which of the following are considered chemical coping risk screening tools?

- A. Pain medication diaries, pill counts, and UDT
- B. Current Opioid Misuse Measure (COMM), Addiction Behavior Checklist (ABC), and UDT
- C. Patient-reported history, SOAPP, and physician's clinical impression
- D. Patient-reported history, behavioral pattern "red flags" such as early refills, and frequent history of lost or stolen medications

Answer 4.42

The correct answer is (C)

The following are chemical coping/opioid addiction risk screening tools: patient-reported history, psychology interview, risk screening questionnaires (SOAPP, Opioid Risk Tool, and Pain Medication Questionnaire), and the physician's clinical impression.

The following are used for chemical coping/opioid addiction risk monitoring: prescription monitoring programs (49 states), pain medication diaries, pill counts, UDT, risk monitoring tools such as COMM and ABC, and behavioral patterns such as requests for early refills or frequent loss or stolen medications.

The educational point of the question is that chemical coping/opioid addiction risk screening tools represent a good starting point in terms of assessment, but the provider should continue to monitor for chemical coping/opioid addiction development during subsequent visits, regardless of the risk screening tool.

Further Reading

Arthur JA, Haider A, Edwards T, et al. Aberrant opioid use and urine drug testing in outpatient palliative care. *J Palliat Med.* 2016;19(7):778–782. doi:10.1089/jpm.2015.0335

Fishman SM, Wilsey B, Yang J, et al. Adherence monitoring and drug surveillance in chronic opioid therapy. *J Pain Symptom Manage.* 2000;20:293–307.

5

Adjuvant Drugs in Pain Management

DAVID R. EIDELSON
AND LARRY C. DRIVER

Question 5.1

Mr. Smith is a 70-year-old male who recently moved to the United States with a history of hypertension, congestive heart failure, renal carcinoma, and arthritis. He currently takes tramadol, acetaminophen, fluoxetine, lisinopril, and rofecoxib.

Which medication could potentially lead to worsening heart failure?

- A. Tramadol
- B. Acetaminophen
- C. Fluoxetine
- D. Rofecoxib
- E. Lisinopril

Answer 5.1

The correct answer is (D)

COX-2 inhibitors, such as rofecoxib, are associated with increased cardiovascular risk (heart failure, death, myocardial infarction (MI), stroke, and thromboembolic event). The risk is increased in a dose-dependent manner. COX-2 inhibitors have an increased risk of mortality in patients with preexisting heart failure.

Risk factors: Acute MI, unstable angina, congestive heart failure, ischemic cardiovascular disease.

Mechanism: Several factors appear to contribute to the cardiovascular risks associated with COX-2 inhibitors, including degree of COX-2 selectivity. Selective COX-2 inhibition is associated with reduced prostaglandin 12 or prostacyclin production by vascular endothelium with little or no inhibition of potentially prothrombotic platelet thromboxane A_2 production. This reduction in prostacyclin activity predisposes to endothelial injury.

Treatment: Avoid COX-2 inhibitors in patients with underlying cardiovascular disease. If an anti-inflammatory is necessary, use the lowest effective dose for the shortest time possible. Rofecoxib is the coxib that carries the clearest risk for ischemic cardiovascular disease, and it has been withdrawn from the market in most countries because of this effect. Celecoxib has a more favorable risk profile and can be used cautiously.

Further Reading

Solomon DH. COX-2 selective inhibitors: Adverse cardiovascular effects. <https://www.uptodate.com/contents/cox-2-selective-inhibitors-adverse-cardiovascular-effects>. Published 2017.

Solomon DH. Nonselective NSAIDs: Adverse cardiovascular effects. <https://www.uptodate.com/contents/nonselective-nsaids-adverse-cardiovascular-effects>. Published 2017.

Question 5.2

Ms. Howard is a 65-year-old female with a history of chronic right leg pain secondary to osteosarcoma for which she takes a pain medication whose name she cannot remember. She presents to your office with new-onset epigastric pain. She endorses the pain is relieved by food. However, she recently has become concerned because her stool has become dark to black, and she has become increasingly more tired. On exam, she looks pale, and lab work shows normocytic anemia.

Which medication most likely caused this situation?

- A. Bleomycin
- B. Gabapentin
- C. Acetaminophen
- D. Morphine
- E. Indomethacin

Answer 5.2

The correct answer is (E)

Nonsteroidal anti-inflammatory drugs (NSAIDs) can have a profound effect on the stomach and bowel, with approximately 15% of patients on longer term NSAIDs developing peptic ulcer disease (PUD). Often, these ulcers are asymptomatic, but the feared complication is bleeding (new-onset anemia, melena, and hematochezia) and perforation.

Epigastric pain is the most common symptom of both gastric and duodenal ulcers. Patients often describe a gnawing or burning sensation that occurs after meals. In the case of gastric ulcers, this occurs soon after meals, whereas with duodenal ulcers, it usually occurs 2 or 3 hours later. Food often will relieve the duodenal ulcer pain.

Risk factors: Duration of therapy—use for a short-term period less than 1 week is unlikely to result in clinically significant gastroduodenal toxicity. However, longer term therapy is associated with increased risk of complications. Other factors include advancing age, higher NSAID dosage, past history of gastroduodenal toxicity from NSAIDs, history of PUD, and concomitant use of other medications (steroids and anticoagulants).

Mechanism: The proposed mechanism for NSAID-induced gastroduodenal injury is through its inhibition of prostaglandin. NSAIDs inhibit cyclooxygenase, which leads to decreased mucosal prostaglandin synthesis. Prostaglandin plays a critical role in maintaining gastric mucosal integrity.

Treatment: Avoid mucosal-damaging anti-inflammatory medication, and consider acetaminophen. Minimize the damage by prescribing a proton pump inhibitor or prostaglandin E analog.

Further Reading

Feldman M. NSAIDs (including aspirin): Pathogenesis of gastroduodenal toxicity. <https://www.uptodate.com/contents/nsaids-including-aspirin-pathogenesis-of-gastroduodenal-toxicity>. Published 2017.

Matsui H, Shimokawa O, Kanek T, et al. The pathophysiology of non-steroidal anti-inflammatory drug (NSAID)-induced mucosal injuries in stomach and small intestine. *J Clin Biochem Nutr*. 2011;48(2):107–111. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3045681>

Question 5.3

Mr. Jones is a 70-year-old male with a history of diabetes, Alzheimer's dementia, and depression. He was brought to the emergency department by his family after he ingested a large amount of an unknown home medication. On arrival, he was lethargic, confused, and hypotensive. An electrocardiogram showed a marked prolongation of the QRS interval.

Which medication was most likely responsible for these findings?

- A. Insulin
- B. Acetaminophen
- C. Aspirin
- D. Amitriptyline

Answer 5.3

The correct answer is (D)

This patient most likely overdosed on his home tricyclic antidepressant (TCA; amitriptyline) medication. Symptoms and signs of TCA toxicity generally consist of vital sign abnormality (tachycardia and hypotension), mental status changes (sedation), seizures, anticholinergic toxicity (hyperthermia, flushing, and dilated pupils), and electrocardiogram (ECG) changes. Cardiac conduction abnormalities are common, and the ECG helps determine the extent of TCA poisoning (prolongation of QRS >100 msec, QRS morphology changes, and size and ratio of R and S waves in aVR >0.7).

TCA toxicity/poisoning

Mechanisms of action: There are multiple mechanisms responsible for the clinical effects of TCA overdose, including blockade of cardiac fast sodium channels, antagonism of central and peripheral muscarinic acetylcholine receptors, antagonism of peripheral α_1 -adrenergic receptors, antagonism of histamine receptors, and antagonism of GABA_A receptors.

Treatment: Sodium bicarbonate for QRS duration >100 msec. Benzodiazepines for TCA-induced seizures. Fluid bolus 500–1000 ml normal saline for hypotension. In the setting of TCA-induced anticholinergic toxicity, physostigmine is contraindicated because it can lead to cardiac arrest.

Further Reading

- Biggs JT, Spiker DG, Petit JM, Ziegler VE. Tricyclic antidepressant overdose: Incidence of symptoms. *JAMA*. 1977;238:135.
- Kerr GW, McGuffie AC, Wilkie S. Tricyclic antidepressant overdose: A review. *Emerg Med J* 2001;18:236–241. <https://www.ncbi.nlm.nih.gov/pubmed/11435353>
- Salhanick SD. Tricyclic antidepressant poisoning. http://www.uptodate.com/contents/tricyclic-antidepressant-poisoning?source=search_result&search=tca+overdose&selectedTitle=1%7E54. Published 2016.

Question 5.4

Ms. Hopkins is a 48-year-old female with a history of multiple sclerosis with severe muscular rigidity, hypertension, and depression. She presents to the emergency department extremely drowsy and dizzy, and upon arrival she has a seizure. Her family brings her home medications, which include the angiotensin-converting enzyme lisinopril, baclofen, acetaminophen, and sertraline.

Which medication did she most likely overdose on?

- A. Lisinopril
- B. Baclofen
- C. Acetaminophen
- D. Sertraline

Answer 5.4

The correct answer is (B)

This patient's symptoms are consistent with baclofen toxicity. Baclofen is a central-acting muscle relaxant. It is commonly used to treat muscle spasms in multiple sclerosis as well as spinal cord injuries. Baclofen is available for both oral and intrathecal administration. There is a black box warning for abrupt discontinuation of intrathecal baclofen because its withdrawal has resulted in high fever, altered mental status, rebound spasticity, and muscle rigidity that can progress to rhabdomyolysis and, in rare circumstances, multiple organ system failure and death.

Baclofen toxicity

Mechanism of action: Baclofen is an agonist on GABA_B receptors, which leads to a decrease in excitatory neurotransmission and an increase in inhibitory signals. It inhibits synaptic transmission through spinal reflex arcs via hyperpolarization of primary afferent fiber terminals.

Side effects: The most common side effects include drowsiness (63%), dizziness (5%–15%), and weakness (5%–15%). Signs of toxicity include neurologic symptoms such as seizures, delirium, and altered mental status. When doses are greater than 200 mg, the heart is affected and tachycardia/bradycardia, hyper/hypotension, and eventually respiratory compromise can be seen.

Treatment: Maintain airway, breathing, and circulation, and supportive care. Anticonvulsants are indicated for seizures. If ingestion was recent, activated charcoal can help bind the drug. If symptoms are severe, hemodialysis can be employed to help clear the drug and reduce the duration of symptoms.

Further Reading

Leung NY, Whyte, IM, Isbister GK. Baclofen overdose: Defining the spectrum of toxicity. *Emerg Med Australas*. 2006;18(1):77–82.
<https://www.ncbi.nlm.nih.gov/pubmed/16454779>

Question 5.5

Ms. Wilson is an 80-year-old female who was recently hospitalized after a syncope episode. She presents to your clinic with dry mouth and is extremely drowsy. She has a history of chronic back pain, muscle spasms, as well as liver disease.

Which medication is most likely responsible for her symptoms?

- A. Metoprolol
- B. Omega fish oil
- C. Tizanidine
- D. Acetaminophen
- E. NSAIDs

Answer 5.5

The correct answer is (C)

Tizanidine's most common side effects include xerostomia (49%), drowsiness (48%), and hypotension (16%–33%). Side effects and overdose are more likely to occur in the setting of liver disease due to extensive hepatic metabolism; therefore, its use is not recommended in patients with hepatic impairment. Furthermore, caution should be taken when prescribing tizanidine to the elderly because clearance decreases by fourfold in this population.

Mechanism of action: Tizanidine is a central α_2 -adrenergic receptor agonist that reduces spasticity by increasing presynaptic inhibition of motor neurons.

Tizanidine is contraindicated when a patient is taking either ciprofloxacin or fluvoxamine (potent CYP1A2 inhibitors) because these prevent the drug from being broken down and can lead to toxicity.

Further Reading

Berry H, Hutchinson DR. A multicentre placebo-controlled study in general practice to evaluate the efficacy and safety of tizanidine in acute low-back pain. *J Int Med Res.* 1988;16(2):75–82. <https://www.ncbi.nlm.nih.gov/pubmed/2967780>

RxList. Zanaflex. <http://www.rxlist.com/zanaflex-drug/clinical-pharmacology.htm>. Published 2017.

Tizanidine. <http://www.uptodate.com/contents/tizanidine-drug-information>. Published 2017.

Question 5.6

Ms. Washington is a 67-year-old female with a history of breast cancer who is currently in remission after multiple rounds of chemotherapy. She was recently seen in your clinic for a shingles outbreak. Today, she complains of increased pain in the area of her prior shingles outbreak. She describes the pain as burning and stabbing in character.

Which drug is US Food and Drug Administration (FDA) approved for postherpetic neuralgia?

- A. Pregabalin
- B. Gabapentin
- C. Baclofen
- D. Tizanidine

Answer 5.6

The correct answer is (A)

Only pregabalin is FDA approved for the management of postherpetic neuralgia. Although pregabalin and gabapentin are both used for the management of neuropathic pain, only pregabalin has FDA approval for postherpetic neuralgia. Pregabalin is FDA approved for diabetic peripheral neuropathy, postherpetic neuralgia, adjunctive therapy with partial-onset seizures, fibromyalgia, and neuropathic pain associated with spinal cord injury. Compared to gabapentin, an advantage of pregabalin is that it requires a much lower dose due to its higher bioavailability, along with its relatively rapid absorption time.

Mechanism of action: Pregabalin binds to the $\alpha_2\delta$ subunit of voltage-gated calcium channels within the central nervous system and modulates calcium influx at the nerve terminals, thereby inhibiting excitatory neurotransmitter release including glutamate, norepinephrine, serotonin, dopamine, substance P, and calcitonin gene-related peptide.

Side effects: The most common side effects include dizziness (12%–28%), drowsiness (19%–21%), and peripheral edema (2%–8%).

Further Reading

Gajraj NM. Pregabalin: Its pharmacology and use in pain management.

Anesth Analg. 2007;105(6):1805–1815.

McAuley DF. How does pregabalin compare to gabapentin in the treatment of neuropathic pain? <http://www.globalrph.com/pregabalin.htm>. Published 2017.

RxList. Lyrica. <http://www.rxlist.com/lyrica-drug/clinical-pharmacology.htm>. Published 2017.

Question 5.7

Mr. Wilcox is a 70-year-old male with a history of liver disease and complicated neuropathic pain for which he takes multiple medications that affect or are impacted by the hepatic cytochrome P450 system.

Which antiepileptic would be most appropriate as an adjunct to the patient's current regimen?

- A. Oxcarbazepine
- B. Carbamazepine
- C. Phenobarbital
- D. Morphine

Answer 5.7

The correct answer is (A)

Oxcarbazepine is a keto-analogue of carbamazepine that is rapidly converted to its active form. This derivative does not pass through the liver cytochrome system, resulting in an improved side effect profile. It has the additional benefit of fewer drug interactions compared to carbamazepine, which is a potent cytochrome P450 inducer. This is especially advantageous in patients who require polypharmacotherapy. Phenobarbital (option C) also affects the cytochrome P450 system, and morphine (option D) is not an anti-epileptic drug.

Mechanism of action: Oxcarbazepine is thought to block voltage-sensitive sodium channels, resulting in stabilization of hyperexcited neural membranes, inhibition of repetitive neuronal firing, and diminution of propagation of spread in the intact brain. Additional effects may include increased potassium conductance and modulation of calcium channels.

Side effects: The most common side effects include dizziness, blurred or double vision, fatigue, headaches, nausea, and vomiting.

Further Reading

Al-Quliti KW. Update on neuropathic pain treatment for trigeminal neuralgia: The pharmacological and surgical options. *Neurosciences (Riyadh)*. 2015;20(2):107–114. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4727618>

Novartis. Trileptal. https://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4254b_07_05_KP%20OxcarbazepineFDAlabel102005.pdf. Published 2006.

RxList. Trileptal. <http://www.rxlist.com/trileptal-side-effects-drug-center.htm>. Published 2017.

6

Cancer-Related Fatigue

SRIRAM YENNURAJALINGAM

Question 6.1

Mrs. Smith is a 75-year-old female retired nurse who was diagnosed with metastatic breast cancer 4 years ago. During the past year, she has had disease progression to the bone and liver. Mrs. Smith was living by herself, but after failure of endocrine therapy, she moved in with her daughter's family due to a history of falls. Mrs. Smith was last treated with weekly paclitaxel regimen, during which she had to delay two cycles due to peripheral neuropathy and low hemoglobin levels; she also experiences ongoing fatigue, especially for a few days after treatment. She is limited in her daily activities and spends more time in bed. Mrs. Smith's daughter reports that her mother has been eating less than two times a day, and the meals are half the regular portion size because Mrs. Smith feels full easily. Mrs. Smith is unwilling to continue treatment because she believes that therapy is starting to affect her quality of life, including fatigue, appetite, functional status, and weight loss.

Contributors to her fatigue syndrome include which of the following?

- A. Depression
- B. Autonomic failure
- C. Anemia
- D. Cachexia
- E. All of the above

Answer 6.1

The correct answer is (E)

Cancer-related fatigue is multifactorial. Various factors contribute to fatigue in patients with advanced cancer, including pain, depression, autonomic failure, anemia, and cachexia. It is therefore essential to screen and treat these factors whenever feasible. For patients who are treated for these factors but the symptoms are still refractory or if the treatment is not feasible, it is important to consider a short trial of methylphenidate or corticosteroid if safe to do so.

Further Reading

- Yennu S, Urbauer DL, Bruera E. Factors associated with the severity and improvement of fatigue in patients with advanced cancer presenting to an outpatient palliative care clinic. *BMC Palliat Care*. 2012;11(1):16.
- Yennurajalingam S, Bruera E. Palliative management of fatigue at the close of life: "It feels like my body is just worn out." *JAMA*. 2007;297(3):295–304.
- Yennurajalingam S, Palmer JL, Zhang T, et al. Association between fatigue and other cancer-related symptoms in patients with advanced cancer. *Supportive Care Cancer*. 2008;16(10):1125–1130.

Question 6.2

Ms. Kim is a 47-year-old Korean woman with refractory ovarian cancer with peritoneal carcinomatosis. She presents to the palliative care clinic with complaints of abdominal distension and shortness of breath. She reports feeling extremely tired and unable to do her daily activities. Laboratory tests are otherwise unremarkable.

All of the following interventions will have symptomatic benefit for alleviating her fatigue *except*:

- A. Vitamin supplementation
- B. Expressive supportive counseling
- C. Short course of corticosteroids
- D. Increased physical activity
- E. Nutritional counseling

Answer 6.2

The correct answer is (A)

Physical activity, psychological interventions, and education have been found to be beneficial in the management of cancer-related fatigue. A short course of corticosteroid has been found to be effective in the management of fatigue. There is no evidence to support the empiric use of vitamin supplementation.

Further Reading

Bennett S, Pigott A, Beller EM, et al. Educational interventions for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev.* 2016;2016(11):CD008144.

Mustian KM, Alfano CM, Heckler C, et al. Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: A meta-analysis. *JAMA Oncol.* 2017;3(7):961–968.

Yennurajalingam S, Frisbee-Hume S, Palmer JL, et al. Reduction of cancer-related fatigue with dexamethasone: A double-blind, randomized, placebo-controlled trial in patients with advanced cancer. *J Clin Oncol.* 2013;31(25):3076–3082.

Question 6.3

Mr. Blum is a 63-year-old male with a history of prostate cancer with bone metastasis. He is currently undergoing chemotherapy. He has low back pain that is well controlled with morphine extended-release 45 mg taken orally every 12 hours. He takes a single dose of morphine immediate-release 15 mg at least once daily for breakthrough pain. He is very comfortable with his pain control; however, he has severe fatigue and daytime drowsiness. He does not have any confusion, myoclonus, or hallucinations.

Which of the following would be recommended to manage his fatigue?

- A. Decrease the dose of long-acting morphine to 30 mg orally every 12 hours
- B. Change the dose of morphine extended-release to 30 mg orally every 8 hours
- C. Add methylphenidate
- D. Add duloxetine

Answer 6.3

The correct answer is (C)

There is inconclusive evidence concerning the efficacy of methylphenidate based on recent trials for the use of psychostimulants for the management of cancer-related fatigue in patients with advance cancer. However, there is level 1 evidence for the use of psychostimulants for the treatment of opioid-related drowsiness. Therefore, a trial of low-dose short-acting methylphenidate at 8 a.m. and 12 noon could be beneficial for the treatment of cancer-related fatigue with drowsiness.

Further Reading

Qu D, Zhang Z, Yu X, et al. Psychotropic drugs for the management of cancer-related fatigue: A systematic review and meta-analysis. *Eur J Cancer Care*. 2016;25(6):970–979.

Yennurajalingam S, Bruera E. Palliative management of fatigue at the close of life: “It feels like my body is just worn out.” *JAMA*. 2007;297(3):295–304.

Question 6.4

Mr. Jones is a 70-year-old Caucasian male with metastatic lung cancer. The patient was diagnosed 14 months ago and is currently on a premetrexed-based regimen. Six weeks ago, the patient was started on dexamethasone 8 mg orally daily for fatigue, appetite, and nausea. He still complains of persistent fatigue and bilateral lower extremity swelling. The family reports that the patient had two episodes of falls during the past few weeks. Laboratory results are unremarkable except for hyperglycemia (fasting blood sugar = 146 mg/dl).

Which of the following is the most likely cause of worsening of Mr. Jones' fatigue and falls?

- A. Steroid-induced myopathy
- B. Steroid-resistant fatigue
- C. Treatment-induced fatigue
- D. Undiagnosed brain metastasis

Answer 6.4

The correct answer is (A)

Patients are at risk of side effects including myopathy, hyperglycemia, candidiasis, and steroid psychosis as a result of chronic exposure to steroids such as dexamethasone. The metabolic abnormalities are usually due to hyperglycemia (as a result of gluconeogenesis), myopathy, and skeletal muscle atrophy (as a result of decreased protein synthesis and increased protein degradation due to activation of the ubiquitin proteasome pathway and inhibition of insulin growth factor-1).

Further Reading

Yennurajalingam S, Bruera E. Role of corticosteroids for fatigue in advanced incurable cancer: Is it a “wonder drug” or “deal with the devil.” *Curr Opin Support Palliat Care*. 2014;8(4):346–351.

Question 6.5

Mr. Price is an 86-year-old African American widower with a history of metastatic prostate cancer. He has been on androgen deprivation therapy and receiving radiation treatments for the past 5 weeks. The patient is currently living with his daughter. He presents to the palliative care clinic with complaints of fatigue, drowsiness, and low back pain. He complains of back pain mainly when walking for more than 5 minutes. The patient denies myoclonus, confusion, anxiety, or sleep disturbances. He is currently on morphine sulfate extended-release 30 mg orally every 8 hours, temazepam 30 mg orally nightly. The patient is also on metoclopramide 10 mg orally every 6 hours for nausea and sennakot 2–4 tablets for constipation.

In addition to a trial of methylphenidate 5 mg orally at 8 a.m. and 12 noon, what is the next step that may be considered for the management of the patient's fatigue?

- A. Increase the dose of morphine sulfate to 60 mg orally twice a day
- B. Conserving energy throughout the day
- C. Good sleep hygiene
- D. Titrate the patient off benzodiazepine

Answer 6.5

The correct answer is (D)

Polypharmacy is a common problem in patients receiving palliative care. The most common medications that contribute to fatigue include chronic use of benzodiazepines, antipsychotics, antihistamines, antihypertensives, and opioids. Because the patient denies complaints of sleep disturbance or anxiety, it is important to consider weaning off medications that may contribute to the fatigue.

Further Reading

Yennurajalingam S, Bruera E. Palliative management of fatigue at the close of life: "It feels like my body is just worn out." *JAMA*. 2007;297(3):295–304.

Question 6.6

Ms. Cruz is a 56-year-old female with advanced metastatic breast cancer who presents to the palliative clinic with severe fatigue and drowsiness. She was diagnosed with breast cancer 15 years ago and subsequently developed metastasis to her spine 4 years ago. She does complain of back pain, but it is fairly controlled with morphine sulfate extended-release 30 mg orally every 12 hours. She denies any history of falls and blood loss, but she has complaints of decreased appetite and constipation lately. Laboratory analysis shows her serum electrolytes to be as follows: Na, 132 mg/l; K, 3.0 mg/l; blood urea nitrogen, 25 mg/dl; Cr, 1.6 mg/dl; Ca, 10.3 mg/dl; and albumin, 3.2 mg/dl. Her hemoglobin is 9.8 g/dl and thyroid-stimulating hormone is 5.8 mIU/l.

For management of the patient's fatigue, all of the following interventions would be beneficial except:

- A. Correction of potassium
- B. Hydration
- C. Correction of hypothyroidism
- D. Correction of hemoglobin

Answer 6.6

The correct answer is (D)

Management of fatigue in advanced cancer should initially focus on treating reversible causes, including correction of electrolytes (e.g., potassium), dehydration, and hypothyroidism. Due to high symptom burden and high frequency of anemia as a result of chronic disease in advanced cancer patients, correction of hemoglobin may not result in improvement of fatigue.

Further Reading

Munch TN, Zhang T, Willey J, et al. The association between anemia and fatigue in patients with advanced cancer receiving palliative care. *J Palliat Med.* 2005;8(6):1144–1149.

Yennurajalingam S, Bruera E. Palliative management of fatigue at the close of life: “It feels like my body is just worn out.” *JAMA.* 2007;297(3):295–304.

Question 6.7

Mrs. Gonzales is an 89-year-old Hispanic female with metastatic lung cancer and severe fatigue. She has been on immunotherapy for the past 3 months. She has been homebound, having difficulty with her energy level. She also has diarrhea as result of the immunotherapy and has low-grade fever. She has no symptoms indicative of depression, and she has a fair appetite. She denies pain and has no history of recent falls.

For the management of the patient's fatigue, which of the following strategies has been found to be beneficial?

- A. Conserving energy throughout the day
- B. Learning about the benefits of exercise
- C. Diet and relaxation
- D. Good sleep hygiene
- E. All of the above

Answer 6.7

The correct answer is (E)

Recent evidence suggests that strategies including education with regard to energy conservation (i.e., to be able to use energy only for the most important activity during a day), physical activity, diet, nutrition, and sleep hygiene have been found to be beneficial in the management of cancer-related fatigue.

Further Reading

Bennett S, Pigott A, Beller EM, et al. Educational interventions for the management of cancer-related fatigue in adults. *Cochrane Database Syst Rev.* 2016;2016(11):CD008144.

7

Anorexia–Cachexia Syndrome and Hydration

EGIDIO G. DEL FABBRO

Question 7.1

A 60-year-old female with newly diagnosed incurable pancreatic cancer is about to start her first cycle of chemotherapy. She reports weight loss of 5 kg from baseline weight of 70 kg. She has used marijuana to increase her appetite but is concerned that the drug is still illegal in her state. She wants to know whether “synthetic” marijuana will improve her appetite and help her gain weight.

Based on the literature regarding cannabinoids in oncology, you suggest which of the following?

- A. Dronabinol increases weight compared to placebo in advanced cancer patients.
- B. Dronabinol increases appetite compared to placebo in advanced cancer patients.
- C. Megestrol combined with dronabinol improves appetite more than either drug alone.
- D. Cannabinoids may be useful for chemotherapy-induced nausea and vomiting (CINV).

Answer 7.1

The correct answer is (D)

Two synthetic cannabinoids, dronabinol and nabilone, are available. Guidelines from professional organizations such as the American Society of Clinical Oncology suggest cannabinoids can be considered for refractory nausea and vomiting and as a rescue antiemetic. Cannabinoids are not first-line treatment, and no randomized controlled trials (RCTs) have compared cannabinoids to the current drugs for CINV, such as 5-HT₃ antagonists or neuroleptics.

Cannabinoids for appetite and weight loss in patients with cancer

Although cannabinoids improved appetite in advanced HIV disease, a three-arm multicenter RCT of 289 patients with advanced cancer showed that dronabinol and cannabis extract had no appetite or weight benefit compared to placebo. An earlier RCT of 469 patients compared megestrol, dronabinol, or the combination of both agents for appetite stimulation. No additional benefit was obtained with the combination.

Further Reading

Jatoi A, Windschitl HE, Loprinzi CL, et al. Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: A North Central Cancer Treatment Group study. *J Clin Oncol*. 2002;20:567–573.

Strasser F, Luftner D, Possinger K, et al. Comparison of orally administered cannabis extract and delta-9-tetrahydrocannabinol in treating patients with cancer-related anorexia–cachexia syndrome: A multicenter, phase III, randomized, double-blind, placebo-controlled clinical trial from the Cannabis-In-Cachexia-Study-Group. *J Clin Oncol*. 2008;24:3394–3400.

Question 7.2

A 65-year-old male with metastatic lung cancer has elected to discontinue chemotherapy and is referred to palliative care for evaluation of 10% weight loss, poor appetite, and depressed mood. He is on mirtazapine and sees a counselor in the clinic at 2-week intervals. After 6 weeks, his depressed mood has improved; however, he continues to experience a poor appetite and requests an appetite stimulant so that he can enjoy meals with his family. You express concern about the potential for side effects, but he is willing to risk side effects if there is a chance of improved appetite.

You suggest megestrol as a possibility but provide informed consent, and you advise the patient which of the following?

- A. Megestrol increases the risk for thromboembolism.
- B. A dose of 800 mg daily is optimal for safety.
- C. Megestrol increases cortisol and decreases testosterone levels.
- D. Megestrol is not associated with an increase in mortality.

Answer 7.2

The correct answer is (A)

Megestrol has a dose-dependent increased risk for thromboembolism and mortality. Patients should be informed of the potentially serious side effects, and therapy should be reserved for those placing a high priority on improved appetite. The optimal dose for weight gain is >400 mg/day, although improvements in appetite have been reported at 160 mg/day. Megestrol also decreases testosterone, and is associated with clinically significant hypoadrenalism requiring stress dose corticosteroids is a potential side effect with prolonged use.

Further Reading

Orme LM, Bond JD, Humphrey MS, et al. Megestrol acetate in pediatric oncology patients may lead to severe, symptomatic adrenal suppression. *Cancer*. 2003;98(2):397–405.

Ruiz Garcia V, Lopez-Briz E, Carbonell Sanchis R, et al. Megestrol acetate for treatment of anorexia–cachexia syndrome. *Cochrane Database Syst Rev*. 2013;2013(3):CD004310.

Question 7.3

A 45-year-old male engineer with metastatic colon cancer is referred for symptom management. The patient reports involuntary weight loss of 20 pounds during the past 3 months from a baseline weight of 240 pounds. His body mass index (BMI) is 31, and his appetite score is 3 (0 being best and 10 worst). He is unable to work because of fatigue and has increasing difficulty performing chores.

The patient has features consistent with the definition of cancer cachexia because of which of the following?

- A. He has weight loss >5% over the past 6 months.
- B. His appetite is poor.
- C. Parenteral nutrition will be required to reverse the weight loss.
- D. He has sarcopenic obesity.

Answer 7.3

The correct answer is (A)

Cancer cachexia is defined as a multifactorial syndrome characterized by ongoing loss of skeletal muscle mass (with or without loss of fat mass) leading to progressive functional impairment, which cannot be fully reversed by conventional nutritional support. Based on this definition, the diagnosis of cachexia centers on a history of involuntary weight loss >5% over 6 months (or 2% when evidence of sarcopenia is present).

Cancer cachexia cannot be reversed by parenteral nutrition. The patient is able to take orally and has mildly impaired appetite, suggesting that decreased caloric intake is not the cause for his profound weight loss. Catabolic processes including proteolysis and lipolysis are likely the major factors in his loss of more than 8% body weight. He may have sarcopenic obesity (requires additional assessment such as dual-energy X-ray absorptiometry (DEXA) or computed tomography (CT) scan for evaluation); however, sarcopenic obesity is not included in the definition for cancer cachexia. Several studies have shown that patients with sarcopenia and a high BMI have a particularly poor prognosis.

Further Reading

Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: An international consensus. *Lancet Oncol.* 2011;12(5):489–495.

Prado CM, Lieffers JR, McCargar LJ, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: A population-based study. *Lancet Oncol.* 2008;9(7):629–635.

Question 7.4

Mrs. P. is a 48 year old female was referred to palliative care 3 months ago with a history of advanced cervical cancer, 15% weight loss, and high symptom burden with Edmonton Symptom Assessment Scale (ESAS) scores including nausea (8/10), depression (7/10), and pain (9/10). She reported constipation and drowsiness on progressively increased doses of morphine for the past 6 months. After an opioid switch, addition of daily laxatives, metoclopramide, and counseling, her symptom scores improved and she was able to gain 5 pounds. However, she has not been able to return to her baseline weight and is still troubled by early satiety and bloating.

The mechanisms of cachexia in this patient may include which of the following?

- A. Increased levels of anti-inflammatory cytokines
- B. Endocrine abnormalities including low serum levels of ghrelin and insulin
- C. Autonomic dysfunction
- D. Myostatin inhibition

Answer 7.4

The correct answer is (C)

Autonomic dysfunction and sympathetic activation are associated with cancer cachexia and cardiac cachexia. Vagus nerve dysfunction is also thought to play a role in gastroparesis and aberrant signaling to the hypothalamus (responsible for appetite control).

Mechanisms of cachexia

Inflammation and the release of pro-inflammatory cytokines are thought to be the dominant mechanism in cancer cachexia, affecting muscle and adipose tissue metabolism and function and modulation of appetite. Cachexia is an insulin- and ghrelin-resistant state, leading to elevated levels of both hormones. Intervention trials using ghrelin and ghrelin mimetics have shown improvement in appetite and lean body mass. Myostatin is a negative regulator of muscle and correlates with cancer-associated cachexia in animal models. Inhibition of myostatin is likely to increase muscle.

Further Reading

Hundsberger T, Omlin A, Haegele-Link S, Vehoff J, Strasser F.

Autonomic dysfunction in cancer cachexia coincides with large fiber polyneuropathy. *J Pain Symptom Manage*. 2014;48(4):611–8.e1.

Onesti JK, Guttridge DC. Inflammation based regulation of cancer cachexia. *Biomed Res Int*. 2014;2014:168407.

Temel JS, Abernethy AP, Currow DC, et al. Anamorelin in patients with non-small-cell lung cancer and cachexia: Results from two randomised, double-blind, phase 3 trials. *Lancet Oncol*. 2016;17(4):519–531.

Question 7.5

A 67-year-old mechanic with head and neck cancer has a weight loss of 5% since diagnosis 3 months ago and is being treated with chemotherapy and radiotherapy. A multidisciplinary approach to managing his symptom burden and weight loss includes nutritional counseling and attention to nutritional impact symptoms such as nausea, depression, and pain.

Which of the following is associated with a better prognosis?

- A. Poor appetite scores
- B. Loss of weight
- C. Low C-reactive protein (CRP)
- D. Multiple nutritional impact symptoms (NIS)

Answer 7.5

The correct answer is (C)

Increased inflammatory markers such as CRP are associated with a poor prognosis. For example, the Glasgow Prognostic Score is a simple systemic inflammation-based approach using assessment of CRP and albumin levels that has prognostic value independent of tumor stage, performance status, and treatment in a variety of advanced common solid tumors.

Patient-reported outcomes and prognosis in cancer cachexia

Health-related quality of life parameters such as appetite loss and pain provide significant prognostic value in addition to sociodemographic (age and sex) and clinical variables (performance status and distant metastases). These parameters increase the predictive accuracy of survival prognoses. In addition, the effects of multiple NIS (e.g., symptoms such as poor appetite, dry mouth, and pain) were evaluated in 635 patients with head and neck cancer prior to chemotherapy or radiotherapy. Those with multiple NIS were more likely to have reduced dietary intake, weight loss, and shortened survival.

Further Reading

- Douglas E, McMillan DC. Towards a simple objective framework for the investigation and treatment of cancer cachexia: The Glasgow Prognostic Score. *Cancer Treat Rev.* 2014;40(6):685–691.
- Farhangfar A, Makarewicz M, Ghosh S, et al. Nutrition impact symptoms in a population cohort of head and neck cancer patients: Multivariate regression analysis of symptoms on oral intake, weight loss and survival. *Oral Oncol.* 2014;50(9):877–883.
- Quinten C, Coens C, Mauer M, et al.; EORTC Clinical Groups. Baseline quality of life as a prognostic indicator of survival: A meta-analysis of individual patient data from EORTC clinical trials. *Lancet Oncol.* 2009;10(9):865–871.

Question 7.6

A 55-year-old female with lymphoma has bulky lymphadenopathy, and her disease has become refractory. She is now being treated at home with hospice care. She complains of early satiety, and the family is concerned about her complaints of dry mouth and is therefore requesting fluids. The patient denies thirst, blood pressure is 140/90, heart rate is 94, and she is on morphine extended-release 60 mg q12 hour PO for pain and transdermal scopolamine for nausea.

You proceed with which of the following?

- A. Start metoclopramide PO for early satiety in addition to scopolamine.
- B. Provide IV fluids to relieve symptoms of dry mouth.
- C. Consider IV fluids because improved outcomes are shown in patients with advanced cancer.
- D. Discuss the possibility of Hypodermoclysis with 1 liter daily if she becomes dehydrated.

Answer 7.6

The correct answer is (D)

Hypodermoclysis is the infusion of fluids in the subcutaneous space for rehydration and opioid analgesics. Approximately 1 liter of fluid administered via a butterfly needle by gravity or infusion pump is sufficient for a 24-hour period.

Hydration and symptom management

Scopolamine should be discontinued because it causes dry mouth in the majority of patients and increases the risk for delirium. Metoclopramide should be given based on a systematic review and consensus recommendations. A blinded RCT in advanced cancer patients enrolled in hospice showed no benefit with 1000 ml of IV normal saline compared to 100 ml daily. Outcomes of delirium, symptom burden, survival, and quality of life were not statistically different. Dry mouth may be related to medications, is associated with poor prognosis, but may not respond to intravenous fluids in patients with advanced cancer.

Further Reading

- Bruera E, Hui D, Dalal S, et al. Parenteral hydration in patients with advanced cancer: A multicenter, double-blind, placebo-controlled randomized trial. *J Clin Oncol*. 2013;31(1):111–118.
- Dalal S, Del Fabbro E, Bruera E. Is there a role for hydration at the end of life? *Curr Opin Support Palliat Care*. 2009;3(1):72–78.
- Walsh D, Davis M, Ripamonti C, et al. 2016 Updated MASCC/ESMO consensus recommendations: Management of nausea and vomiting in advanced cancer. *Support Care Cancer*. 2017;25(1):333–340.

Question 7.7

A 65-year-old male with newly diagnosed gastric cancer has 10% weight loss and complains of decreased energy and poor appetite. He has read about some medications improving cachexia in clinical studies and asks you for more information.

All of the following assessments have been used as outcome measures in cachexia clinical trials *except*:

- A. Lean body mass using CT abdomen scan measuring L4 musculature
- B. Lean body mass using DEXA scan
- C. Magnetic resonance imaging (MRI) of visceral adipose tissue
- D. Quality of life scales focused on appetite and weight loss

Answer 7.7

The correct answer is (C)

MRI may have an important future role in evaluating skeletal muscle quality, particularly with components such as intramyocellular lipid. However, visceral fat measured by MRI has not been used as an outcome in cachexia trials.

Outcome measures in clinical trials

Increasing lean body mass is an important focus of cachexia research. Existing appetite stimulants such as corticosteroids and megestrol produce gains in fat or fluid rather than muscle. DEXA is considered the gold standard for measuring body composition in patients with cachexia. DEXA is relatively inexpensive, accurate, and safe with very low-dose radiation. Unfortunately, DEXA scans may overestimate lean body mass when fluid retention is present. CT scans measuring musculature at L3 have been validated as an outcome measure and used in intervention trials. Although the expense and higher doses of radiation are limiting factors, CT scans may become useful for evaluating cachexia in clinical practice because of their routine use for evaluating tumor response to chemotherapy.

Further Reading

- Prado CM, Heymsfield SB. Lean tissue imaging: A new era for nutritional assessment and intervention. *JPEN J Parenter Enteral Nutr.* 2014;38(8):940–953.
- Salsman JM, Beaumont JL, Wortman K, et al. Brief versions of the FACIT-Fatigue and FAACT subscales for patients with non-small cell lung cancer cachexia. *Support Care Cancer.* 2015;23(5):1355–1364.

Question 7.8

A 65-year-old banker with a history of New York Heart Association functional class IV heart failure reports dyspnea and weight loss of approximately 20 pounds. The weight loss is a change from his premorbid weight and is unrelated to hypervolemia and diuresis.

Which of the following statements regarding cachectic patients with heart failure is true?

- A. Weight loss >8% of premorbid body weight is associated with a poor prognosis in heart failure.
- B. Beta-blockers contribute to weight loss.
- C. Cachectic patients have decreased levels of norepinephrine, cortisol, and tumor necrosis factor- α (TNF- α).
- D. Altered intestinal function does not contribute to weight loss.

Answer 7.8

The correct answer is (A)

Recommendations are that >7.5% weight loss be considered cachectic in cardiac patients. Studies of left ventricular dysfunction showed that weight loss $\geq 6\%$ was associated with poor prognosis. Beta-blockers may help prevent weight loss and have been used in other disease states, such as cancer cachexia, with some preliminary success. Patients with cardiac cachexia have immune-endocrine abnormalities that include increased cytokine levels such as TNF- α and interleukin-6 and endocrine dysfunction with elevated norepinephrine, epinephrine, and insulin and abnormally low insulin-like growth factor-1 levels. Other mechanisms of cachexia include gastrointestinal edema with dysfunctional intestinal barriers, increased permeability, and exposure to endotoxins and chronic inflammation that impairs mucosa function and nutrient uptake and facilitates protein loss.

Further Reading

Anker SD, Coats AJ. Cardiac cachexia: A syndrome with impaired survival and immune and neuroendocrine activation. *Chest*. 1999;115(3):836–847.

Trippel TD, Anker SD, von Haehling S. The role of micronutrients and macronutrients in patients hospitalized for heart failure. *Heart Fail Clin*. 2013;9(3):345–357.

Question 7.9

A 77-year-old male with chronic obstructive pulmonary disease (COPD) has 20% weight loss over the past year and reports increasing weakness. He is being managed by bronchodilators, prednisone, and physical rehabilitation.

Which of the following statements regarding the mechanisms of cachexia in COPD is false?

- A. Ubiquitin proteasome system activity is increased in the muscles of cachectic COPD patients.
- B. A shift of muscle fiber type II to type I occurs in COPD cachexia.
- C. Resting energy expenditure is increased, particularly in patients with emphysema.
- D. Decreased dietary intake and chemosensory abnormalities contribute to weight loss.

Answer 7.9

The correct answer is (B)

A well-known qualitative change in the skeletal muscle of COPD patients is the loss of oxidative capacity, characterized by a muscle fiber type I to type II shift (slow twitch to fast twitch).

Mechanisms of pulmonary cachexia

Muscle wasting in COPD is accompanied by an increase in activation of the ubiquitin proteasome system. This increase in catabolic activity among cachectic COPD patients is site specific, involving limb rather than respiratory muscles. Other protein degradation pathways that may be altered include the autophagy–lysosome pathway. Disturbed energy balance is another mechanism contributing to pulmonary cachexia. Patients with an emphysematous subtype are more likely to be hypercatabolic with increased resting energy expenditure. Finally, compromised dietary intake due to a variety of factors, including nutritional impact symptoms and altered satiety, plays a role.

Further Reading

Miki K, Maekura R, Nagaya N, et al. Ghrelin treatment of cachectic patients with chronic obstructive pulmonary disease: A multicenter, randomized, double-blind, placebo-controlled trial. *PLoS One*. 2012;7(5):e35708.

Sanders KJ, Kneppers AE, van de Boel C, Langen RC, Schols AM. Cachexia in chronic obstructive pulmonary disease: New insights and therapeutic perspective. *J Cachexia Sarcopenia Muscle*. 2016;7(1):5–22.

Question 7.10

A 48-year-old female with metastatic melanoma is referred to your clinic for 10% weight loss and symptoms of poor appetite, early satiety, and constipation.

Your initial assessment of poor appetite, weight loss, and nutritional impact symptoms may include all of the following *except*:

- A. ESAS and BMI
- B. Patient-Generated Subjective Global Assessment (PG-SGA)
- C. Serum ghrelin level
- D. Mid-arm muscle area

Answer 7.10

The correct answer is (C)

Serum ghrelin is not a standard test for the assessment of cachexia in daily practice.

Cachexia assessments for daily clinical practice

The 10-item ESAS is often used in palliative care practice and research. The ESAS evaluates symptom severity, including appetite, on a 0 to 10 scale but does not assess other relevant symptoms, such as constipation, early satiety, or dysgeusia. A more comprehensive evaluation of cachexia requires an additional assessment, such as the PG-SGA. This validated tool endorsed by the American Dietetic Society identifies reversible factors contributing to poor oral intake. A brief (a-PG-SGA) version of the PG-SGA is validated and provides additional diagnostic and prognostic value in evaluating patients with cancer. The a-PG-SGA can be completed in less than 5 minutes and includes information about severity and rate of weight loss, food intake, nutritional symptoms, and function.

Measuring mid-arm muscle area (MAMA) in lean, non-obese patients is reasonably accurate for assessing muscle mass compared with CT. MAMA can be done at bedside with a tape measure and skin calipers measuring triceps skinfold thickness.

Further Reading

Del Fabbro E, Jatoi A, Davis M, et al. Health professionals' attitudes toward the detection and management of cancer-related anorexia–cachexia syndrome, and a proposal for standardized assessment. *J Community Support Oncol.* 2015;13(5):181–187.

Saito R, Ohkawa S, Ichinose S, et al. Validity of mid-arm muscular area measured by anthropometry in nonobese patients with increased muscle atrophy and variation of subcutaneous fat thickness. *Eur J Clin Nutr.* 2010;64(8):899–904.

8

Management of Psychological Symptoms Including Anxiety and Depression

MARVIN OMAR DELGADO GUAY

Question 8.1

A 42-year-old male patient with advanced carcinoma is evaluated in your palliative care clinic. He has been receiving chemotherapy for the past 4 months. He presents to you with a complaint of feeling “bummed out” for the past 2 months. He was recently divorced. He is not working anymore. He is still able to be independent in all his activities of daily living. He has had mild changes in sleep habits. He expresses having some meaning in his life.

Which of the following is the most likely diagnosis?

- A. Adjustment disorder with depressed mood
- B. Schizophrenia
- C. Anxiety disorder
- D. Manic–depressive disorder
- E. Major depressive episode

Answer 8.1

The correct answer is (A)

Adjustment disorder is the most prevalent psychiatric problem associated with life-threatening illness, especially in cancer patients. Its frequency varies from 20% to 30% of all such patients. It can be associated with emotional or behavioral symptoms occurring as a result of a triggering event or stressor. It can present with depressed mood, anxiety, disturbance of conduct, mixed anxiety and depressed mood, and mixed disturbance of emotions and conduct. The onset of adjustment disorder must occur within 3 months of the triggering event. It usually does not last more than 6 months after the termination of the stressor.

Further Reading

Akechi T, Okuyama T, Sugawara Y, et al. Major depression, adjustment disorders, and post-traumatic stress disorder in terminally ill cancer patients: Associated and predictive factors. *J Clin Oncol*. 2004;22:1957.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

Question 8.2

A 58-year-old male presents to your clinic with a diagnosis of advanced carcinoma. His illness continues to progress despite therapy. In talking about the future course of his illness, he begins to cry. His wife is also tearful.

Besides having facial tissues available, which of the following is the next best approach?

- A. Be silent.
- B. Continue with the discussion.
- C. Reassure him.
- D. Tell them to stop crying.

Answer 8.2

The correct answer is (A)

Conversations about sensitive topics can be particularly challenging with patients who have life-threatening illness. One of the foundational skills to provide a patient-centered communication is active listening and allowing for appropriate silence in the conversation. Being silent is an appropriate response in this case to let the patient express his emotions, worries, and fears. Other important elements to provide a patient-centered communication are to propose open-ended and exploratory questions; be able to recognize emotions; and to respond to those emotions with empathy rather than biomedical information, avoiding technical jargon and providing small chunks of information.

Further Reading

- Beckman HB, Frankel RM. Training practitioners to communicate effectively in cancer care: It is the relationship that counts. *Patient Educ Couns*. 2003;50:85–89.
- Delgado-Guay MO, De La Cruz MG, Epner DE. I don't want to burden my family: Handling communication challenges in geriatric oncology. *Ann Oncol*. 2013;24(7):30–35.
- Epstein RM, Street RL Jr. *Patient-Centered Communication in Cancer Care: Promoting Healing and Reducing Suffering*. Bethesda, MD: National Cancer Institute; 2007.

Question 8.3

Your team is evaluating a young patient with advanced AIDS and Kaposi sarcoma. He has been nonadherent with his anti-retroviral therapy. He has lost weight and reports a poor appetite. He sleeps poorly. He also reports a lack of energy and spends most of his time on his couch or in bed. He expresses to the team that he is not interested in anything in his life. He is comfortable talking about the fact that he will die.

A clinical suspicion of major depression is most supported by which of the following?

- A. Changes in appetite and sleep patterns
- B. Lack of energy
- C. Feelings of hopelessness and helplessness
- D. Comfort in talking about the prospect of death

Answer 8.3

The correct answer is (C)

Assessing psychological distress in patients under palliative treatment is complicated due to the simultaneous presence of physical and psychological symptoms. Hopelessness, helplessness, and anhedonia are important symptoms to recognize in patients who are having major depression.

Further Reading

Breitbart W, Rosenfeld BD, Passik SD. Interest in physician-assisted suicide among ambulatory HIV-infected patients. *Am J Psychiatry*. 1996;153(2):238–242.

Grassi L, Indelli M, Marzola M, et al. Depressive symptoms and quality of life in home-care assisted cancer patients. *J Pain Symptom Manage*. 1996;12(5):300–307.

Hotopf M, Chidgey J, Addington-Hall J, Ly KL. Depression in advanced disease: A systematic review Part 1. Prevalence and case finding. *Palliat Med*. 2002;16(2):81–97.

Question 8.4

An elderly male patient with advanced life-threatening illness has had a history of fatigue, insomnia, decreased appetite, and poorly controlled pain. He also reports feelings of sadness and not finding hope in his situation. His wife reports that he often states he feels helpless and no longer enjoys his hobbies or spending time with her or her family. She states he has had these feelings for at least 2 months, and they have been getting progressively worse. His medications include ranitidine, gabapentin, and lorazepam. He uses opiate analgesics as needed for pain. Examination reveals nonspecific neurological abnormalities. His vital signs are normal. There is no evidence of cognitive impairment.

What is the psychological issue this patient is experiencing?

- A. Adjustment disorder
- B. Schizoaffective disorder
- C. Major depression
- D. Expected symptoms related to the advanced illness
- E. None of the above

Answer 8.4

The correct answer is (C)

Depression occurs in as many as 25% of terminally ill patients, depending on the tool used to make the diagnosis. Depression at the end of life affects the dying person as well as the family and caregivers. In the patient, depression reduces quality of life and increases both desire for physician-assisted suicide and risk of suicide. Hopelessness, helplessness, and anhedonia are important symptoms to recognize in patients who are having major depression. It is important to ensure that there is no cognitive impairment contributing to the emotional distress that the patient presents.

Further Reading

- Back AL, Starks H, Hsu C, et al. Clinician–patient interactions about requests for physician-assisted suicide: A patient and family view. *Arch Intern Med.* 2002;162(11):1257–1265.
- Hotopf M, Chidgey J, Addington-Hall J, Ly KL. Depression in advanced disease: A systematic review Part 1. Prevalence and case finding. *Palliat Med.* 2002;16(2):81–97.

Question 8.5

A 60-year-old male patient with advanced life-threatening illness presents to the palliative care clinic accompanied by his wife, who is the main caregiver. He is complaining of a history of having some episodes of feeling down, although he does not feel this way all the time. He expresses worry about his family and what is going to happen to them when he is not there for them. He does not want to cause them more suffering; he sometimes thinks about his death and does not want to be a burden on anyone. He has not thought about ending his life. He has not been able to rest well at night because he cannot stop thinking about the future. He is still able to function at home, and he enjoys when his adult children and his friends visit him. You acknowledge his emotions and worries, and you express empathy to him and his wife.

What would be the most appropriate next step in his care?

- A. Start an antidepressant immediately.
- B. Provide a supportive–expressive therapy. Involve your psychological counselors and continue to monitor closely.
- C. Re-evaluate him in a couple of weeks to find out how he is feeling, and ask his wife to call you if there are any changes in his psychological status.
- D. Give him a benzodiazepine so he can sleep well and rest.
- E. All of the above.

Answer 8.5

The correct answer is (B)

Patients living with life-threatening illness who have adjustment disorder have positive outcomes when they are treated with brief psychotherapy. Early intervention in counseling is very important in the management of these patients. Psychotherapy for adjustment disorder addresses illness-related stressors directly by focusing on immediate problems in living caused by the disease and providing techniques to enhance coping skills.

Further Reading

Akechi T, Okuyama T, Sugawara Y, et al. Major depression, adjustment disorders, and post-traumatic stress disorder in terminally ill cancer patients: Associated and predictive factors. *J Clin Oncol.* 2004;22:1957.

Sifneos, P. Brief dynamic and crisis therapy. In: Kaplan H, Sadock, B, eds. *Comprehensive Textbook of Psychiatry.* 5th ed., vol. 2. Baltimore, MD: Williams & Wilkins; 1989:1562.

Question 8.6

Your team evaluates a patient with advanced and progressive illness despite multiple treatments. After the comprehensive evaluation by your team, the patient asks you to help him commit suicide.

You should respond by saying which of the following?

- A. "Where do you have pain?"
- B. "Tell me more about what you have in mind."
- C. "I would never do that."
- D. "Are you having trouble sleeping?"
- E. "Do you want me to prescribe some antidepressant and a "benzo" so you can rest well?"

Answer 8.6

The correct answer is (B)

For patients, depression reduces quality of life and increases both desire for physician-assisted suicide and risk of suicide.

Patient-centered communication is a key approach to exploring emotional conversations and establishing healing and also trusting relationships. Important skills include eliciting patients' and families' perspectives in an open-ended manner, listening intently, and responding to emotions with empathy. Asking the patient an open-ended question such as "Tell me more about what you have in mind?" will help the clinician explore what is triggering those thoughts and distress related to that request. It is extremely important to involve all the psychological and spiritual members of the team, in addition to consultation with psychiatrist.

Further Reading

- Back AL, Starks H, Hsu C, et al. Clinician–patient interactions about requests for physician-assisted suicide: A patient and family view. *Arch Intern Med*. 2002;162(11):1257–1265.
- Breitbart W, Rosenfeld BD, Passik SD. Interest in physician-assisted suicide among ambulatory HIV-infected patients. *Am J Psychiatry*. 1996;153(2):238–242.

Question 8.7

A 38-year-old female patient with advanced life-threatening illness is being evaluated by you. The patient is single and has been living with her parents for the past few months. She states that she has been losing interest in attending her regular yoga classes, and she has felt less enjoyment in going out with her friends. She prefers to stay home most of the time. She used to enjoy listening to classical music but does not anymore. Her interest in attending church has also decreased. She still has a good relationship with God. She denies any suicidal ideation or plan. In addition to starting counseling with your psychology team and providing chaplain support, based on the clinical findings you decide to start her on an antidepressant.

Which of the following must you consider when starting an antidepressant for a patient with a life-threatening illness?

- A. The selective serotonin reuptake inhibitors (SSRIs) are the first line of treatment in patients with advanced illness, especially when life expectancy is more than 2 or 3 weeks.
- B. The SSRIs have few anticholinergic effects, and they might produce gastrointestinal distress and sexual dysfunction.
- C. Tricyclic antidepressant use is limited due to the development of more anticholinergic side effects (dry mouth and constipation) and cardiac arrhythmias.
- D. Mirtazapine in low doses can improve sleep, appetite, nausea, and anxiety.
- E. The use of methylphenidate needs to be monitored due to cardiac decompensation, especially in elderly patients and patients with a history of heart disease/arrhythmias.
- F. All of the above.

Answer 8.7

The correct answer is (F)

The use of pharmacologic interventions is the mainstay of management for patients with moderate to severe levels of depression. These medications are safe and effective in this setting. Antidepressants might provide better control of the depressive affect, irritability, emotional lability, and social withdrawal. The use of antidepressant treatment can improve depression in terminally ill patients. The American College of Physicians recommends that clinicians should regularly assess and treat depression in patients with serious illness at the end of life.

Further Reading

Walker J, Hansen CH, Martin P, et al. Integrated collaborative care for major depression comorbid with a poor prognosis cancer (SMaRT Oncology-3): A multicentre randomised controlled trial in patients with lung cancer. *Lancet Oncol.* 2014;15:1168.

Williams S, Dale J. The effectiveness of treatment for depression/depressive symptoms in adults with cancer: A systematic review. *Br J Cancer.* 2006;94:372.

Question 8.8

A 29-year-old female with advanced malignancy, currently receiving treatment, presents with an attack of severe shortness of breath, palpitations, shaking, and an intense fear of dying. These attacks are not precipitated by any known factor or event. She denies alcohol or drug use. In addition, she is particularly afraid to leave her house unless someone accompanies her. Her physical examination is completely normal. A whole “battery” of tests, including thyroid functions, electrolytes, electrocardiogram, computed tomography of the chest, and Holter monitoring, has been normal.

In addition to cognitive–behavioral therapy, which of the following is the best initial therapy for this woman?

- A. Diazepam
- B. Sertraline
- C. Lithium
- D. Flurazepam
- E. Nortriptyline

Answer 8.8

The correct answer is (B)

SSRIs are the best initial medical therapy for panic attacks/disorder. In general, trials have shown that SSRIs reduce the frequency of panic attacks, severity of anticipatory anxiety, and degree of phobic avoidance, which are the main components of panic disorder.

Further Reading

Otto MW, Tuby KS, Gould RA, et al. An effect-size analysis of the relative efficacy and tolerability of serotonin selective reuptake inhibitors for panic disorder. *Am J Psychiatry*. 2001;158:1989.

Stein M, Goin M, Pollack M, et al. Practice guideline for the treatment of patients with panic disorder: Second edition. *Am J Psychiatry*. 2009;166(2):1.

Question 8.9

You have been following a 72-year-old male patient with end-stage congestive heart failure, 3 months following a myocardial infarction. He reports that he has been having problems with severe insomnia. He cannot fall asleep easily and wakes up at approximately 4:30 a.m. each morning. He has had increased fatigue since his myocardial infarction. He has been feeling sad, but not with hopelessness or helplessness. He has noticed that he is more forgetful, with increased problems concentrating. Other medical problems include gastroesophageal reflux disease, benign prostatic hyperplasia, and a history of stroke with related seizure disorder.

In addition to sleep hygiene and cognitive-behavioral therapy, which of the following would you recommend?

- A. Mirtazapine
- B. Zolpidem
- C. Amitriptyline
- D. Nortriptyline
- E. Bupropion

Answer 8.9

The correct answer is (A)

Among the options to help the patient with his depressed mood and insomnia, mirtazapine is the most appropriate. Mirtazapine can be classified as a noradrenergic and specific serotonergic antidepressant because it antagonizes presynaptic α_2 -adrenergic receptors and postsynaptic serotonin 5-HT₂ and serotonin 5-HT₃ receptors. Also, it has high affinity for histamine H₁ receptors; this can contribute to the medication's sedative properties. Tricyclic antidepressants block muscarinic M₁, histamine H₁, and α -adrenergic receptors; they produce several side effects, including cardiac effects, anticholinergic effects, antihistaminic effects, decreased seizure threshold, sexual dysfunction, diaphoresis, and tremor.

Bupropion is contraindicated in patients with bulimia nervosa; anorexia nervosa; use of monoamine oxidase inhibitors in the past 2 weeks; seizure disorders; and abrupt withdrawal from alcohol, benzodiazepines, or other sedatives. It is important to note that it must be used with caution in patients receiving other drugs that can decrease the seizure threshold.

Further Reading

- American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2015;63(11):2227–2246.
- Anderson IM, Ferrier IN, Baldwin RC, et al. Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2000 British Association for Psychopharmacology guidelines. *J Psychopharmacol.* 2008;22:343.
- Rush AJ, Trivedi MH, Wisniewski SR, et al. Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. *N Engl J Med.* 2006;354:1231.

Question 8.10

Which of the following factors must be considered when you evaluate patients with life-threatening illness who have persistent depressive symptoms?

- A. Wrong diagnosis (e.g., Does the patient have bipolar disorder?)
- B. Comorbid psychiatric disorders (e.g., dementia and post-traumatic stress disorder)
- C. Untreated or ineffectively treated chronic pain, insomnia, and alcohol or prescription or nonprescription substance misuse
- D. Medical problems or medications that may cause or worsen depression
- E. All of the above

Answer 8.10

The correct answer is (E)

Patients who present with persistent/recurrent depression despite multiple courses of antidepressant medications and psychotherapy should be evaluated for potential contributors to this psychiatric issue. These contributors include the presence of a wrong diagnosis or depression (e.g., Does the patient have bipolar disorder?); the presence of comorbid psychiatric disorders (e.g., dementia and post-traumatic stress disorder); the presence of untreated or ineffectively treated chronic pain, insomnia, or alcohol or prescription or nonprescription substance misuse; the presence of medical problems or medications that may cause or worsen depression; and severe psychological or social stressors or other problems with treatment adherence.

Further Reading

Iosifescu DV, Nierenberg AA, Alpert JE, et al. Comorbid medical illness and relapse of major depressive disorder in the continuation phase of treatment. *Psychosomatics*. 2004;45(5):419–425.

Unutzer J. Older adults with severe, treatment-resistant depression: “I got my mother back.” *JAMA*. 2012;308(9):909–918.

9

Sleep Disturbance in Palliative Care

REBECCA BURKE AND
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Question 9.1

Mr. K has uncontrolled hypertension, morbid obesity, end-stage renal disease, and peripheral neuropathy. He presents to the palliative clinic with insomnia and fatigue. He frequently naps throughout the day and has trouble falling asleep at night. His wife complains about his loud snoring and episodes of confusion during the day. His medications include furosemide, enalapril, metoprolol, and gabapentin.

What would be the most appropriate next step in management of this patient's insomnia?

- A. Trazodone at night
- B. Basic metabolic panel, complete blood count, and thyroid-stimulating hormone
- C. Polysomnography
- D. Increase night-time gabapentin dose

Answer 9.1

The correct answer is (C)

Sleep apnea is a commonly overlooked etiology for insomnia. Standardized screening of all palliative care patients may detect this underdiagnosed condition more frequently. In one study in advanced cancer patients who screened positive for sleep disorder (Edmonton Symptom Assessment Scale score >4), the frequency of obstructive sleep apnea was 61%. Any patient presenting with some of the cardinal symptoms of sleep apnea, such as loud snoring, nocturnal gasping or choking, frequent daytime naps, fatigue, and poor concentration, should undergo further testing.

Once a patient is confirmed to have sleep apnea, treatment options include weight loss, continuous positive airway pressure (CPAP), alcohol avoidance, and oral appliances. For patients with persistent daytime sleepiness, stimulants have been shown to improve symptoms. Underlying medical conditions such as hypothyroidism or acromegaly should be treated as appropriate. If the underlying cause is anatomical, such as a tumor compressing the airway, the anti-inflammatory component of steroids can prove beneficial.

Further Reading

Schwartz JR, Khan A, McCall WV, Weintraub J, Tiller J. Tolerability and efficacy of armodafinil in naive patients with excessive sleepiness associated with obstructive sleep apnea, shift work disorder, or narcolepsy: A 12-month, open-label, flexible-dose study with an extension period. *J Clin Sleep Med.* 2010;6(5):450–457.

Yennurajalingam S, Balachandran D, Pedraza Cardozzo SL, et al. Patient-reported sleep disturbance in advanced cancer: Frequency, predictors and screening performance of the Edmonton Symptom Assessment System sleep item. *BMJ Support Palliat Care.* 2017;7(3):274–280.

Question 9.2

Mrs. S is a 67-year-old female with metastatic endometrial cancer. She has been taking melatonin at night for insomnia but still has trouble falling asleep and staying asleep. She is taking morphine for abdominal pain. Her previous doctor prescribed her alprazolam as needed for sleep, and she requests a refill.

What information should you provide her with before you proceed?

- A. Tolerance can occur rapidly with this medication.
- B. Respiratory depression is an uncommon side effect.
- C. Alprazolam will not help her fall asleep but will help her stay asleep.
- D. Alprazolam will help her fall asleep but not stay asleep.

Answer 9.2

The correct answer is (A)

Benzodiazepines promote sleep by binding to γ -aminobutyric acid receptors. They reduce sleep latency, prolong stage 2 sleep, and increase sleep duration. Respiratory depression is a common side effect, and caution should be used in patients concurrently using opioids. Another limitation to the use of benzodiazepines long term is that tolerance is a well-documented phenomenon.

Behavioral interventions are the most cost-effective treatment for insomnia and may include education on sleep hygiene, stimulus control, relaxation, sleep restriction therapy, cognitive therapy, and cognitive-behavioral therapy (CBT). CBT for insomnia has been proven to improve sleep outcomes, and it should be the first line of treatment prior to consideration of pharmacologic options. In fact, the addition of medication to CBT does not improve symptoms relative to treatment with CBT alone.

Further Reading

- Buscemi N, Vandermeer B, Friessen C, et al. The efficacy and safety of drug treatments for chronic insomnia in adults: A meta-analysis of RCTs. *J Gen Intern Med*. 2007;22(9):1335–1350.
- Morin CM, Beaulieu-Bonneau S, Bélanger L, et al. Cognitive-behavior therapy singly and combined with medication for persistent insomnia: Impact on psychological and daytime functioning. *Behav Res Ther*. 2016;87:109–116.
- Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, Part I: Sleep and psychological effects. *J Clin Oncol*. 2005;23(25):6083–6096.

Question 9.3

Mr. L has prostate cancer and was recently found to have spinal metastasis after complaining of lower back pain. He admits that this new finding has been a source of distress to him. He was started on dexamethasone and hydromorphone to alleviate his pain. He says his back pain is better controlled, but now he is having trouble sleeping at night. He asks for something to help.

What do you recommend?

- A. Zolpidem at night
- B. Increase hydromorphone at night
- C. Positron emission tomography scan to check for disease progression
- D. Olanzapine at night

Answer 9.3

The correct answer is (D)

After secondary causes of insomnia have been treated, such as optimization of pain control, pharmacologic treatment should be considered in the palliative care setting. Careful review of patients' medications is an important initial step. Glucocorticoid-induced sleep disturbances have been reported, especially with split doses that may interfere with the normal pattern of diurnal cortisol production. Earlier daytime dosing or single dosing of glucocorticoid may alleviate this concern.

Patients being treated with opioids are at an increased risk of respiratory depression, especially when therapy is combined with benzodiazepines or sedative-hypnotics. For patients in the palliative care setting who benefit from treatment with opioids but suffer from insomnia and/or mood disorders, atypical antipsychotics should be considered. All second-generation antipsychotics are histaminic (H_1) antagonists and therefore have the potential to cause drowsiness. Olanzapine specifically also blocks serotonin ($5-HT_2$) receptors, targeting both insomnia and anxiety.

Further Reading

Felton M, Weinbert R, Pruskowski J, et al. Olanzapine for nausea, delirium, anxiety, insomnia, and cachexia. *J Palliat Med.* 2016;19(11):1224–1225.

Opioid Pain or Cough Medicines Combined with Benzodiazepines: Drug Safety Communication—FDA Requiring Boxed Warning About Serious Risks and Death. N.p., n.d. Web. 19 Oct. 2016.

Question 9.4

Mr. D has amyotrophic lateral sclerosis and lives with his son. His wife was his primary caretaker until she died from breast cancer 1 year ago. Since then, Mr. D has become increasingly despondent, preferring to be left alone in his room for most of the day. He no longer enjoys playing golf with his friends. His appetite has decreased, and he stays awake for most of the night. His son is concerned about his lack of sleep at night.

Which class of medication would be the best option for this patient?

- A. Antihistamine
- B. Benzodiazepine
- C. Selective serotonin reuptake inhibitor
- D. Gabapentin

Answer 9.4

The correct answer is (C)

Although emotional distress is normal in patients suffering from a terminal illness, differentiating between a normal adjustment reaction and an underlying psychological disorder can be challenging. Identifying depression in patients is essential to providing appropriate treatment options. According to the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*, in order to diagnose major depressive disorder, five (or more) specified depressive symptoms have to be present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms has to be depressed mood or loss of interest or pleasure. As always, treatment of the underlying medical disorder will be the most efficacious treatment for patients presenting with sleep disorders. Antidepressants have been proven to be efficacious for the treatment of depression in palliative care.

Individuals suffering from grief may commonly present with a complaint of insomnia. In these patients, often grief counseling and support from family, friends, or clergy may be sufficient. The World Health Organization has made strong recommendations against the use of benzodiazepines as treatment for patients without a mental disorder experiencing bereavement.

Further Reading

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

Rayner L, Price A, Evans A, et al. Antidepressants for the treatment of depression in palliative care: Systematic review and meta-analysis. *Palliat Med*. 2011;25(1):36–51. doi:10.1177/0269216310380764

Tol WA, Barbui C, van Ommeren M. Management of acute stress, PTSD, and bereavement: WHO recommendations. *JAMA*. 2013;310(5):477–478.

Question 9.5

Mr. P is an 85-year-old nursing home resident on hospice care for metastatic prostate cancer. Throughout the day, he has become increasingly agitated. By evening, he begins hitting the nurses and yelling obscenities. His medications include a daily multivitamin, metoprolol, acetaminophen, and diphenhydramine. The nurse calls you asking for recommendations.

What should be the next step in management for his behavior?

- A. Computed tomography scan of the head
- B. Ativan as needed
- C. Physical restraints
- D. Bladder scan

Answer 9.5

The correct answer is (D)

Sleep disorders in elderly patients particularly require a more in-depth search for an underlying cause. This patient is most likely sun downing, a symptom indicative of delirium. Without finding the underlying cause of delirium, treatment with additional medications could worsen the delirium. Sun downing can easily be confused for insomnia, even more so in hypoactive delirium. Careful review of medications is a fundamental initial step to determine the underlying cause. Caution is advised when using any anticholinergic in older patients. Although diphenhydramine is a first-generation antihistamine used for allergic symptoms, it possesses anticholinergic properties as well. Anticholinergic drugs can cause acute urinary retention, confusion, hallucinations, blurred vision, dry mouth, and constipation, all of which can lead to delirium in an elderly patient. Steroids are another class of medications known to induce delirium. A bladder scan would be the diagnostic test of choice to rule out urinary retention. Hypoxemia, dehydration, uncontrolled pain, and/or any source of infection are other risk factors for acute delirium and may simply present with agitation in an elderly patient. These conditions should be treated accordingly and the delirium state may resolve, although not always in patients nearing the end of life. Terminal delirium will not resolve with correction of underlying abnormalities.

According to the American Geriatrics Society Beers criteria, all types of benzodiazepines should be avoided when treating insomnia, agitation, or delirium in the geriatric population. However, in patients at risk of seizure (brain metastasis, epilepsy, and recent stroke) and terminal delirium, risk versus benefit should be weighed when using benzodiazepines. Physical restraints generally are not recommended.

Further Reading

American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2012;60(4):616–631.

10

Nausea and Vomiting

SHALINI DALAL

Question 10.1

Ms. L is a patient with colon cancer who has known metastasis to the liver. She has been reporting nausea and decreased oral intake for approximately 2 weeks, and she presented to the emergency center where she was found to have liver and renal dysfunction. She has not had significant pain concerns and has not been on opioids.

The patient's nausea symptoms are most likely due to the activation of which of the following?

- A. Chemoreceptor trigger zone (CTZ)
- B. Gastrointestinal (GI) tract
- C. Higher brain cortical areas
- D. Vestibular apparatus

Answer 10.1

The correct answer is (A)

Pathophysiology of nausea and vomiting

Two distinct sites in the brainstem (medulla) are critical for the control of emesis: the vomiting center (VC) and the CTZ. The VC is the site where four major afferent neuronal pathways from various sources converge: (a) higher cortical centers in response to sensory and psychogenic stimuli, (b) vestibular apparatus in response to vertigo and visuospatial disorientation, (c) CTZ, and (d) peripheral pathways (via the vagus and splanchnic nerves) from the GI tract in response to contraction or distension of gut.

The CTZ is located in the area postrema of the medulla, and unlike the VC, it is functionally located outside the blood–brain barrier and is therefore able to sample emetogenic toxins, metabolic abnormalities such as uremia or hypercalcemia, or drugs in the blood and spinal fluid. The GI tract activates the VC directly, as well as indirectly via the CTZ.

Further Reading

Dalal S, Del Fabbro E, Bruera E. Symptom control in palliative care—Part I: Oncology as a paradigmatic example. *J Palliat Med.* 2006;9(2):391–408.

Hornby PJ. Central neurocircuitry associated with emesis. *Am J Med.* 2001;111(Suppl. 8A):106S.

Question 10.2

Which of the following groups of antiemetics share the same mechanism of action?

- A. Metoclopramide, haloperidol, ondansetron, and chlorpromazine
- B. Dronabinol, promethazine, dexamethasone, and lorazepam
- C. Chlorpromazine, haloperidol, metoclopramide, and prochlorperazine
- D. Scopolamine, promethazine, hyoscyamine, and glycopyrrolate

Answer 10.2

The correct answer is (C)

Generally, vomiting occurs when an area of the brain in the medulla (the VC) is activated by neuronal impulses from the CTZ, the GI tract, higher cortical areas, and the vestibular apparatus. Recognized major nausea receptors associated with nausea and vomiting in the brain include dopamine (D)-2 (CTZ: chlorpromazine, haloperidol, metoclopramide, and prochlorperazine); histamine (H)-1 (vestibular: promethazine, diphenhydramine, meclizine, and hydroxazine); acetylcholine (Ach) (vestibular: scopolamine (transdermal), hyoscyamine, and glycopyrrolate); serotonin (5-HT)-3 (GI and CTZ: ondansetron, granisetron, and dolasetron); neurokinin (NK)-1; higher cortical areas (dexamethasone and lorazepam); and cannabinoid (CB)-1 receptors (dranabinol).

Further Reading

- Dalal S, Del Fabbro E, Bruera E. Symptom control in palliative care—Part I: Oncology as a paradigmatic example. *J Palliat Med.* 2006;9(2):391–408.
- Glare P, Miller J, Nikolova T, Tickoo R. Treating nausea and vomiting in palliative care: A review. *Clin Interv Aging.* 2011;6:243–259.

Question 10.3

The mechanism of action of antiemetics such as metoclopramide, prochlorperazine, chlorpromazine, and haloperidol is which of the following?

- A. 5-HT₃ receptor antagonism, in the GI tract and the CTZ
- B. D₂ receptor antagonism, in the CTZ
- C. H₁ receptor antagonism, in the vestibular apparatus
- D. All of the above

Answer 10.3

The correct answer is (B)

Phenothiazines and other antipsychotic agents, such as haloperidol and olanzapine, block D_2 receptors found in the CTZ. All but haloperidol have a broad spectrum of activity, also blocking histaminic, anticholinergic, serotonergic, and/or α -adrenergic receptors that contribute to their individual side effects. Among these, metoclopramide is unique in that it also produces vagal blockade in the GI tract, contributing to its prokinetic activity.

Further Reading

- Dalal S, Del Fabbro E, Bruera E. Symptom control in palliative care—Part I: Oncology as a paradigmatic example. *J Palliat Med.* 2006;9(2):391–408.
- Glare P, Miller J, Nikolova T, Tickoo R. Treating nausea and vomiting in palliative care: A review. *Clin Interv Aging.* 2011;6:243–259.

Question 10.4

GH is a 58-year-old female with stage IV ovarian cancer with liver metastasis and peritoneal carcinomatosis who presents to the emergency center with progressive symptoms of nausea, vomiting, abdominal pain, and constipation. A month prior, she stopped chemotherapy because of progression, partial small bowel obstruction, and poor performance status. Scans now reveal a complete malignant small bowel obstruction with further progression in liver and peritoneum. The patient is started on parenteral hydration, and a nasogastric tube (NGT) is placed. After 24 hours in the medical ward, she is transferred to the palliative care unit. On arrival, the patient is noted to have ongoing abdominal pain, NGT output over 1.5 liters, and nausea.

Which of the following are options to consider next for symptomatic management?

- A. Haloperidol IV/SC, octreotide SC, metoclopramide IV/SC, hyoscine butylbromide IV/SC, and morphine IV/SC
- B. Haloperidol IV/SC, metoclopramide IV/SC, ondansetron IV, hyoscine butylbromide IV/SC, and consultation for venting gastrostomy
- C. Morphine IV/SC, octreotide SC, metoclopramide IV/SC, haloperidol IV/SC, and dexamethasone IV/SC
- D. Dexamethasone IV/SC, morphine IV/SC, haloperidol IV/SC, octreotide SC, and consultation for venting gastrostomy

Answer 10.4

The correct answer is (D)

Most advanced GI cancers causing malignant bowel obstruction (MBO) are inoperable, and medical treatment remains the major modality for relieving symptoms in MBO. Antiemetic agents that do not affect bowel motility (e.g., haloperidol) or those that inhibit bowel motility (antispasmodic effect) and decrease GI secretions (e.g., hyoscine butylbromide) are useful in MBO management. Corticosteroids such as dexamethasone may be used to decrease inflammatory edema and decrease water and salt secretion in bowel. Somatostatin analogs such as octreotide are increasingly being used to control symptoms in inoperable MBO when vomiting is intractable or there is high output from NGTs. They reduce gastric and intestinal secretion and bile flow. Venting gastrostomy is an option for patients with intractable vomiting despite medical management, especially when there is high intestinal obstruction. Venting gastrostomy can be considered as a long-term alternative to an NGT provided it is feasible and agreeable to the patient. Metoclopramide is an antiemetic (D_2 antagonistic), but because of its prokinetic effects in the stomach and possibly duodenum, it is not useful in the setting of complete bowel obstruction.

Further Reading

Laval G, Marcelin-Benazech B, Guirimand F, et al. Recommendations for bowel obstruction with peritoneal carcinomatosis. *J Pain Symptom Manage.* 2014;48(1):75–91.

Question 10.5

Which of the following statements about cannabinoids such as dronabinol is false?

- A. They are associated with weight gain in advanced cancer patients with cachexia.
- B. They improve nausea and vomiting symptoms from chemotherapy in cancer patients.
- C. They improve appetite, nausea, and mood in AIDS patients.
- D. Side effects include somnolence, dizziness, and perceptual disturbances.

Answer 10.5

The correct answer is (A)

A recent systematic review of cannabinoids for patients experiencing refractory nausea/vomiting from chemotherapy (23 trials; years 1974–1991) found cannabinoids to be superior to placebo and with similar efficacy as prochlorperazine. None of these trials compared cannabinoids to 5-HT₃ receptor antagonists. In a large three-arm randomized trial conducted in advanced cancer patients, comparison was made between oral megestrol acetate 800 mg/day, dronabinol 2.5 mg twice daily, and the combination of both megestrol and dronabinol. This study found the megestrol alone arm to be superior to dronabinol alone (75% vs. 49%, respectively) for improving appetite, and the addition of dronabinol did not improve megestrol responses. Another three-arm trial of cannabis alone, cannabis plus cannabidiol, and placebo in advanced cancer patients demonstrated no differences in appetite, nausea, weight, or quality of life and was terminated early because of futility. In contrast to cancer anorexia, cannabinoids have been shown to be useful in improving appetite in AIDS/HIV patient. Side effects are dose-dependent central nervous system effects and include sedation, abnormal thinking, paranoia, and dizziness.

Further Reading

- Beal JE, Olson R, Laubenstein L, et al. Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *J Pain Symptom Manage*. 1995;10(2):89–97.
- Davis MP. Cannabinoids for symptom management and cancer therapy: The evidence. *J Natl Compr Canc Netw*. 2016;14(7):915–922.
- Jatoi A, Windschitl HE, Loprinzi CL, et al. Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: A North Central Cancer Treatment Group study. *J Clin Oncol*. 2002;20:567–573.
- Smith LA, Azariah F, Lavender VT, et al. Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy. *Cochrane Database Syst Rev*. 2015;2015(11):CD009464.

11

Delirium

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Question 11.1

A 76-year-old male is admitted to the palliative care unit for pain management related to his prostate cancer with bone metastases. On your afternoon rounds, you note that he is unusually withdrawn and slightly somnolent. On further exam, he is disoriented to time and place, also a change from his baseline. He denies the presence of pain or other symptoms.

Which of the following is the most likely diagnosis?

- A. Hypoactive delirium
- B. New-onset dementia
- C. Major depressive episode
- D. Terminal phase of his illness

Answer 11.1

The correct answer is (A)

Delirium is frequently missed or misdiagnosed by the health care team. This may relate to symptom fluctuation and transient lucidity, in addition to overlapping clinical features with dementia and depression, and compounded by a lack of or inadequate delirium screening. Notably, hypoactive delirium, a common subtype in palliative care inpatients, is often overlooked. Patients with hypoactive delirium have impaired cognition but become somnolent and withdrawn, with no visible agitation, and may be misdiagnosed as having depression or fatigue or as being in the terminal phase. Delirium superimposed on dementia also presents challenges in recognition because signs of delirium may be mistaken for psychological symptoms of dementia, and deficits in attention may occur in severe dementia.

Delirium screening

Although delirium is a clinical diagnosis, its detection may be improved by the routine use of nursing observational and cognitive screening tools or brief tests of attention (e.g., naming the months of the year in reverse order). A collateral history from a caregiver of an acute change in mental status from baseline should prompt further assessment for delirium.

Further Reading

Lawlor PG, Bush SH. Delirium in patients with cancer: Assessment, impact, mechanisms and management. *Nat Rev Clin Oncol*. 2015;12:77–92.

Question 11.2

You are consulted to assist the treating team in determining the goals of care for an 87-year-old female admitted to the hospital with end-stage heart failure. During your initial assessment, the patient has clear difficulty concentrating on your discussion and answering your questions appropriately, does not seem concerned by her surroundings or her illness, and admits to the occasional visual hallucination. You worry that she may be in a delirium and question her capacity to fully participate in a goals of care discussion. The team argues that she is completely oriented and calm and therefore not delirious.

What would be your best next step?

- A. Agree that it is unlikely she is in a delirium because she is oriented to person, place, and time and continue with determining goals of care with the patient.
- B. Educate the team that although oriented, she presents many features of delirium and this should be further assessed.
- C. Conclude that this is most likely an undiagnosed dementia, but obtain collateral information to confirm your diagnosis.
- D. Question if she is suffering from a depressive episode, and obtain a psychiatry consult prior to proceeding.

Answer 11.2

The correct answer is (B)

Delirium is diagnosed clinically, with the psychiatric interview as the standard diagnostic reference. Patients may remain oriented despite having full syndromal delirium. Subsyndromal delirium, with the presence of some delirium features but not meeting full diagnostic criteria, may also occur.

Delirium diagnosis

The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* provides itemized diagnostic criteria for delirium, with the essential feature of a disturbance of attention and awareness. In addition, delirium develops over a short period of time (usually hours to days) with a fluctuating level of severity over the course of a day. Delirium prodromal features may occur and include anxiety, restlessness, irritability, disorientation, as well as sleep disturbances.

Further Reading

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

Question 11.3

A 67-year-old female with known metastatic colon cancer is admitted to the hospital with urosepsis and delirium. Her medical history is significant for a severe anxiety disorder and coronary artery disease. She is somnolent, and therefore all her home medications, which include metoprolol, lorazepam, and aspirin, are held. She is treated with IV antibiotics, fluids, and haloperidol as needed. On day 1 of admission, you note an improvement in her awareness and cognition. However, on day 2, she is very agitated.

Which of the following is the most likely explanation for her worsening delirium?

- A. This is an expected fluctuation in her delirium symptoms.
- B. Electrolyte imbalance.
- C. Antibiotic resistance.
- D. Drug withdrawal.

Answer 11.3

The correct answer is (D)

Although benzodiazepines are potentially deliriogenic medications, the sudden withdrawal of long-standing benzodiazepines (lorazepam in this case) can precipitate delirium.

Causes of delirium

The development of delirium signifies underlying pathology and is usually associated with multifactorial etiology. Delirium arises from the complex interaction between predisposing (baseline) and acute precipitating factors. Common predisposing risk factors for delirium include increasing age ≥ 65 years and preexisting cognitive impairment, including dementia. Thus, frail and elderly people with preexisting cognitive impairment may develop delirium with a relatively minor precipitant, whereas younger people with no predisposing risk factors are much less likely to develop delirium with minor precipitants as compared with more noxious precipitants. A previous delirium episode is also a risk factor for the development of a further delirium. Other risk factors include pre-existing visual and hearing impairment and polypharmacy.

Note that there is frequently more than a single cause for a patient's delirium episode. In advanced cancer patients, there is a median of three (range, one to six) precipitants per delirium episode.

Further Reading

Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet* 2014;383:911–922.

Lawlor PG, Bush SH. Delirium in patients with cancer: Assessment, impact, mechanisms and management. *Nat Rev Clin Oncol*. 2015;12:77–92.

Question 11.4

A 67-year-old female with metastatic pancreatic cancer is at home for end-of-life care. She is on morphine 10 mg subcutaneous regularly every 4 hours to control her severe abdominal pain. In the past 24 hours, you note that she has required eight breakthrough doses, whereas she had previously only required the occasional one or two doses. The family tells you these have been given as she has been grimacing and moaning. On exam, the patient is somnolent but confused and unable to answer your questions. She is afebrile, lungs are clear, and abdomen is soft. You note myoclonus but no focal neurological abnormalities.

Which of the following is a likely predominant cause for her delirium?

- A. Infection
- B. Hyperglycemia
- C. Hypercalcemia
- D. Opioid neurotoxicity

Answer 11.4

The correct answer is (D)

Patients with delirium at the end of life often have an increased expression of pain due to disinhibition. If a patient's delirium is unrecognized, his or her moaning and grimacing may be misinterpreted as pain. This can lead to the administration of extra unnecessary doses of opioids, potentially increasing the delirium severity.

Opioid-induced neurotoxicity

Opioid-induced neurotoxicity (OIN) is a syndrome of neuropsychiatric side effects seen with opioid therapy. The components of OIN are severe sedation, hallucinations, cognitive impairment or delirium, myoclonus and seizures, allodynia, and hyperalgesia. These symptoms may occur as a single feature or in varying combinations. OIN may be managed by opioid dose reduction if pain is controlled. Another strategy is opioid rotation or switching. Depending on the goals of care, there may be a role for hydration.

Assessment of agitated patient

It is important to rule out other treatable causes of increased patient agitation, such as urinary retention. Performing a bladder scan is simple, with urinary catheterization providing instantaneous symptom relief. Other potential causes for increased patient agitation include fecal impaction; uncontrolled pain; medication-induced akathisia; and drug, alcohol, or nicotine withdrawal.

Further Reading

Lawlor PG, Bush SH. Delirium in patients with cancer: Assessment, impact, mechanisms and management. *Nat Rev Clin Oncol*. 2015;12:77–92.

Question 11.5

An 86-year-old male with end-stage kidney disease is at home for end-of-life care. During your first visit, family members explain that he has been getting increasingly confused and agitated. In response to this, they have minimized all distractions and interactions with the patient, assuring that he can rest peacefully in his bedroom, with the curtains closed at all times. They also discourage him from getting up to a chair or ambulating, stating he needs to rest.

What would be the next best step in counseling this family?

- A. Normalize delirium at the end of life and reassure they are doing everything right.
- B. Insist that the patient walk to the bathroom to maintain his strength as long as possible.
- C. Educate about the benefits of optimizing sleep–wake pattern and encouraging mobility on delirium.
- D. Recommend an admission to hospital to investigate possible causes for his delirium.

Answer 11.5

The correct answer is (C)

Environmental and other nonpharmacological strategies are used for both prevention and treatment of delirium. In addition to patient orientation, use of communication aids (eye glasses, hearing aids, and dentures), and encouraging mobility, a normal sleep–wake pattern should be facilitated with exposure to daylight during the daytime and reduced lighting and noise at night.

Nonpharmacological approaches

It is estimated that approximately one-third of delirium episodes can be prevented using multicomponent nonpharmacological strategies. The original Hospital Elder Life Program (HELP; <http://www.hospitalelderlifeprogram.org>), led by volunteers and family, targets the following risk factors in older patients: cognitive impairment, sleep deprivation, immobility, visual and hearing impairment, and dehydration. However, the efficacy and applicability of these approaches for terminally ill patients are not clear.

Further Reading

Hshieh TT, Yue J, Oh E, et al. Effectiveness of multicomponent nonpharmacological delirium interventions: A meta-analysis. *JAMA Intern Med.* 2015;175:512–520.

Question 11.6

A 72-year-old female with metastatic colon cancer presents to the emergency room with a few days' history of increasing confusion, agitation, and weakness. Prior to this, she was cognitively intact, able to ambulate short distances, but required help for bathing. She is unable to answer your questions reliably and appears to be hallucinating and very frightened. Her children wish to investigate and treat potentially reversible causes to her delirium. Meanwhile, you would like to ensure symptoms are well managed.

What would be your best next step?

- A. Haloperidol 1 mg subcutaneously q6 hours regular and q2 hours PRN
- B. Lorazepam 1 mg sublingual TID and q4 hours PRN
- C. Haloperidol 0.5 mg subcutaneously q4 hours PRN
- D. Chlorpromazine 12.5 mg subcutaneously q4 hours regular and q4 hours PRN

Answer 11.6

The correct answer is (C)

Low-dose antipsychotics may be used in the management of delirium if there are distressing perceptual disturbances or safety concerns. Benzodiazepines should not be used first-line as single agents because they are deliriogenic.

Pharmacological management of delirium symptoms

The 2012 Cochrane Review by Candy et al. concluded that there was insufficient evidence on the role of drug therapy in the treatment of delirium in terminally ill patients. The National Institute for Health and Care Excellence (NICE) Clinical Guideline 103 for adults with delirium, which excludes “people receiving end-of-life care,” recommends that the short-term use of antipsychotics such as haloperidol and olanzapine may be employed in the management of distressing perceptual disturbances (e.g., hallucinations and illusions) or severe agitation where the delirious patient is considered a risk to him- or herself or others.

Because benzodiazepines can exacerbate delirium, they should be avoided as first-line agents in the pharmacological management of delirium. Use of benzodiazepines as first-line agents is limited to the management of alcohol or sedative-hypnotic withdrawal.

Further Reading

Candy B, Jackson KC, Jones L, et al. Drug therapy for delirium in terminally ill adult patients. *Cochrane Database Syst Rev.* 2012;2012(11):CD004770.

Young J, Murthy L, Westby M, Akunne A, O'Mahony R. Diagnosis, prevention, and management of delirium: summary of NICE guidance. *BMJ.* 2010;341:c3704.

Question 11.7

A 44-year-old male with metastatic testicular cancer is admitted to the palliative care unit with delirium. Haloperidol 1 mg PO q8 hours is prescribed as he presents with frightening visual hallucinations. A few days into his admission, you note that he is becoming increasingly restless. He describes feeling anxious and a sensation of “needing to move all the time.”

What would be your next best step?

- A. Increase the dose of his haloperidol because his delirium seems to be worsening.
- B. Start a dopamine receptor agonist, such as pramipexole or rotigotine.
- C. Start a midazolam infusion in order to control his restlessness and anxiety.
- D. Minimize the use of antipsychotics because you question if this is a possible adverse effect.

Answer 11.7

The correct answer is (D)

This patient has developed acute akathisia secondary to haloperidol. It is important to recognize increasing agitation in a delirious patient that is due to adverse effects of antipsychotic treatment, as opposed to delirium symptomatology.

Acute extrapyramidal side effects of antipsychotics

It is thought that blocked dopamine D_2 receptors in the nigrostriatal pathways lead to medication-induced extrapyramidal side effects (EPSEs). Although EPSEs are less likely with atypical antipsychotics, they can occur at higher doses of these medications.

Clinical risk factors for developing EPSEs include antipsychotic potency, rapidly increasing antipsychotic dose (especially in the first days of treatment), increasing age and age <30 years, and dementia. Parenteral administration of haloperidol causes less EPSEs compared with the oral route.

Acute EPSEs (dystonia, akathisia, and antipsychotic-induced parkinsonism) are often missed or misdiagnosed, potentially leading to further treatment with more antipsychotic. For acute akathisia and dystonia, the causative medication should be reduced or stopped whenever possible. Prescription of an oral anticholinergic drug (e.g., benztropine) or an antihistaminic antimuscarinic drug (e.g., diphenhydramine) may reduce extrapyramidal symptoms. If ongoing antipsychotic therapy is warranted, consider switching to an atypical antipsychotic.

Further Reading

Forcen FE, Matsoukas K, Alici Y. Antipsychotic-induced akathisia in delirium: A systematic review. *Palliat Support Care*. 2016;14:77–84.

Question 11.8

A 57-year-old male with non-small cell lung cancer with metastases to brain, liver, and bone is at home for end-of-life care. Despite increasing doses of haloperidol to manage his delirium, he remains very agitated. This is extremely distressing to the family and also the staff who have been attending to his care. A decision was made a few weeks ago that he did not wish to return to the hospital for investigations and did not wish any further treatment to prolong his life. The patient has now not had any oral intake for 2 days. After a discussion with his family, it is decided that palliative sedation is indicated.

With regard to the pharmacological management, what would be the best choice?

- A. Start a midazolam subcutaneous infusion at 5 mg/hr and gradually titrate down to the lowest effective dose.
- B. Start a midazolam infusion at 1 mg/hr and gradually titrate up if needed to control the refractory agitation.
- C. Continue with the current dose of haloperidol but add midazolam subcutaneously q30 minutes as needed for agitation.
- D. Discontinue the haloperidol and start midazolam subcutaneously q30 minutes as needed for agitation.

Answer 11.8

The correct answer is (B)

Midazolam is the drug of first choice for palliative sedation due to its rapid onset of action and short half-life, as well as dose-dependent sedative effect. Midazolam is given as a continuous subcutaneous or intravenous infusion in initial rates of 0.5–1 mg/hr. Midazolam doses titrated up to 6 mg/hr have been reported.

Refractory agitated delirium at the end of life

The pharmacological management for palliative sedation is derived from case series and expert opinion, and currently there is insufficient high-level evidence regarding its efficacy for symptom control.

In addition to midazolam, other medications that have also been used for palliative sedation include lorazepam, levomepromazine (also known as methotrimeprazine—not available in the United States), chlorpromazine, phenobarbital (phenobarbitone), propofol, and dexmedetomidine.

Further Reading

Cherny NI, Radbruch L. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med.* 2009;23:581–593.

Question 11.9

You are on call for the palliative care unit and get paged late evening about an inpatient. He is a 54-year-old male with metastatic cancer admitted earlier that day with new delirium. While pending the results of workup for underlying causes, he was given a dose of haloperidol for distressing visual hallucinations. The nurse now calls because he has become progressively more agitated and just pulled out his IV. She is concerned he will harm himself.

Which of the following would be the best initial medical management?

- A. Haloperidol 1 mg PO stat and q4 hours PRN
- B. Quetiapine 25 mg PO q8 hours regularly and reassess in a few days
- C. Lorazepam 1 mg sublingual stat and q4 hours PRN
- D. Haloperidol 1 mg subQ and lorazepam 0.5 mg subQ stat, then both q4 hours PRN

Answer 11.9

The correct answer is (D)

Although the nonpharmacological management of delirium is a key component of care, delirious patients who are very distressed or a potential risk to themselves or others may require pharmacological management for their symptoms, including “rescue” doses of midazolam or lorazepam if not responding to antipsychotics. Lower doses of benzodiazepines should be used in very elderly or frail patients or if co-administered with an antipsychotic.

Alcohol or benzodiazepine withdrawal requires the first-line use of a benzodiazepine as a single agent.

Role of benzodiazepines in delirium

Benzodiazepine administration may be associated with an increased risk of delirium, particularly in higher doses. In Breitbart’s randomized trial in AIDS patients, all six patients receiving lorazepam developed side effects or refused to continue taking it. However, recent studies have reported the efficacy of combined haloperidol and midazolam for the management of agitated palliative care patients over haloperidol alone. (Lorazepam 1 mg is equivalent to midazolam 2 mg.)

Further Reading

Breitbart W, Marotta R, Platt M, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. *Am J Psychiatry*. 1996;153(2):231–237.

Ferraz Gonçalves J, Almeida A, Costa I, Silva P, Carneiro R. Comparison of haloperidol alone and in combination with midazolam for the treatment of acute agitation in an inpatient palliative care service. *J Pain Palliat Care Pharmacother*. 2016;30(4):284–288.

Question 11.10

A 73-year-old female with known dementia with Lewy bodies (DLB) is admitted to the hospital with end-stage renal disease. She is noted to be hypervigilant, with increased psychomotor activity. Although she is known for visual hallucinations at baseline, these have worsened considerably since admission, are frightening, and cause significant agitation. Goals of care are palliative, and you would like to address these distressing delirium symptoms.

Which of the following is the best next step?

- A. Prescribe haloperidol 0.25–0.5 mg PO q4 hours PRN for agitation
- B. Prescribe lorazepam 0.5–1 mg PO q4 hours for agitation
- C. Prescribe low-dose quetiapine to be given q4 hours PRN for agitation
- D. Avoid any antipsychotic or benzodiazepine so as to not worsen her DLB

Answer 11.10

The correct answer is (C)

In general for delirium management, the regular use of antipsychotics should be avoided, and PRN doses should be used. If a first-generation antipsychotic such as haloperidol is used in a delirious patient with preexisting DLB or Parkinson's disease, there is a risk of extrapyramidal side effects, as well as an increased risk of disease exacerbation. Quetiapine, a second-generation antipsychotic, is preferred if therapy with an antipsychotic is required. Moreover, particularly for these patient groups, a PRN benzodiazepine may be an alternative pharmacotherapeutic strategy for the management of agitation. (Lorazepam 1 mg is equivalent to midazolam 2 mg.)

Clinical features of Dementia with Lewy bodies

Dementia with Lewy bodies can be confused with delirium. The core clinical features of DLB are fluctuating cognition with pronounced variations in attention and alertness, recurrent complex visual hallucinations that are typically well formed and detailed, and spontaneous features of parkinsonism. Delusions may also be present.

Further Reading

Hogan DB, Fiest KM, Roberts JJ, et al. The prevalence and incidence of dementia with Lewy bodies: A systematic review. *Can J Neurol Sci.* 2016;43(Suppl. 1):S83–S95.

McKeith I, Fairbairn A, Perry R, Thompson P, Perry E. Neuroleptic sensitivity in patients with senile dementia of Lewy body type. *BMJ.* 1992;305:673–678.

Peeling L, Illiffe S. A woman with forgetfulness and falls. *BMJ.* 2011;343:d7412.

12

Dyspnea

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Question 12.1

A 58-year-old male with stage III adenocarcinoma of the lung (diagnosed 1 year ago) currently on maintenance therapy with pembrolizumab presented to the emergency center with complaints of gradually worsening shortness of breath and nonproductive cough over the past 3 weeks. He denied fever, chills, chest pain, hemoptysis, palpitations, pedal edema, or orthopnea. On examination, he was afebrile and in mild respiratory distress. No jugular venous distention was noted. His chest examination showed a focal wheeze over the right middle lobe. Oxygen saturation at rest was 94%, decreasing to 88% with ambulation. Laboratory assessment included a normal total leukocyte, platelet count, and hemoglobin. A complete metabolic panel was normal. Two blood cultures were negative. Chest radiograph showed new right middle lobe infiltrates. Contrast-enhanced chest computed tomography (CT) revealed new focal airspace opacities in the right middle lobe, with no evidence of acute pulmonary embolism, and residual spiculated tumor noted in the right upper lobe.

What is the immediate next step in the management of the patient?

- A. Stop pembrolizumab and start the patient on prednisone with taper
- B. Continue with pembrolizumab and start the course of antibiotics
- C. Intensify the regimen due to the possibility of lymphangitic spread
- D. Perform bronchoscopy with bronchoalveolar lavage
- E. Perform echocardiogram to evaluate for pericardial effusion

Answer 12.1

The correct answer is (D)

Lung cancer is the leading cause of cancer-related mortality in the United States. There have been significant advancements in the treatment of molecularly defined non-small cell lung cancer (NSCLC), but the prognosis has only modestly improved. A plateau has been reached with traditional chemotherapy and angiogenesis inhibitors. Immunotherapy is a new modality, different from chemotherapy and targeted therapy. Immunotherapy works by stimulating immune response against foreign tumor cells and relieving inhibition of the immune system that allows tumor growth. Pembrolizumab is an example of an antineoplastic agent that works as an anti-PD1 monoclonal antibody. Toxicities of immunotherapy include, but are not limited to, immune suppression, pneumonitis, nephritis, colitis, and hyperthyroidism. The differential diagnosis of pulmonary infiltrates in the immunocompromised patient includes both infectious and non-infectious etiologies. The radiological presentation of drug-induced pneumonitis is similar to pneumonia, and a high index of clinical suspicion is necessary for identification. It is advisable to obtain a bronchoscopy with bronchoalveolar lavage to rule out infection before starting steroids for the management of drug toxicity.

Further Reading

- Champiat S, Lambotte O, Barreau E, et al. Management of immune checkpoint blockade dysimmune toxicities: A collaborative position paper. *Ann Oncol*. 2016;27:559.
- Naidoo J, Page DB, Li BT, et al. Toxicities of the anti-PD-1 and anti-PD-L1 immune checkpoint antibodies. *Ann Oncol*. 2015;26:2375.

Question 12.2

A 53-year-old female with locally advanced (IIIa) adenocarcinoma of the lung was admitted to the oncology floor with complaints of progressively worsening facial swelling over the past 8 days. Family members also reported that she complained of a throbbing headache and increasing somnolence. She had completed six cycles of taxane and platinum-based chemotherapy with radiotherapy. Her physical examination revealed facial edema, swelling in her neck and upper extremities, and prominent venous collaterals on her chest wall. A chest radiograph showed no progression of the disease in either hemi thorax at the time of symptom presentation. Laboratory data were as follows: white blood cell count 5000/mm³, hemoglobin 9.4 g/dl, and platelets 300. Contrast-enhanced chest CT demonstrated a thrombus inside her superior vena cava. Magnetic resonance imaging (MRI) of the head showed new cerebral edema.

What is the next appropriate step in the management of the patient?

- A. Start the patient on diuresis and repeat MRI brain in 2 weeks
- B. Start the patient on steroids and repeat the MRI brain in 1 week
- C. Start the patient on therapeutic enoxaparin and repeat chest CT in 1 week
- D. Consult radiation–oncology and interventional radiology immediately
- E. Immediately start antineoplastic therapy

Answer 12.2

The correct answer is (D)

Superior vena cava (SVC) syndrome is caused by the obstruction of blood flow through the SVC due to an extrinsic compression or intrinsic thrombus formation. An intrathoracic malignancy is responsible for 60%–80% of the total number of cases. Altered mental status due to cerebral edema and stridor due to either central airway obstruction or laryngeal edema constitute emergent situations in which immediate treatment with radiation therapy or stent placement is warranted.

Further Reading

Fagedet D, Thony F, Timsit JF, et al. Endovascular treatment of malignant superior vena cava syndrome: Results and predictive factors of clinical efficacy. *Cardiovasc Intervent Radiol*. 2013;36:140.

Rowell NP, Gleeson FV. Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus: A systematic review. *Clin Oncol (R Coll Radiol)*. 2002;14:338.

Question 12.3

An 87-year-old male with a past medical history of recently diagnosed stage IV lung cancer presented to the emergency department with a 2-day history of acutely worsening dyspnea with exertion. The patient also had a history of diabetes and renal insufficiency. In the emergency center, his vitals were as follows: blood pressure 120/80 mm Hg, heart rate 120 beats per minute, respiratory rate 25 breath/minute, SpO₂ 92% on 3 liters of oxygen/minute via nasal cannula, temperature 37.3°C. Physical examination revealed decreased breath sounds in the right posterior mid to lower hemothorax, no wheezing, no jugular venous distention, no S3 or S4, and no lower extremity edema. Chest radiograph showed complete opacification of the right hemothorax, with contralateral shifting of the trachea. CT chest pulmonary embolism protocol was negative. Cardiac enzymes and echocardiogram were unremarkable. Laboratory data revealed no leukocytosis, and coagulation parameters were normal. Bedside thoracentesis was performed and revealed an exudative pleural effusion with the presence of malignant cells. The patient declined treatment for his cancer. The patient was discharged from the emergency center with an outpatient appointment to see a pulmonologist in 2 weeks.

What would be the next step in the management of this patient if he returns to the emergency room within 1 week with similar symptoms?

- A. Repeat the therapeutic thoracentesis again and discharge the patient
- B. Consult palliative medicine
- C. Start workup for depression and dementia, and challenge the patient's ability to make decisions by the court
- D. Discuss the benefits of placing a tunneled indwelling pleural catheter before performing therapeutic thoracentesis
- E. Consult CT surgery for decortication

Answer 12.3

The correct answer is (D)

Malignant pleural effusion is commonly associated with advanced malignancy, most commonly lung, breast, and ovarian carcinomas, or lymphoma. Management options for malignant pleural effusion have traditionally included therapeutic thoracentesis, chemical pleurodesis, and tunneled indwelling pleural catheters. Tunneled indwelling pleural catheters have emerged as first-line therapy for palliation and symptom relief for recurrent malignant pleural effusion.

Multiple studies have compared chemical pleurodesis and tunneled indwelling pleural catheters in terms of efficacy and complications, and pleural catheters have been shown to decrease pleural effusion, improve symptoms, and even induce spontaneous pleurodesis. Tunneled indwelling pleural catheters may be performed at the bedside regardless of performance status. They are associated with minimal side effects, improved quality of life, as well as decreased length of hospital stay because they can be performed in an outpatient setting.

Two general guidelines can be used in selecting patients for the appropriate pleural intervention. First, if the fluid accumulates slowly (>1 month) or the patient has a short expected survival rate (<3 months) or has poor performance status, then pleural effusion is managed with repeated therapeutic thoracentesis. Second, if pleural fluid accumulates rapidly, then aggressive interventions are employed: tunneled indwelling pleural catheter placement or chemical pleurodesis.

Placement of an indwelling pleural catheter with intermittent drainage by the patient, family, or medical personnel has the additional advantage of relieving dyspnea at home or hospice without the need for repeated invasive interventions.

Further Reading

Davies HE, Mishra EK, Kahan BC, et al. Effect of an indwelling pleural catheter vs. chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: The TIME2 randomized controlled trial. *JAMA*. 2012;307:2383.

Sabur NF, Chee A, Stather DR, et al. The impact of tunneled pleural catheters on the quality of life of patients with malignant pleural effusions. *Respiration*. 2013;85:36.

Question 12.4

A 75-year-old male presents with dyspnea with minimal exertions. He also reports chest pain on his right side worse with inspiration, as well as a constant cough with occasional hemoptysis. Imaging confirms multiple large pulmonary masses with evidence of lymphangitic spread and a large right-sided pleural effusion. He was diagnosed with NSCLC. After consultation with an oncologist, it is determined that he is not a candidate for chemotherapy. He was started on palliative radiation therapy for bony metastasis. Despite escalating doses of short-acting narcotic medication, he continues to have severe dyspnea.

At this point, what would be the best plan to help alleviate his pain?

- A. Increase the dose of short-acting narcotic to the maximum dose
- B. Discontinue short-acting narcotic and instead administer a long-acting narcotic
- C. Administer a long-acting narcotic around the clock with a short narcotic for breakthrough pain
- D. Order additional radiation therapy to the leg
- E. Add an antidepressant medication to the short-acting narcotic medication

Answer 12.4

The correct answer is (C)

Guidelines for management of dyspnea from the American College of Chest Physicians, the American College of Physicians, the American Thoracic Society, the Canadian Thoracic Society, and the National Comprehensive Cancer Network all recommend the use of systemic opioids for relief of dyspnea in patients with advanced terminal disease with appropriate caution regarding the risk of respiratory depression. A systematic review of the evidence from approximately the past 15 years showed the potential benefit of the strong opioid in the modest alleviation of dyspnea in cancer.

In this particular case, we are dealing with metastatic lung cancer to both the lung parenchyma and the pleural cavity. The main focus should be on the palliation of dyspnea. An optimal treatment includes the use of long-acting narcotics. Any breakthrough is controlled with short-acting narcotics. If the breakthrough episodes are frequent, then the dosages of long-acting medications should be increased.

Further Reading

- Johnson MJ, Hui D, Currow DC. Opioids, exertion and dyspnea: A review of the evidence. *Am J Hosp Palliat Care*. 2016;33(2):194–200.
- Vargas-Bermudez A, Cardenal F, Porta-Sales J. Opioids for the management of dyspnea in cancer patients: Evidence of the last 15 years—A systematic review. *J Pain Palliat Care Pharmacother*. 2015;29(4):341–352.

Question 12.5

A 53-year-old female with stage IV breast cancer (ER-positive, PR-positive, HER2-negative) that has spread to thoracic vertebrae, liver, and brain underwent whole brain radiation therapy 4 months ago. Currently, she is on both hormonal therapy and chemotherapy. She currently weighs 160 kg, having lost 10 kg in the past 3 months. She was referred to palliative medicine 6 months ago for back pain and was started on long-acting morphine with short-acting morphine for breakthrough pain. Currently, her pain is not well controlled, so her oncologist increased her long-acting morphine doses and set up a palliative care appointment for the upcoming week. Overnight, she was found to be unresponsive by her family members, and she was rushed to the hospital. In the emergency room, she had a respiratory rate of 12 breaths/minute, blood pressure of 84/40 mm Hg, pinpoint pupils, and pulse oximetry showing oxygen saturation at approximately 82%. She was intubated and transferred to the intensive care unit. Naloxone 0.4 mg was administered intravenously, but her mental state has not improved.

What is the most likely diagnosis of her clinical presentation?

- A. Cerebral edema due to tumor
- B. Acute liver failure due to metastasis
- C. Aspiration pneumonia
- D. New brain metastatic lesions

Answer 12.5

The correct answer is (C)

Aspiration pneumonia usually requires either compromise of the defenses that protect the lower airways or an inoculum deleterious to lower airways. A number of clinical signs and symptoms, such as choking, coughing during and after meals, or dysphagia, should alert the clinician that a potential swallowing disorder could be causing aspiration. Excessive sedation due to opioids or sedative–hypnotic medication or metabolic encephalopathy may potentiate these effects.

Video fluoroscopic swallowing study or fiber-optic examination of oropharyngeal swallowing are non-invasive tests that examine the oral, pharyngeal, and cervical esophageal stages of swallowing. Efficient and safe swallowing are important criteria for continued oral nutrition. Antibiotic treatment is given in case of an aspiration event. If swallow evaluation fails, then feeding gastrostomy or jejunostomy tubes can be placed endoscopically.

In this case, the patient's sedative dosages were increased, and she was at increased risk for obstructive sleep apnea given her weight and oral airway. That likely compromised the defenses such as glottis closures and cough reflexes during her sleep, resulting in an aspiration event.

Further Reading

Ashford JR, Skelley M. Oral care and the elderly. *Perspect Swallowing Swallowing Disorders (Dysphagia)*. 2008;17:19.

Karagiannis M, Karagiannis TC. Oropharyngeal dysphagia, free water protocol and quality of life: An update from a prospective clinical trial. *Hell J Nucl Med*. 2014;17(Suppl. 1):26.

Question 12.6

A 42-year-old male with stage IV non-Hodgkin's lymphoma presented with a 2-month history of hoarseness and stridor, which had become more severe over the previous 2 days. Direct laryngoscopy showed submucosal fullness of the entire supra glottis and minimal vocal cord abduction. CT of the neck showed above findings with normal caliber of the distal trachea. He has widespread lymphoma resistant to prior chemotherapy. He requested that all attempts should be made to avoid surgical intervention. He was admitted to the intensive care unit with the plan for radiation therapy and a trial of new chemotherapeutic regimen.

In addition to the radiation and chemotherapy regimen, what other intervention should be added to his treatment plan to relieve work of breathing aside from tracheostomy?

- A. Add long-acting opioids around the clock
- B. Push IV morphine PRN to relieve dyspnea
- C. Add benzodiazepines to the treatment
- D. Add inhaled heliox to the treatment
- E. Add inhaled nitric oxide to the treatment

Answer 12.6

The correct answer is (D)

Heliox is a mixture of helium and oxygen. Helium is an inert gas. Heliox has a low density and has the potential to decrease the proportion of turbulent airflow relative to laminar flow. Decreasing turbulent flow due to airway stenosis decreases airway resistance and helps reduce the work of breathing. Heliox acts as a temporizing therapy and may provide a bridge to definitive treatment that includes palliative chemotherapy, radiation therapy, or stent placement.

Further Reading

Milner QJ, Abdy S, Allen JG. Management of severe tracheal obstruction with helium/oxygen and a laryngeal mask airway. *Anesthesia*. 1997;52:1087.

Smith SW, Biros M. Relief of imminent respiratory failure from upper airway obstruction by use of helium–oxygen: A case series and brief review. *Acad Emerg Med*. 1999;6:953.

Question 12.7

A 49-year-old male with recently diagnosed squamous cell lung cancer was admitted with complaints of dysphagia. CT chest showed that this mass was in the left hilar area with obstruction of the left mainstem bronchus and proximal portions of the left upper and lower lobe bronchi, as well as invasion of the carina, adjacent esophagus, and left main pulmonary artery surrounding the descending thoracic aorta. A 12-cm covered esophageal stent was inserted to relieve dysphagia, and chemotherapy was started. Approximately 1 month later, the patient revisited the emergency department with increased dyspnea and coughing. The patient was tachypneic with a respiration rate of 34 breaths/minute, along with accessory muscle use, so intubation was performed. In the intensive care unit, increased bloody secretions were noted from the endotracheal tube. Labs showed an acute drop in hemoglobin and no evidence of coagulopathy. Chest radiography showed that the left lung had totally collapsed. A bronchoscopic examination demonstrated the presence of an endoluminal protruding mass with complete compression of the left main bronchus. There was diffuse bleeding from the mucosal surface of the mass without a localized focus. Epinephrine was sprayed on the area to control the bleeding. However, this was only temporarily effective, and the bleeding continued intermittently. Surgical resection also could not be considered because of the advanced stage of the cancer.

What is the next step in the management of the bleeding?

- A. Start the patient on anti-fibrinolytic therapy
- B. Infuse 2 units of fresh frozen plasma and 2 units of platelets
- C. Proceed with bronchial stent placement
- D. Repeat CT angiography in 2 days

Answer 12.7

The correct answer is (C)

The initial step in the management of hemoptysis includes determining the site of bleeding. All coagulopathy should be reversed. A bronchoscopy should be performed, whenever possible, to assess and attempt to control the bleeding (iced saline, balloon tamponade, and topical vasoconstrictor or electrocautery). If the bronchoscopic intervention fails, then the next step is an interventional radiology-guided angiographic embolization or surgery.

Further Reading

Hsiao EI, Kirsch CM, Kagawa FT, et al. Utility of fiberoptic bronchoscopy before bronchial artery embolization for massive hemoptysis. *AJR Am J Roentgenol.* 2001;177:861.

Pereira J, Phan T. Management of bleeding in patients with advanced cancer. *Oncologist.* 2004;9:561.

Sakr L, Dutau H. Massive hemoptysis: An update on the role of bronchoscopy in diagnosis and management. *Respiration.* 2010;80:38.

Question 12.8

A 43-year-old female patient diagnosed with stage IIIB NSCLC with bilateral rib metastases presented to the emergency room with complaints of shortness of breath. Her past medical history was significant for osteoarthritis, depression, and anxiety. Her medication includes extended-release hydromorphone 32 mg orally daily and immediate-release hydromorphone 4 mg every 4 hours for pain control. On examination, she was hemodynamically stable and was saturating 86% on room air. Chest auscultation revealed decreased breath sounds in bilateral lung fields. Her respiratory rate was 8 breaths per minute. She was sleepy but arousable with normal-sized pupils. Chest radiograph showed low lung volumes with no focal consolidation. Laboratory data were normal, but arterial blood gas revealed the following: pH 7.26, $p\text{CO}_2$ 88 mm Hg, and $p\text{O}_2$ 50 mm Hg. Code status was discussed with the patient, and she stated her wishes to be DNR.

What is the next plan in the management?

- A. Intubate the patient and start mechanical ventilation
- B. Start the patient on non-invasive positive pressure ventilation and administer naloxone
- C. Only administer naloxone
- D. Start the patient on nasal cannula with oxygen delivered at 10 l/min

Answer 12.8

The correct answer is (B)

Non-invasive positive pressure ventilation (NPPV) refers to positive pressure ventilation that is delivered through a non-invasive interface such as a nasal mask, face mask, or nasal prongs rather than a more invasive measure such as an endotracheal tube or tracheostomy. The clinical benefit of NPPV has been shown in acute respiratory acidosis, exacerbations of chronic obstructive pulmonary disease, hypoxemic respiratory failure due to cardiogenic pulmonary edema, and in patients with advanced neuromuscular disorders such as amyotrophic lateral sclerosis. NPPV may be used to manage an episode of acute reversible respiratory failure in a patient who has an advanced serious and/or life-threatening illness and wishes to avoid invasive mechanical ventilation. In this particular clinical scenario, the patient is hypercapnic and hypoxemic likely due to hypoventilation secondary to opioids. In this case, the patient's DNR/DNI status suggests that NPPV should be used to provide ventilation. NIPPV is contraindicated in confused or obtunded patient.

Further Reading

Freichels TA. Palliative ventilatory support: Use of noninvasive positive pressure ventilation in terminal respiratory insufficiency. *Am J Crit Care.* 1994;3:6.

Gifford AH. Noninvasive ventilation as a palliative measure. *Curr Opin Support Palliat Care.* 2014;8:218.

Yeow ME, Mehta RS, White DB, Szmulowicz E. Using noninvasive ventilation at the end of life #230. *J Palliat Med.* 2010;13:1149.

Question 12.9

A 75-year-old male with metastatic small cell lung cancer to the liver and spine on palliative radiation is transitioning to end-of-life care. He was admitted to the hospital for a 1-day history of shortness of breath and sharp chest pain worsened by respiration. On physical examination, he had blood pressure 112/70 mm Hg, pulse of 99 beats per minute, temperature 99.5°F, and oxygen saturation 88% on room air. He was in mild respiratory distress, and lung auscultation was clear. Home medications include extended-release oxycodone, morphine as needed, and senna. Laboratory tests were within normal limits except for mild anemia (hemoglobin 10.3). Electrocardiogram showed sinus tachycardia. On chest radiograph, there was decrease lung markings on the right upper lobe but no infiltrate seen.

CT angiogram of the chest was performed, and the patient was found to have embolism of the ascending branch of the right pulmonary artery. No right ventricular strain was seen on echocardiogram.

What is the next best step in the management?

- A. Emergent catheter-directed thrombolysis
- B. Start heparin drip and transition to warfarin
- C. Discuss the patient's preference on starting low-molecular-weight heparin (LMWH) after counseling him on the benefits and potential bleeding risk associated with anticoagulation
- D. Stop all medications and transfer to hospice facility

Answer 12.9

The correct answer is (C)

Thromboembolic diseases are common in cancer patients due to the hypercoagulable state induced by different host- and tumor-related factors. Current guidelines advocate life-long anticoagulation for patients with active cancer and a history of thromboembolism, preferably with LMWH rather than warfarin.

This patient is hemodynamically stable and does not have right heart strain, so catheter-directed thrombolysis is not indicated.

The question of whether to anticoagulate patients with terminal illness and venous thromboembolic disease in hospice is still controversial, and the risk:benefit ratio is not well studied. One reason to continue anticoagulation at the end of life is the possibility that discontinuing it in patients with thromboembolism may hasten death. The annual thromboembolic recurrence rate after discontinuing warfarin after at least 3 months of therapy is between 3.2% and 10.9%. On the other hand, anticoagulation at the end of life increases the risk of bleeding, especially in patients with renal insufficiency, low body weight, and malnutrition. The largest study on anticoagulation use in hospice populations reviewed patients with lung cancer and venous thromboembolism and/or atrial fibrillation retrospectively and found that the strongest predictor of anticoagulant choice was geographic region: Hospices in the Northeast were associated with significantly higher rates of LMWH prescription compared to those in other regions.

Further Reading

Holmes H, Bain KT, Zalpour A, et al. Predictors of anticoagulation in hospice patients with lung cancer. *Cancer*. 2010;116(20):4817–4824.

Question 12.10

A 70-year-old male with locally advanced pancreatic cancer undergoing chemotherapy with gemcitabine is referred to a pulmonologist for management of severe chronic obstructive pulmonary disease (COPD). The patient was a 90 pack year smoker, but he stopped smoking 2 years ago. He complains of worsening shortness of breath and inability to perform any of his daily activity for the past 3 weeks. He is on maximum medical treatment (chronic oral steroids, budesonide–formoterol twice a day, tiotropium inhaler daily, and albuterol inhaler as needed) and 4 l/min of supplemental oxygen via nasal cannula. The patient has had three hospitalization within the past year for COPD exacerbations followed by pulmonary rehabilitation after each one. On physical examination, vital signs are stable, oxygen saturation is 94% on 4 liters nasal cannula, and body mass index (BMI) is 17. He looks fatigued. Chest radiograph shows flattening of the diaphragm and distension of the lung field.

What is the next best step in the management?

- A. Refer to pulmonary rehabilitation
- B. Prednisone and antibiotics for 5 days
- C. Assess for depressive symptoms and begin low-dose opioid medications
- D. Refer for lung reduction surgery

Answer 12.10

The correct answer is (C)

Shortness of breath is a very distressing symptom and should be appropriately addressed to help provide psychological relief. The patient has very severe COPD on maximal medical therapy and oxygen. Worsening dyspnea is likely a progression of his COPD rather than another exacerbation. He is fully dependent on others for his daily activities and has very low BMI, both of which are suggestive of end-stage COPD. Given his very poor prognosis, he should be considered for end-of-life care.

Dyspnea is an almost universal symptom in advanced COPD, and it is one of the most significant contributors to the poor quality of life experienced by these patients. Exacerbations of COPD present with increased cough, sputum production, and worsened dyspnea. A majority of patients with COPD experience considerable problems arising out of breathlessness, leading to immobility, dependency on others, and social isolation. It can be easily speculated that such patients have their preferences, desires, and demands to lead a better quality of life.

Even prior to the terminal phase, COPD is strongly associated with anxiety and depression, particularly in those who are hypoxic or severely dyspneic. Patients will benefit from starting an antidepressant.

The only drugs with a proven effect on dyspnea are opioids. The mechanism of action of morphine is not well understood, but it is thought to decrease the respiratory drive and air hunger. Moreover, opioids have anxiolytic properties further diminishing dyspnea.

Further Reading

- Claudine P. Morphine-induced relief of dyspnea: What are the mechanisms? *Am J Respir Crit Care Med.* 2011;184(8):867–869.
- Seamark D, Seamark C, Halpin D. Palliative care in chronic obstructive disease: A review for clinicians. *J R Soc Med.* 2007;100 (5):225–233.
- Spathis A, Booth S. End of life care in chronic obstructive pulmonary disease: In search of a good death. *Int J Chron Obstruct Pulmon Dis.* 2008;3(1):11–29.

13

**Constipation and
Bowel Obstruction**

MARIEBERTA VIDAL

Question 13.1

Mr. Jones is a 68-year-old male with a history of bony pain due to a history of metastatic prostate cancer. The patient takes morphine extended-release 60 mg every 8 hours for pain. During the past week, his pain has been worse, requiring six breakthrough doses of morphine immediate-release 15 mg. Today, he presents with confusion and pain, and his last bowel movement was 5 days ago despite senna bid.

What is the next best step?

- A. Treatment with administration of enema
- B. Treat with lactulose
- C. Treat with naltrexone
- D. Opioid rotation
- E. Check calcium levels

Answer 13.1

The correct answer is (E)

It is important to rule out other causes for constipation. This patient has evidence of bone metastasis, and in the clinical picture of constipation and confusion, hypercalcemia needs to be ruled out.

Further Reading

Gardner EC Jr, Hersh T. Primary hyperparathyroidism and the gastrointestinal tract. *South Med J.* 1981;74:197.

Question 13.2

Which of the following is not recommended in the management of constipation for patients with a prior history of fecal impaction and poor oral intake?

- A. Polyethylene glycol
- B. Bulk fiber
- C. Senna
- D. Lactulose
- E. Bisacodyl suppositories

Answer 13.2

The correct answer is (B)

Bulk laxatives such as fiber will soften hard stool but also harden a loose one. They are not the first option in palliative care patients because they need to be taken with plenty of water (at least 200–300 ml), and their consistency can be difficult to manage in very ill patients. Patients with poor water intake are at higher risk of developing fecal impaction again if fiber or bulking agents are used.

Further Reading

Lembo A, Camilleri M. Chronic constipation. *N Engl J Med*. 2003;349:1360.

Sykes N. Constipation and diarrhoea. In: Hanks G, Cherney NI, Christakis NA, et al. eds. *Oxford Textbook of Palliative Medicine*. 4th ed. New York, NY: Oxford University Press; 2010;833–849.

Question 13.3

Mrs. Z is a 49-year-old female patient with advanced endometrial cancer with carcinomatosis and ascites. She takes morphine 45 mg every 12 hours and morphine immediate-release 15 mg as needed for her lower abdominal pain. She presented to the emergency room with nausea, vomiting, and abdominal pain, and her last bowel movement was 6 days ago.

Which of the following is contraindicated?

- A. Morphine infusion
- B. Haloperidol IV
- C. Methylnaltrexone
- D. Hydromorphone infusion
- E. None of the above

Answer 13.3

The correct answer is (C)

Methylnaltrexone is an opioid antagonist that targets the mu receptors of the gastrointestinal tract without crossing the blood–brain barrier or impairing analgesia by opioids. Cases of bowel perforation have been documented in patients with any compromised bowel integrity. Methylnaltrexone is contraindicated in patients with clinical evidence or prior history of bowel obstruction.

Further Reading

Portenoy RK, Thomas J, Moehl Boatwright ML, et al. Subcutaneous methylnaltrexone for the treatment of opioid-induced constipation in patients with advanced illness: A double-blind randomized, parallel group, dose-ranging study. *J Pain Symptom Manage*. 2008;35(5):458–468.

Thomas J, Karver S, Cooney GA, et al. Methylnaltrexone for opioid-induced constipation in advanced illness. *N Engl J Med*. 2008;358(22):2332–2343.

Question 13.4

For the management of constipation in a patient receiving palliative care, which of the following agents is an osmotic laxative?

- A. Polyethylene glycol
- B. Docusate
- C. Mineral oil
- D. Psyllium
- E. All of the above

Answer 13.4

The correct answer is (A)

Laxatives can be divided into those that soften the stool and those that increase gut peristalsis. Lubricant or surfactant laxatives such as docusate sodium increase water penetration and soften the stool. Bulk-forming agents such as bran and psyllium increase stool bulk and cause a stretch response that can cause mechanical irritation. Stimulant laxatives such as senna and bisacodyl increase intestinal peristalsis and secretions. Emollient laxatives such as mineral oil act as a lubricant and stool softener. Osmotic agents such as polyethylene glycol, lactulose, and sorbitol increase stool osmolality, leading to fluid accumulation in the colon.

Further Reading

Dipalma JA, Cleveland MV, McGowan J, Herrera JL. A randomized, multicenter, placebo-controlled trial of polyethylene glycol laxative for chronic treatment of chronic constipation. *Am J Gastroenterol.* 2007;102:1436.

Question 13.5

What is the best treatment and prophylaxis for opioid-induced constipation (OIC)?

- A. Keep the opioid dose low
- B. Oral intake of at least 1.5 liters of water daily
- C. Daily ambulation
- D. Schedule daily laxatives
- E. All of the above

Answer 13.5

The correct answer is (D)

The best treatment and prophylaxis for OIC is use of daily laxatives. The majority of patients with chronic opioid use will experience chronic constipation. A low dose of laxatives should be started at night and slowly titrated to achieve regular soft stools. Good fluid intake and ambulation may help with constipation but will not prevent constipation. Keeping a low dose of opioid due to the concern for OIC is not recommended. The goal for symptom control should be to control the pain adequately and adjust the laxatives as needed.

Further Reading

Clemens KE, Klaschik E. Management of constipation in palliative care patients. *Curr Opin Support Palliat Care*. 2008;2:22.

Grunkemeier DM, Cassara JE, Dalton CB, Drossman DA. The narcotic bowel syndrome: Clinical features, pathophysiology, and management. *Clin Gastroenterol Hepatol*. 2007;5:1126.

14

Palliative Care Emergencies

SRIRAM YENNURAJALINGAM

Question 14.1

Mrs. Smith is a 59-year-old White female who presents with a history of stage III breast cancer s/p treatment 10 years ago with new-onset back pain. Pain is dull and constant, and it is aggravated by lying flat and coughing. Workup revealed recurrent breast cancer, metastatic to thoracic spine and ribs. Metastatic workup including full spine magnetic resonance imaging (MRI) was positive for T4 disease with cord compression and rib disease. Her neurological exam showed diminished power in the lower extremities of 3/5, absent joint position sense in the lower extremities.

All of the following statements are true *except*:

- A. Surgery is indicated for spinal instability, rapid neurological deterioration, previous radiotherapy, and intractable pain.
- B. Pain control can be achieved with opioids and an aggressive bowel regimen.
- C. High doses of steroids are always beneficial compared to moderate doses of steroids.
- D. Radiation therapy usually includes external beam radiotherapy of 30 Gy in 10 fractions.

Answer 14.1

The correct answer is (C)

A Cochrane Review suggests that it is unclear if high doses of steroids offer benefits compared to moderate doses or no steroids at all.

Spinal cord compression is the second most common neurological complication of cancer after brain metastasis. The most common site is at the thoracic level (60%). Workup includes MRI spine or computed tomography (CT) myelogram. Lumbar puncture is contraindicated. Goals of management include restoration of neurological function and stabilization of the spine. This includes bed rest, steroids, consult neurosurgery and/or radiation oncology, and cancer-specific treatment for chemosensitive tumors. Other measures include pain control with opioids and use of a Philadelphia collar if the cervical spine is involved.

Further Reading

George R, Jeba J, Ramkumar G, Chacko AG, Tharyan P. Interventions for the treatment of metastatic extradural spinal cord compression in adults. *Cochrane Database Syst Rev.* 2015;2015(9):CD006716.

Question 14.2

A 52-year-old female with a history of metastatic breast cancer with metastasis to the spine and ribs presents to the emergency center with symptoms of extreme fatigue, nausea, constipation, and confusion for the past 3 days. On examination, she has postural hypotension, dry mucosa, and diminished reflexes in all four extremities. Her laboratory tests reveal serum calcium levels of 14 mg/dl, serum phosphorus is 4.6 mg/dl, serum creatinine is 2.0 mg/dl, and albumin level is 3.3 g/dl.

Which of the following statements is true?

- A. Volume expansion with isotonic fluid, calcitonin, and concurrent bisphosphonate therapy is the best initial therapy.
- B. Use of loop diuretics with volume expansion is the best initial therapy.
- C. Pamidronate is preferred over zoledronic acid in patients with normal to moderately impaired renal function.
- D. The 1-year survival after the diagnosis of hypercalcemia of malignancy is 50%.

Answer 14.2

The correct answer is (A)

Treatment of hypercalcemia usually includes administration of intravenous hydration with 0.9% sodium chloride 2–4 l/day for 2 or 3 days, calcitonin 4–8 units/kg SQ q6–12 hours for 2 or 3 days, and zoledronic acid 3 or 4 mg IV for 15–30 minutes. Zoledronic acid is preferred over pamidronate in patients with normal to moderately impaired renal function. Fever, bone pain during infusion (15%), and osteonecrosis of maxilla and mandible (1%) are important side effects of bisphosphonates. The diagnosis of hypercalcemia of malignancy is associated with poor survival. The use of diuretics is not routine with the advent of bisphosphonates and should be considered only after hydration. In a retrospective study of 8,000 patients with hypercalcemia due to malignancy, the 12-month survival was 25%.

Further Reading

Sternlicht H, Glezerman IG. Hypercalcemia of malignancy and new treatment options. *Ther Clin Risk Manag.* 2015;11:1779–1788. doi:10.2147/TCRM.S83681

Question 14.3

A 61-year-old White male with metastatic lung cancer s/p multiple prior therapies, including prior high-dose endobronchial radiation, who is not a candidate for cancer-directed therapies is admitted to the palliative care service with fever and cough. The patient was started on empiric antibiotics for pneumonia. Within 24 hours of admission, the patient has 700 cc of hemoptysis and becomes severely short of breath.

All of the following treatments are appropriate in the management of bleeding in this patient *except*:

- A. Mask bleeding with dark-colored towels
- B. Prevent aspiration by positioning the patient to the lateral decubitus position with affected lung in the dependent position
- C. Empathetic communication with the patient's family
- D. Endotracheal intubation and bronchial artery embolization

Answer 14.3

The correct answer is (D)

Hemoptysis is commonly seen in lung cancer patients (20%). In patients at risk of bleed, plan ahead. Have parenteral opioids and sedatives on hand, and have dark towels and bedding available in case of a hemoptysis event. Aggressive interventions such as endotracheal intubation are seldom indicated in palliative care patients. In patients who are in the earlier stages of illness, treatments including external beam radiotherapy, endobronchial techniques, bronchial artery embolization, and chemotherapy may be considered. In a terminal ill patient with massive hemoptysis, palliative sedation with midazolam/lorazepam may be the best approach.

Further Reading

Simoff MJ, Lally B, Slade MG, et al. Symptom management in patients with lung cancer: Diagnosis and management of lung cancer, 3rd ed.: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013;143(5 Suppl.):e455S–e497S.

Question 14.4

A 56-year-old Caucasian male has metastatic renal cell cancer with metastasis in the lung and bones (spine and pelvis). The patient also has a history of diabetes mellitus type 2 controlled with metformin extended-release 1,000 mg daily. Life expectancy is less than 6 months. The patient now prefers to focus on better quality of life. He follows up regularly with the palliative care team on an outpatient basis. The patient presents to the emergency center with a complaint of new left lower extremity pain. As per the patient's report, he states that he slipped and fell down while in the shower. X-ray done in the emergency center reveals a fracture of the left femur:

What is the best treatment choice at this time?

- A. Radiation
- B. Surgical intervention
- C. Chemotherapy
- D. None of the above

Answer 14.4

The correct answer is (B)

Indications for surgical intervention in metastatic bone disease include (a) fracture of femur, tibia, or weight-bearing portions of pelvis; and (b) spinal fracture or instability with epidural compromise. However, surgery is contraindicated in patients with very limited prognosis and/or extensive comorbidities. Surgical intervention is usually recommended for patients with a life expectancy of at least 1 month and a pathologic fracture that is functionally limiting.

Further Reading

Kollender Y, Bickels J, Price WM, et al. Metastatic renal cell carcinoma of bone: Indications and technique of surgical intervention. *J Urol.* 2000;164:1505.

Wolanczyk MJ, Fakhrian K, Adamietz IA. Radiotherapy, bisphosphonates and surgical stabilization of complete or impending pathologic fractures in patients with metastatic bone disease. *J Cancer.* 2016;7:121.

Question 14.5

A 66-year-old African American female has multiple myeloma with extensive disease involving the spine and pelvis. The patient follows up regularly with the palliative care team on an outpatient basis for back pain. The patient has a history of smoking, coronary artery disease, and chronic obstructive pulmonary disease. She presents to the emergency center with a complaint of new-onset confusion. Her laboratory tests reveal serum calcium levels of 15 mg/dl, serum phosphorus 5.0 mg/dl, serum creatinine 4.5 mg/dl, and albumin 3.2 g/dl.

Which of the following statements is true regarding the management of hypercalcemia due to malignancy?

- A. Dialysis is used to treat hypercalcemia in select patients with renal insufficiency or heart failure or patients unable to tolerate hydration.
- B. Calcitonin usually is beneficial to treat severe hypercalcemia (≥ 14 mg/dl) when combined with intravenous hydration and bisphosphonates.
- C. Use of pamidronate is contraindicated in patients with severe renal insufficiency (creatinine mg/dl).
- D. Glucocorticoids are used to treat hypercalcemia due to lymphomas, sarcoid, and other granulomatous disease.
- E. All of the above.

Answer 14.5

The correct answer is (E)

The initial treatment of hypercalcemia includes administration of IV hydration with 0.9% sodium chloride 2–4 l/day for 2 or 3 days, calcitonin 4–8 units/kg SQ q6–12 hours for 2 or 3 days, and zoledronic acid 3 or 4 mg IV for 15–30 minutes. Denosumab is an option for patients with hypercalcemia that is refractory to zoledronic acid or in whom bisphosphonates are contraindicated due to severe renal impairment. Dialysis is used to treat hypercalcemia in select patients with renal insufficiency or heart failure or patients unable to tolerate hydration.

Further Reading

Bech A, de Boer H. Denosumab for tumor-induced hypercalcemia complicated by renal failure. *Ann Intern Med.* 2012;156:906.

Koo WS, Jeon DS, Ahn SJ, et al. Calcium-free hemodialysis for the management of hypercalcemia. *Nephron.* 1996;72:424.

Stewart AF. Clinical practice: Hypercalcemia associated with cancer. *N Engl J Med.* 2005;352:373.

Question 14.6

A 74-year-old African American male has multiple myeloma with extensive disease involving the spine. The patient presents to the emergency center with a complaints of new-onset lethargy and somnolence. His laboratory tests reveal serum calcium level of 14.2 mg/dl, serum phosphorus is 4.6 mg/dl, serum creatinine is 2.0 mg/dl, and albumin is 3.0 g/dl. The initial treatment of his hypercalcemia included administration of IV hydration with 0.9% sodium chloride, calcitonin, and zoledronic acid.

All of the following are acute side effects of bisphosphonate therapy except:

- A. Nephrotoxicity (nephrotic-range proteinuria and acute renal insufficiency)
- B. Conjunctivitis, uveitis, scleritis, and orbital inflammation
- C. Pain, infection, and necrotic bone in the mandible or maxilla
- D. Fever, chills, bone pain, headache, nausea, myalgias, and arthralgias
- E. All of the above

Answer 14.6

The correct answer is (C)

Nephrotoxicity due to bisphosphonates is both dose- and infusion time-dependent. The risk of nephrotoxicity is higher among patients who receive the drug over less than 2 hours. Ocular inflammation requires a prompt ophthalmologic evaluation, and further treatment with the offending bisphosphonate is not recommended. Fever, chills, bone pain, headache, nausea, myalgias, and arthralgias occur as part of an acute phase reaction after initial administration of bisphosphonates, and these symptoms resolve within a few days. Medication-related osteonecrosis of the jaw typically presents as pain, infection, and necrotic bone in the mandible or maxilla in a patient receiving long-term treatment with bisphosphonates (seen in <2% cases).

Further Reading

Chang JT, Green L, Beitz J. Renal failure with the use of zoledronic acid. *N Engl J Med.* 2003;349:1676.

Perazella MA, Markowitz GS. Bisphosphonate nephrotoxicity. *Kidney Int.* 2008;74:1385.

Tanvetyanon T, Stiff PJ. Management of the adverse effects associated with intravenous bisphosphonates. *Ann Oncol.* 2006;17:897.

Question 14.7

A 62-year-old female has metastatic lung cancer s/p multiple prior therapies. The patient is admitted to the emergency center with worsening shortness of breath, cough, headaches, and blurred vision. On examination, vital signs are stable except for a distinct stridor. There is facial swelling and venous distension of the neck and chest wall.

All of the following measures are urgently needed to manage the symptoms *except*:

- A. Sit the patient upright or elevate head of bed
- B. Corticosteroids
- C. Diuretics
- D. Oxygen/opioids as needed
- E. Intravenous fluids using upper arm access
- F. Immediate radiation or stent placement

Answer 14.7

The correct answer is (E)

The superior vena caval syndrome includes symptoms and signs resulting from obstruction of the superior vena cava commonly due to the tumor. The management of superior vena caval syndrome includes radiation or stent placement after diagnosis with CT scan with contrast or MRI if contrast allergy is present. Intravenous fluids using upper arm access may exacerbate the symptoms.

Further Reading

Wilson LD, Detterbeck FC, Yahalom J. Superior vena cava syndrome with malignant causes. *N Engl J Med.* 2007;356:1862–1869.

Question 14.8

A 52-year-old female with newly diagnosed metastatic lung cancer presents to the emergency center with worsening shortness of breath, cough, and headaches. The patient has no history of seizures. On examination, vital signs are stable. Examination is unremarkable. CT chest reveals a 2-cm left upper lobe mass. MRI of the brain shows one metastatic lesion in the left brain.

All of the following measures are needed to manage the symptoms *except*:

- A. Stereotactic radiosurgery for brain metastasis
- B. Corticosteroids
- C. Levetiracetam for 2 years
- D. Opioids as needed
- E. None of the above

Answer 14.8

The correct answer is (C)

Seizure prophylaxis is not indicated in primary or metastatic brain tumors in the absence of seizure history. However, postoperative seizure prophylaxis for up to 3 months is advised to prevent early postoperative seizures.

Further Reading

Sirven JI, Wingerchuk DM, Drzakowski JF, Lyons MK, Zimmerman RS.

Seizure prophylaxis in patients with brain tumors: A meta-analysis.
Mayo Clin Proc. 2004;79(12):1489–1494.

Weston J, Greenhalgh J, Marson AG. Antiepileptic drugs as prophylaxis for post-craniotomy seizures. *Cochrane Database Syst Rev.* 2015;2015(3):CD007286.

Question 14.9

A 62-year-old female with refractory ovarian cancer with extensive peritoneal disease presents to the emergency center with severe abdominal pain, nausea, and obstipation. Exam shows hyperactive bowel sounds. X-ray of the abdomen shows multiple air fluid levels.

Management of the symptoms in this patient includes all of the following *except*:

- A. Subcutaneous or intravenous hydration
- B. Hyoscine butylbromide
- C. Metaclopramide
- D. Dexamethasone
- E. Nasogastric decompression

Answer 14.9

The correct answer is (C)

Metoclopramide is a prokinetic agent and therefore may further increase the severity of the symptoms. Conservative symptomatic management for patients with advanced disease is the most common option in the palliative setting. Surgery may be beneficial if the obstruction is present at a single level. Venting gastrostomy can also be beneficial for symptom relief.

Further Reading

DeEulis TG, Yennurajalingam S. Venting gastrostomy at home for symptomatic management of bowel obstruction in advanced/recurrent ovarian malignancy: A case series. *J Palliat Med.* 2015;18(8):722–728. doi:10.1089/jpm.2014.0355

Jatoi A, Podratz KC, Gill P, Hartmann LC. Pathophysiology and palliation of inoperable bowel obstruction in patients with ovarian cancer. *J Supportive Oncol.* 2004;2(4):323–337.

Question 14.10

A 48-year-old White female has metastatic lung cancer s/p multiple prior therapies, including prior high-dose endobronchial radiation. The patient not a candidate for cancer-directed therapies. She is admitted to the palliative care service with severe shortness of breath and anxiety. Her exam is remarkable for heart rate of 126 beats per minute and pallor inspiratory stridor. Pulse oximetry shows oxygen saturation of 94%. Chest X-ray shows bilateral lung masses and bibasilar haziness. The patient is started on empiric antibiotics for pneumonia.

All of the following treatments are appropriate in the management of acute breathlessness in this patient *except*:

- A. Systemic opioids
- B. Bronchodilators
- C. Corticosteroids
- D. Oxygen

Answer 14.10

The correct answer is (D)

Management of distressing symptoms such as dyspnea includes use of oxygen but only in hypoxemic patients. Several randomized trials and at least four systematic reviews demonstrate the benefits of systemically administered opioids in treating dyspnea. Morphine is the most widely studied drug.

Further Reading

Bausewein C, Booth S, Gysels M, Higginson I. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. *Cochrane Database Syst Rev.* 2008;2008(2):CD005623.

15

Other Symptoms

*Xerostomia, Hiccups, Pruritus, Pressure Ulcers
and Wound Care, Lymphedema,
and Myoclonus*

PAUL W. WALKER

Question 15.1

A 59-year-old male has just completed radiation therapy for treatment of his base of tongue cancer. He now complains of dry mouth with difficulty chewing food, swallowing, and speaking. He finds his dry mouth is one of his most unremitting symptoms. He asks you what can be done for this problem.

You recommend which of the following?

- A. Reviewing his medication list for possible anticholinergic, antihistamine, psychotropic, and other classes of drugs that can worsen dry mouth
- B. Regular oral hygiene with regular brushing of the teeth with fluoride toothpaste to reduce caries and periodontal disease
- C. Supplement oral moisture with regular sips of fluid, ice chips, popsicles, chewing sugarless gum, or sucking on sugar-free candy
- D. All of the above

Answer 15.1

The correct answer is (D)

Xerostomia is a complex and challenging problem that is often underestimated by the clinician but often mentioned by the patient. Many causes can contribute to dry mouth, including medications, radiation therapy, systemic diseases that decrease saliva flow, dehydration, and mouth breathing. Medications such as pilocarpine and cevimeline offer moderate benefit, but their use raises concerns for glaucoma, cardiac side effects, increased sweating, lacrimation, and dizziness. Often, the most benefit can be achieved using simple strategies such as oral hydration, hygiene, and minimizing drugs that can contribute to the problem.

Further Reading

- Brimhall J, Jhavan MA, Yepes JF. Efficacy of cevimeline vs. pilocarpine in the secretion of saliva: A pilot study. *Spec Care Dentist*. 2013;33(3):123–127.
- Lalla RV, Peterson DE. Oral symptoms. In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:937–46.
- Lovelace TL, Fox NF, Sood AJ, Nguyen SA, Day TA. Management of radiotherapy-induced salivary hypofunction and consequent xerostomia in patients with oral head and neck cancer: Meta-analysis and literature review. *Oral Surg Oral Med Oral Pathol Oral Radial*. 2014;117(5):595–607.

Question 15.2

You are consulted on a 46-year-old male with non-small cell lung cancer who has developed acute hiccups after his chemotherapy regimen. You review his medication list and note he is receiving morphine, dexamethasone, and lorazepam.

Which of the following would be your first consideration to relieve his hiccups?

- A. Increase the dexamethasone to reduce inflammation that may be causing hiccups.
- B. Stop or taper the dexamethasone and lorazepam because these drugs are associated with causing hiccups.
- C. Have the patient perform breath-holding maneuvers, pharyngeal and gag reflex stimulation, and vagal maneuvers because these traditional folk remedies are very effective.
- D. Start the patient on an as-needed dose of chlorpromazine because this is what you learned when in medical school.

Answer 15.2

The correct answer is (B)

Searching for and eliminating the cause of hiccups can be the most effective treatment for hiccups. Most clinicians have little knowledge of the cause and treatment of hiccups. It is underappreciated that corticosteroids and benzodiazepine drugs are associated with causing hiccups. Reducing or eliminating these drugs alone can resolve the problem. Starting chlorpromazine can be helpful, but it is not the recommended initial therapy. Traditional folk remedies involving pharyngeal stimulation and breath-holding have a low likelihood of improving persistent hiccups.

Further Reading

- Smith HS. Hiccups. In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:894–898.
- Thomas T, Wade R, Booth S. Other respiratory symptoms (cough, hiccup, and secretions). In: Bruera E, Higginson IJ, Ripamonti C, von Gunten C, eds. *Textbook of Palliative Medicine*. Oxford, UK: Hodder Arnold; 2006:663–672.

Question 15.3

You are consulted on a 46-year-old male with non-small cell lung cancer who has developed acute hiccups after his chemotherapy regimen. You review his medication list and note he is receiving morphine, dexamethasone, and lorazepam, and you try to taper the offending agents. Hiccups are persisting in this patient despite your best efforts to eliminate a cause. It is unclear what the etiology may be. The patient reports becoming fatigued and disheartened by the recurring episodes of hiccups and has difficulty speaking and eating when they occur.

Which of the following should be your first consideration for drug therapy?

- A. Metoclopramide 10 mg q4 hours IV or SC together with a proton pump inhibitor
- B. Start baclofen 5 mg tid
- C. Start gabapentin 100–300 mg tid
- D. Start haloperidol 3–5 mg PO/SC tid

Answer 15.3

The correct answer is (A)

The recommended agents to use first for hiccups are metoclopramide and a proton pump inhibitor because gastroesophageal reflux disease is an important inciting factor in many patients. These drugs are also less likely to cause serious side effects compared to other agents. Baclofen has been reported to be the most effective agent when other drugs have failed, but it is only available orally and can have significant side effects. Therefore, it is not recommended first line. Haloperidol, chlorpromazine, gabapentin, nifedipine, and sertraline have been reported to be helpful in case reports.

Further Reading

- Ramirez FC, Graham DY. Treatment of intractable hiccup with baclofen: Results of a double-blind randomized, controlled, crossover study. *Am J Gastroenterol.* 1992;87(12):1789–1791.
- Smith HS. Hiccups. In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:894–898.
- Thomas T, Wade R, Booth S. Other respiratory symptoms (cough, hiccup, and secretions). In: Bruera E, Higginson IJ, Ripamonti C, von Gunten C, eds. *Textbook of Palliative Medicine*. Oxford, UK: Hodder Arnold; 2006:663–672.

Question 15.4

A 37-year-old female with lymphoma has been referred to you for the problem of generalized pruritus.

What would be the best initial step to take?

- A. Order an antihistamine medication to be administered IV as needed for the itch.
- B. Request laboratory tests to determine the patient's hepatic and renal function because liver and kidney disease are causes of itch.
- C. Perform a history focusing on whether new topical or drug treatments have been administered, whether other family members have complained of itch, and whether symptoms of neurological disease or a history of psychiatric disorder is present?
- D. Order a topical lotion to sooth itch.

Answer 15.4

The correct answer is (C)

Although this patient may have pruritus secondary to her malignancy, it is important to do a careful history to determine the cause of the itch and rule out common causes, such as drug reactions, irritating topical agents, infectious causes, and neurological or psychiatric diseases. Following this, physical examination of the skin may be helpful in revealing causes such as urticaria, xerosis, or scabies. Dermatological referral and investigation for liver and kidney disease are steps to take if the diagnosis remains in doubt.

Further Reading

Davidson S, Moser H, Geisler G. Ascending pathways for itch.

In: Carstens E, Akiyama T, eds. *Itch: Mechanisms and Treatment*. Boca Raton, FL: CRC Press; 2014.

Misery L, Brenaut E, Le Garrec R, et al. Neuropathic pruritus. *Nat Rev Neurol*. 2014;10(7):408–416.

Summey BT. Pruritus. In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:910–913.

Question 15.5

Correct management of wounds requires determination of the cause of the wound.

Common causes of wounds in seriously ill patients may include which of the following?

- A. Pressure ulceration and surgical dehiscence
- B. Infection and malignancy
- C. Venous and arterial insufficiency
- D. All of the above

Answer 15.5

The correct answer is (D)

To correctly direct wound care, the cause of the wound needs to be diagnosed. Wounds in severely ill patients are commonly due to pressure ulceration, malignancy, venous stasis, arterial insufficiency, infection, and surgical dehiscence. Evaluating patients with these common causes in mind is helpful.

Further Reading

Froiland KG. Pressure ulcers/wounds. In: Bruera E, Higginson IJ, Ripamonti C, von Gunten C, eds. *Textbook of Palliative Medicine*. Oxford, UK: Hodder Arnold; 2006:768–772.

Schulz VN, Kozell KM, Martins LM. Pressure ulcers and wound care. In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:478–484.

Question 15.6

Which of the following is the primary cause of a pressure ulcer?

- A. Thin skin
- B. Loss of adipose tissue
- C. Loss of mobility resulting in unrelieved pressure over a bony prominence
- D. Poor nutritional status

Answer 15.6

The correct answer is (C)

Loss of mobility resulting in unrelieved pressure over a bony prominence is the cause of pressure ulcers. Ischemia develops when capillary pressure is exceeded. Increasing patient mobility with frequent position changes and turning, if possible, is the hallmark of good care. Relief of pressure over the area of the wound is the most important strategy. The assessment of a physical or occupational therapist can be of great assistance. However, at the end of life, position changes may not be acceptable or appropriate, and wound healing may not be possible. Proper dressings and nutrition are further considerations.

Further Reading

Gillespie BM, Chaboyer WP, McInnes E, Whitty JA, Thalib L.

Repositioning for pressure ulcer prevention in adults. *Cochrane Database Syst Rev.* 2004;2004(4):CD009958.

Reddy M, Gill SS, Kalkar SR, et al. Treatment of pressure ulcers: A systematic review. *JAMA.* 2008;300(22):2647–2662.

Question 15.7

The goal of wound dressing is predominately to do which of the following?

- A. Cover the wound to prevent infection
- B. Cover the wound to prevent odor in the room
- C. Cover the wound to prevent bleeding due to inadvertent trauma
- D. Cover the wound to allow moist wound healing

Answer 15.7

The correct answer is (D)

Preventing the wound from becoming dry and allowing moist wound healing is of primary importance in the selection of dressing type. It is also important to address wounds with excess exudate by using a dressing that can absorb large amounts of fluid. Neither too dry nor too wet is the goal. It is important to clean the wound between dressing changes. Nontoxic liquids such as normal saline, Ringer's lactate, or sterile water are appropriate. The assistance of a wound–ostomy care nurse can be helpful in selecting dressings because choices are many.

Further Reading

- Froiland KG. Pressure ulcers/wounds. In: Bruera E, Higginson IJ, Ripamonti C, von Gunten C, eds. *Textbook of Palliative Medicine*. Oxford, UK: Hodder Arnold; 2006:768–772.
- Schulz VN, Kozell KM, Martins LM. Pressure ulcers and wound care. In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:478–484.

Question 15.8

Which of the following signs and symptoms may be produced by lymphedema?

- A. The sensation of limb heaviness and discomfort
- B. Decreased range of motion of a limb
- C. Concerns related to body image
- D. All of the above

Answer 15.8

The correct answer is (D)

Lymphedema can decrease quality of life in many ways, such as causing limb heaviness and discomfort, decreased range of motion and functionality of a limb, and concerns about body image. This is a change that is visibly apparent, and family members as well as the patient often state that it is their major concern. In severe cases, bullae and spontaneous drainage of serous fluid may develop (lymphorrhea), necessitating the use of absorbent dressings.

Further Reading

Guo Y, Konzen B. Lymphedema. In: Bruera E, Higginson IJ, Ripamonti C, von Gunten C, eds. *Textbook of Palliative Medicine*. Oxford, UK: Hodder Arnold; 2006:787–796.

Towers A. Lymphedema. In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:474–478.

Question 15.9

A 43-year-old female has developed lymphedema of the left upper extremity as a result of radiotherapy, surgery, and tumor recurrence at the axilla.

Which of the following treatments is not of proven benefit?

- A. Diuretic medication
- B. Use of a compressive garment
- C. Referral to a lymphedema therapist for combined/complex decongestive therapy
- D. A schedule of upper limb exercises

Answer 15.9

The correct answer is (A)

The use of diuretic medications is not beneficial in most cases of lymphedema and may place the patient at risk of electrolyte disturbances, hypotension, and even dehydration if fluid intake is not adequate. Referral to a lymphedema therapist is the most intensive of management options. This usually entails the use of techniques termed combined or complex decongestive therapy. These include education on skin care, manual lymph drainage massage or pneumatic compression utilizing electric pumps, and compressive bandaging or garments. These garments are individually fitted to maintain the reduction in swelling obtained thorough massage or compressive techniques. Patients with lower extremity lymphedema may benefit from elevation of the limb, massage toward the heart, and the wearing of support or compression hose. For years it was thought that exercise would be harmful to women with breast cancer who experience upper extremity lymphedema. Relatively recent clinic evidence documents that this is not the case, and exercise is now recommended to improve function. It is important to exclude deep venous thrombosis and cellulitis as causes before starting lymphedema therapy.

Further Reading

- Leung EY, Tiriapur SA, Meads C. The management of secondary lower limb lymphedema in cancer patients: A systematic review. *Palliat Med.* 2015;29(2):112–119.
- Szolnoky G, Dobozy A, Kemeny L. Towards an effective management of chronic lymphedema. *Clin Dermatol.* 2014;32(5):685–691.

Question 15.10

A 62-year-old male with non-small cell lung cancer has spinal metastasis and back pain that you are treating with a regimen of oral morphine. After a recent increase in his morphine doses, he has developed episodic twitching/muscular jerks of his upper and lower extremities. This is accompanied by some mild confusion and visual hallucinations that the family reports.

What is causing the muscle twitching and how should it be managed?

- A. This is a rare and unknown condition, and a neurologist needs to be consulted.
- B. The patient is having focal seizures, and an anticonvulsant is required.
- C. Opioid-induced neurotoxicity is occurring, and the morphine needs to be decreased or rotation to an alternative opioid should be performed.
- D. Brain metastasis may be the root cause. A corticosteroid should be started, and imaging of the brain with contrast computed tomography or magnetic resonance imaging is indicated.

Answer 15.10

The correct answer is (C)

Opioid-induced neurotoxicity (OIN) is a common complication of opioid management. It is the most likely cause of the symptoms in this patient and is due to the recent increase in the morphine dose. Myoclonus is one of the symptoms included in OIN, along with confusion/delirium, hallucinations, and allodynia or hyperalgesia. All of these possible complications do not need to be present to diagnose OIN. The opioid needs to be considered as the possible cause in any patient on an opioid analgesic who presents with focal or generalized myoclonus. If left untreated, the myoclonus can progress to the development of seizures. Accumulation of opioid metabolites is recognized as the cause of OIN. If pain is well controlled, it can be treated with a decrease in the opioid dose. If pain is not well controlled, a rotation to an alternative opioid will allow the morphine metabolites to clear and the neurotoxicity to resolve while analgesia is provided by an alternative medication. Rapid opioid escalation and renal insufficiency are factors that can predispose to OIN. Ensuring adequate hydration can help allow clearance of the opioid metabolites.

Further Reading

Burhard PR. Acute and subacute drug-induced movement disorders.

Parkinsonism Relat Disord. 2014;20(Suppl. 1):S108–S112.

Lawlor P, Lucey M, Creedon B. Opioid side effects and overdose.

In: Walsh TD, Caraceni AT, Fainsinger R, et al., eds. *Palliative Medicine*. Philadelphia, PA: Saunders; 2009:1411–1416.

16

Frequent Pharmacological Interactions in Palliative Care

KELLY MENDOZA,
JESSICA GEIGER-HAYES,
AND MARY LYNN McPHERSON

Question 16.1

DB is a 13-year-old Ethiopian male hospitalized for a sickle cell crisis receiving high-dose intravenous dexamethasone for acute chest syndrome and codeine for pain relief. The palliative medicine team is consulted, and during rounds, DB states that the codeine is not working and that he is still in pain.

What is the underlying issue(s) that could be contributing to DB's complaint?

- A. Potential ultra-rapid metabolism of the 2D6 enzyme
- B. Inadequate codeine dose
- C. Concurrent use of dexamethasone with codeine
- D. Both A and C

Answer 16.1

The correct answer is (D)

Codeine is an inactive prodrug that requires metabolism by the hepatic enzyme cytochrome CYP2D6 to the active analgesic morphine. Dexamethasone is an inducer of the 2D6 enzyme and increases its activity, resulting in a decrease in the effect of codeine. This is an example of a pharmacokinetic drug interaction involving drug metabolism.

CYP2D6 ultra-rapid metabolism

CYP2D6 metabolism is part of the metabolic pathway of codeine, and it is a required initial step for the opioid's analgesic effect. CYP2D6 is encoded by a highly polymorphic gene on chromosome 22, and genotypes can be categorized into groups based on the enzyme's activity. Extensive metabolizers have normal enzyme activity, intermediate metabolizers have decreased enzyme activity, poor metabolizers have absent or little enzyme activity, and ultra-rapid metabolizers have greater than normal activity. Ultra-rapid metabolism leads to rapid clearance of the substrate drug, providing minimal or brief therapeutic effect. Studies performed in many countries have demonstrated significant inter-ethnic differences in CYP2D6 allele frequencies, and it is estimated that 29% of Ethiopians have the ultra-rapid metabolizer phenotype. Ultra-rapid metabolizer patients will not respond to codeine for pain relief due to rapid drug activation and clearance, leading to ineffective analgesia.

Further Reading

Bernard S, Neville KA, Nguyen AT, Flockhart DA. Interethnic differences in genetic polymorphisms of CYP2D6 in the U.S. population: Clinical implications. *Oncologist*. 2006;11(2):126–135.

Yee MM, Josephson C, Hill CE, et al. Cytochrome P450 2D6 polymorphisms and predicted opioid metabolism in African American children with sickle cell disease. *J Pediatr Hematol Oncol*. 2013;35(7):e301–e305.

Question 16.2

EP is a 68-year-old male diagnosed with lung cancer and wide-spread metastases. His pain is well controlled on methadone 5 mg by mouth twice daily. He has developed thrush and has been experiencing myoclonus. The prescriber starts both fluconazole and phenobarbital to control these symptoms.

How are these medications likely to affect the methadone metabolism?

- A. Both will inhibit
- B. Both will induce
- C. Fluconazole will inhibit; phenobarbital will induce
- D. Fluconazole will induce; phenobarbital will inhibit

Answer 16.2

The correct answer is (C)

Methadone is implicated in numerous drug interactions. In this case, methadone metabolism will be slowed by the introduction of fluconazole (inhibits 2C19 and 3A4 enzymes primarily) and increased by the introduction of phenobarbital (induces 2B6 and 3A4 enzymes primarily).

Drug interactions with methadone

Drug interactions with methadone may be pharmacodynamic (exaggerating or negating the therapeutic or toxic effect) or pharmacokinetic (altering the absorption, distribution, metabolism, or excretion of methadone). Pharmacodynamic drug interactions include increased sedation and risk of respiratory depression when given with central nervous system (CNS) depressants such as benzodiazepines. Many medications also prolong the QTc interval, increasing the risk of torsades de Pointes when given concurrently with methadone.

Pharmacokinetic drug interactions associated with methadone overwhelmingly pertain to metabolism in the gastrointestinal tract and liver by the cytochrome P450 enzymes. The major enzymes involved in methadone metabolism include CYP2B6, CYP2C19, CYP3A4, and CYP2D6; less involved are CYP2C8 and CYP2C9. In cases such as this example in which there are opposing effects on methadone metabolism, it is difficult to predict the clinical impact. When unsure, it is prudent to empirically reduce the methadone dose and encourage use of an analgesic for breakthrough pain.

Further Reading

Chang Y, Fang WB, Lin S-N, Moody DE. Stereo-selective metabolism of methadone by human liver microsomes and cDNA-expressed cytochrome P450s: A reconciliation. *Basic Clin Pharmacol Toxicol*. 2011;108(1):55–62.

Gerber JG, Rhodes RJ, Gal J. Stereoselective metabolism of methadone N-demethylation by cytochrome P4502B6 and 2C19. *Chirality*. 2004;16(1):36–44.

Question 16.3

Ms. O has stage IV ovarian cancer. She is experiencing acute on chronic pain that is described as sharp. Her chronic pain had been controlled with morphine extended-release (ER) 60 mg q12 hours and morphine immediate-release (IR) 15 mg q1 hour PRN. She has used five breakthrough doses of morphine IR in the past 24 hours; previously, she did not use PRN doses. She also takes lorazepam 0.5 mg tid and 0.5 mg every q4 hours PRN (uses one or two PRN doses of lorazepam/day), a multivitamin, and an iron supplement. Her husband reports that she is much sleepier than usual and is slightly agitated.

The increased sedation and agitation are likely due to which of the following?

- A. Scheduled morphine ER
- B. Scheduled lorazepam
- C. PRN lorazepam use
- D. PRN morphine use

Answer 16.3

The correct answer is (D)

Increased use of the breakthrough doses of morphine IR can contribute to increased CNS depression. Morphine ER and lorazepam both have CNS depression as a potential side effect. This is an example of a pharmacodynamic drug interaction.

Central nervous system depression

Patients taking one or more CNS depressant medications may experience sedation, agitation, and/or confusion and may progress to respiratory depression. This is due to the effect these medications have on the CNS that results in slowing the brain activity.

Common classes of medications that can cause CNS depression include the following: opioids, benzodiazepines, nonbenzodiazepine sedative–hypnotic agents, barbiturates, alcohol, antipsychotic agents, antidepressants, antihistamines (especially first generation), antiemetics, anticonvulsants, and illicit drugs. Less obvious CNS depressants include cimetidine; anticholinergic agents; and drugs that reduce glomerular filtration, such as nonsteroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors.

Further Reading

Kotlinska-Lemieszek A, Klepstad P, Haugen DF. Clinically significant drug–drug interactions involving opioid analgesics used for pain treatment in patients with cancer: A systematic review. *Drug Design Dev Ther.* 2015;9:5255–5267.

McPherson ML, Lockman K. Frequent pharmacological interactions in palliative care. In: Yennurajalingam S, Bruera E, eds. *Oxford American Handbook of Hospice and Palliative Medicine and Supportive Care.* 2nd ed. New York, NY: Oxford University Press; 2016:323–344.

Question 16.4

Mr. P has chronic nausea, vomiting, and pain. He came to the emergency room with fever and chills, and he was admitted for further workup. Blood cultures were drawn, and he was found to have candidemia. The infectious disease team started IV fluconazole to treat his infection. Home medications include haloperidol and methadone. He is still taking both medications.

What additional test should be ordered to determine if the other medications should be adjusted with initiation of fluconazole?

- A. Liver function tests
- B. Electrocardiogram
- C. Arterial blood gases
- D. Urine culture

Answer 16.4

The correct answer is (B)

An electrocardiogram should be ordered to evaluate QTc. Haloperidol and methadone both have the potential for causing QT prolongation, as does fluconazole. These medications can have additive effects on the QTc. This is an example of a pharmacodynamic drug interaction.

QT interval prolongation

QT prolongation can be defined as a QTc longer than 430 msec for males and 450 msec for females. A QTc interval longer than 500 msec places a patient at high risk for development of torsades de pointes. Many medications used for symptom management in palliative care have the potential for causing QTc prolongation, which can lead to the life-threatening arrhythmia of torsades de pointes. Common palliative medications that can increase the QT interval include, but are not limited to, antipsychotics, methadone, prokinetic agents, tricyclic antidepressants, antifungals, antibiotics, and cardiac medications. For a more complete listing of medications that can prolong the QTc, refer to the website <http://www.crediblemeds.com>. Consider adjusting medications if the QTc approaches 500 msec.

Further Reading

Cruciani RA, Sekine R, Homel P, et al. Measurement of QTc in patients receiving chronic methadone therapy. *J Pain Symptom Manage*. 2005;29(4):385–391.

McPherson ML, Lockman K. Frequent pharmacological interactions in palliative care. In: Yennurajalingam S, Bruera E, eds. *Oxford American Handbook of Hospice and Palliative Medicine and Supportive Care*. 2nd ed. New York, NY: Oxford University Press; 2016:323–344.

QT drug lists by risk group. Arizona Cert: Center for Education and Research on Therapeutics. <http://www.crediblemeds.com>. Accessed September 18, 2016.

Question 16.5

TP is a 58-year-old female suffering from advanced amyotrophic lateral sclerosis (ALS) and is being started on Nuedexta (dextromethorphan/quinidine) for the treatment of pseudobulbar affect, a condition characterized by involuntary, sudden, and frequent episodes of laughing and/or crying. The pharmacist on the team mentions that the mechanism of action of Nuedexta is one whereby the presence of quinidine in the combination enables dextromethorphan to reach therapeutic concentrations in the body.

What kind of drug–drug interaction is this medication combination exploiting?

- A. Absorption
- B. Distribution
- C. Metabolism
- D. Excretion

Answer 16.5

The correct answer is (C)

Dextromethorphan is a sigma-1 receptor agonist and an uncompetitive NMDA receptor antagonist. Quinidine increases plasma levels of dextromethorphan by competitively inhibiting cytochrome 2D6, which is the enzyme that catalyzes a major biotransformation pathway for dextromethorphan. This is an example of a pharmacokinetic drug interaction involving drug metabolism. Whereas most instances of drug interactions in medicine are avoided or monitored intensely for any adverse effects, in the case of this combination product, the inhibition of CYP2D6 by quinidine is exploited to provide an increase in serum levels of dextromethorphan, which is the drug used for therapeutic effect in treating pseudobulbar affect.

Further Reading

Nuedexta prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021879s000lbl.pdf. Accessed September 23, 2016.

17

Hospice Approach to Palliative Care

Medicare Hospice Benefit

SRIRAM YENNURAJALINGAM

Question 17.1

Mrs. Ross is a 78-year-old female with advanced Alzheimer's dementia. She is eligible for hospice with a Functional Assessment Staging (FAST) score of 7B and weight loss.

In order to be admitted into hospice care and receive the Medicare hospice benefit, which of the following eligibility criteria needs to be fulfilled?

- A. Primary terminal condition
- B. Certified as terminally ill by two physicians
- C. Documentation of current subjective and objective findings, current medications, and treatments
- D. All of the above

Answer 17.1

The correct answer is (D)

In addition to referral and prognosis determination, the patient should have a terminal condition and should be certified as having a terminal illness by two physicians. The patient elects the benefit. After an initial certification period of 90 days, a second 90-day recertification is needed. During the hospice admission, if needed, the patient can have blood transfusions, antibiotics, radiation therapy, and procedures such as paracentesis/thoracentesis.

Further Reading

National Hospice and Palliative Care Organization. Facts and figures: Hospice care in America. https://www.nhpco.org/sites/default/files/public/quality/Pediatric_Facts-Figures.pdf. Published September 2015.

Question 17.2

The role of the hospice medical director (as per the Medicare hospice benefits) includes which of the following?

- A. Admission process
- B. Regulatory compliance
- C. Face-to-face visits
- D. Pharmacy utilization
- E. All of the above

Answer 17.2

The correct answer is (E)

The role of the hospice medical director is important and well defined. In addition to patient care, which includes the admission process and direct/indirect patient care, it involves several administrative aspects, including regulatory compliance, audit reviews, face-to-face visit documentation, and pharmacy utilization/relatedness.

Further Reading

National Hospice and Palliative Care Organization. Facts and figures: Hospice care in America. https://www.nhpco.org/sites/default/files/public/quality/Pediatric_Facts-Figures.pdf. Published September 2015.

Question 17.3

Mr. Smith is a 64-year-old ex-smoker with chronic obstructive pulmonary disease (COPD) who has chronic cough, sputum production, dyspnea with mild exertion, and ankle edema. His forced expiratory volume in 1 second (FEV1) is 30% of predicted, and his partial pressure of oxygen (pO_2) at rest is 57 mm Hg. His physician has prescribed the use of oxygen by nasal cannula at 2 l/min.

Patients will be considered to be in the terminal stage of pulmonary disease so as to qualify for hospice admission if they have severe shortness of breath at rest, poorly responsive to bronchodilators, resulting in decreased functional capacity and hypoxemia ($pO_2 \leq 55$ mm Hg or oxygen saturation $\leq 88\%$), and which of the following?

- A. Right heart failure secondary to pulmonary disease
- B. Unintentional progressive weight loss $>10\%$ of body weight over the preceding 6 months
- C. Resting tachycardia >100 beats/minute
- D. All of the above

Answer 17.3

The correct answer is (D)

Patients are considered to be in the terminal stage of pulmonary disease if they have severe shortness of breath at rest, poorly responsive to bronchodilators, resulting in decreased functional capacity (FEV <30% of predicted value after bronchodilator use) and hypoxemia ($pO_2 \leq 55$ mm Hg or oxygen saturation $\leq 88\%$). In addition, they need the following supporting documentation: (a) right heart failure secondary to pulmonary disease, (b) unintentional progressive weight loss >10% of body weight over the preceding 6 months, and (c) resting tachycardia >100 beats/minute. These criteria refer to patients with various forms of advanced pulmonary disease who eventually follow a final common pathway.

Further Reading

The National Hospice Organization. Medical guidelines for determining prognosis in selected non-cancer diseases. *Hosp J*. 1996;11(2):47–63.

Question 17.4

Mrs. Jones is a 69-year-old female with breast cancer, metastatic to lungs. She complains of severe pain and is unable to move her left leg. She had a fall, and X-ray revealed a fractured left hip. She has been on home hospice for approximately 3 weeks. She has comorbidities of COPD, hypertension, and diabetes. The hip repair demonstrated no metastatic disease in the involved leg (not a pathologic fracture). The patient and her family have requested a brief course of rehabilitation at a local skilled nursing facility so she can return to optimum functioning because she was previously able to manage a fair amount of her self-care.

Which of the following is the correct choice?

- A. She may enroll in the skilled nursing facility rehabilitation at the local long-term care facility for rehabilitation of the hip fracture and remain in hospice.
- B. She may enroll in the rehabilitation program at the skilled nursing facility, but hospice will be responsible for payment.
- C. She must revoke hospice services while in treatment and can return to hospice following completion of the rehab program.
- D. All of the above.

Answer 17.4

The correct answer is (A)

Her hip fracture is unrelated to her terminal illness. The patient may seek curative treatment for illness not related to the terminal diagnosis.

If the fracture were pathologic, rehabilitation would be related to the condition and thus subject to coverage by the hospice. Even if the patient remains in hospice and receives rehab, many physicians are uncertain about payment/billing and misunderstand the Medicare hospice benefit.

The patient and family always have the option of revocation if desired, but the patient remains eligible for hospice alongside the treatment, particularly to focus on pain management and goals of care.

Further Reading

Javier N, Montagnin M. Rehabilitation of the hospice and palliative care patient. *J Palliat Med.* 2011;14(5):638–648.

Miller S. A model for successful nursing home–hospice partnerships. *J Palliat Med.* 2010;13(5):525–533.

Question 17.5

Mr. Hill is a 92-year-old veteran with advanced Alzheimer's dementia. He is eligible for hospice with FAST 7B and weight loss. His family does not wish a gastrostomy tube (PEG) and they are interested in hospice. The patient is attended by a Nurse Practitioner affiliated with the Veterans Home Visit Service; the nurse practitioner has not formal relationship with the hospice and wishes to remain attending for this patient.

Which statement is correct?

- A. The nurse practitioner can be attending and certify patients' eligibility for hospice as she knows him best.
- B. The attending nurse practitioner can do the face-to-face evaluation at the 3rd benefit period as long as it is within 30 days of the next benefit period.
- C. The nurse practitioner must relinquish management of her patient to the hospice medical director.
- D. The nurse practitioner can remain attending, but hospice physician must certify eligibility and do face-to-face evaluations for this patient.

Answer 17.5

The correct answer is (D)

Under Medicare regulations, a physician must certify eligibility for hospice, but the nurse practitioner may be attending to patient, if the patient or his family selects the nurse practitioner. Only NPs with a contractual/employment relationship with the hospice can do face-to-face evaluations for the hospice at 3rd and subsequent benefit periods.

Further Reading

Medicare COP Code of Federal Regulations, Title 42, Chapter IV, Subchapter B, Part 418: Hospice care. https://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=f719f310f64cec28f62878a8e9e132f4&tpl=/ecfrbrowse/Title42/42cfr418_main_02.tpl. Published 2017.

Question 17.6

Mr. Johnson, a 68-year-old male with brain metastases due to metastatic lung cancer, has been in home-based hospice for the past 10 weeks. His wife is his primary caregiver, and he has done well with medications for pain, agitation, and dyspnea. The last 3 days, she has called daily about her husband's restlessness, and she has been unable to sleep at night. She is exhausted and wishes something be done or she will take him back to the hospital.

Which of the following is the best choice?

- A. Respite for 5 days to allow the wife to sleep and get rest; also increase number of visits by the social worker to aid the wife in coping with her husband's terminal illness
- B. Increase the patient's temazepam to 30 mg per night and discuss sleep hygiene with the wife
- C. Recommend placement in a nursing facility because the wife cannot handle the patient
- D. Admit the patient to an inpatient unit for workup and management of suspected delirium and medication adjustment
- E. Start continuous home care in their home to minimize the husband's distress and send the wife to a spa for 2 days to relieve her burnout

Answer 17.6

The correct answer is (D)

It is appropriate to admit this patient to an inpatient unit for uncontrolled symptoms. The Medicare hospice benefit affords patients four levels of care to meet their clinical needs: routine home care, general inpatient care, continuous home care, and inpatient respite care. Respite is appropriate for 5 days to allow the family members a break or to get away, but symptoms should be well controlled in this level of care. The patient's escalating symptoms merit further investigation and could well be delirium. Continuous home care that is predominately nursing care in a patient's home is provided between 8 and 24 hours a day to manage pain and other acute medical symptoms. During continuous home care in the home, family members are expected to remain in the home because this is not a custodial strategy.

Further Reading

42 CFR 418.3, 418.52-116. Hospice conditions of participation. 2008. NHPCO national data set and/or NHPCO member database. 2012.

Question 17.7

Mrs. Rogers, a 78-year-old female with end-stage COPD, has returned to the emergency department on Friday evening for the third time in the past month. Her children have come to town to discuss goals of care. They wish to consider hospice. The emergency department physician is willing to certify that she is terminally ill and states in fact that he believes she might die within 48–72 hours in the absence of intubation and treatment in the intensive care unit. The patient is profoundly dyspneic and anxious. The patient has a Palliative Performance Scale score of 30%; is oxygen dependent, cachectic, and dyspneic; and is asking to be kept comfortable. She has signed an out-of-hospital DNR. The family wishes to avoid the acute care hospital setting, does not wish intubation nor further treatment other than comfort measures, and prefers to take her home to die. The patient was in hospice care last year but signed out.

Do you admit this patient to hospice today? Which of the following decisions is least optimal from the standpoint of the patient's needs and hospice regulations?

- A. You direct the emergency room physician to send the patient home, and you will admit the patient on Monday when a hospice physician is available because a face-to-face evaluation has not been done by a hospice physician within the past 30 days.
- B. You agree to admit to home crisis care immediately because if the patient dies within 2 days of admission, the face-to-face is considered “completed,” and this patient seems to be actively dying.
- C. You agree to admit to home crisis care because for emergent admissions on weekends and when the Centers for Medicare and Medicaid Services database is unavailable it is acceptable to admit to home crisis care without a face-to-face evaluation first.
- D. You offer the hospice inpatient unit for uncontrolled symptoms because a hospice physician is present and can do the face-to-face evaluation today prior to the patient's admission assessment.

Answer 17.7

The correct answer is (A)

Because the patient is an emergent admission on the weekend, the face-to-face prior to admission can be waived and done later. If she should die within 2 calendar days of admission (and physicians historically are “optimistic”), the face-to-face is considered “completed.” She can go home to crisis care because she has symptoms that require skilled nursing management: dyspnea, anxiety, and possibly pain. The inpatient unit is another alternative for her care, and if a physician sees her prior to nursing assessment/admission, the regulations have been met. Due to her significant symptoms, she is an emergent admission.

Further Reading

Hospice face-to-face FAQ. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/Hospice/Downloads//hospice_face2Face_FAQ_032511.pdf. Published March 2011.

Question 17.8

A local primary care physician has decided it is time to refer his 78-year-old patient with weight loss and asthenia to hospice care. His referral diagnosis is “failure to thrive.” The family is in agreement with this plan.

What is the next step in this situation?

- A. Request medical records to verify the patient’s weight loss and poor functional status in accordance with the Failure to Thrive Local Coverage Determination.
- B. Call the physician and tell him that hospice no longer accepts patients with this diagnosis.
- C. Request medical records and discuss with the attending physician the patient’s other medical conditions and trajectory of illness.
- D. Refer the patient to a home health program.

Answer 17.8

The correct answer is (C)

Failure to thrive and debility are no longer accepted as the primary hospice diagnosis, but they can be a secondary diagnosis. This patient may still be eligible for hospice if she has another medical condition, such as significant congestive heart failure, moderately severe Alzheimer's dementia, COPD, or another illness that impacts her prognosis. For referral to home health, the patient should meet criteria for that level of care: homebound status except for visits to the physician, church, the beauty shop, and so on, and leaving the home should create a burden. It is not clear from the information that she is a candidate for home health. Communicating with the community attending physician is one of the roles of a hospice medical director.

Further Reading

Periyakoil VS. Frailty as a terminal illness. *Am Fam Physician*. 2013;88(6):363–368.

18

**Cultural Issues
in Palliative Care**

SRIRAM YENNURAJALINGAM

Question 18.1

A 62-year-old Arabic female with metastatic pancreatic cancer presents to the supportive care clinic for uncontrolled pain and lack of appetite. The patient has a performance status of 3. She is refractory to two lines of chemotherapy. The patient is being considered for an experimental trial. In addition to symptom control, you plan to discuss advance care planning with her. Prior to the meeting with the patient, however, her spouse and son take you aside in the clinic hallway and specifically tell you not to discuss end-of-life planning or mention anything related to death with the patient. Subsequently during the patient interview via a medical interpreter, the patient delegates the medical decision-making to her son.

With regard to discussions about end of life for certain patients, which of the following statements is false?

- A. Information about end-of-life options must be offered to all patients irrespective of cultural considerations.
- B. Information about end-of-life options should be offered and delivered in a manner that is sensitive to cultural and religious beliefs.
- C. Health care providers should be informed about the common beliefs, traditions, and values of the patients they see regularly in their practices.
- D. Health care providers are required by law to provide counseling about end-of-life options even if the patient declines the offer.

Answer 18.1

The correct answer is (D)

In certain cultures, it is a taboo to discuss end-of-life options and topics related to death. The law does not provide an exemption from its requirements based on cultural considerations. Information and counseling about end-of-life options must be offered to all patients, but if a patient declines the offer, health care providers are not required to provide it. The patient's decision to decline the information and counseling should be documented in the medical record.

Further Reading

LaVera M, Marchall PA, Lo B, Koenig BA. Strategies for culturally effective end-of-life care. *Ann Intern Med.* 2002;136:670–673.

Question 18.2

A 35-year-old Arabic female with metastatic lung cancer is admitted to the intensive care unit (ICU) with respiratory distress and sepsis. The patient continues to have worsening respiratory distress requiring intubation and vasopressor support. During her ICU stay, the patient continues to deteriorate and has neurological changes manifested by irregular pupils. Computed tomography scan of the patient's head reveals multiple infarcts. There is concern that the patient is clinically brain-dead.

Prior to discussing brain death criteria and end-of-life issues with the patient's family in a family meeting, which of the following options should you consider?

- A. Proceed with the meeting and inform the family that per US law, you will perform the exam to confirm that the patient is brain-dead .
- B. Obtain assistance from an Arabic translator to convince the family to proceed with the brain death exam.
- C. Obtain assistance from chaplaincy as well as an Arabic translator to proceed with brain death exam.
- D. Obtain assistance from chaplaincy as well as an Arabic translator and meet with the family to begin to discuss the patient's current condition and to understand the family's perspective.
- E. Meet with chaplaincy and an Arabic translator first to understand the cultural and religious issues, and then meet with the family as a group.

Answer 18.2

The correct answer is (E)

Prior to discussing brain death criteria and end-of-life issues with the patient's family, you should obtain as much information as possible to understand the cultural and spiritual background of the patient and the family, which may influence the family's decision-making. Assistance from the multidisciplinary team to understand the patient's background as well as help during the family meeting is also important.

Further Reading

Doolen J, York NL. Cultural differences with end-of-life care in the critical care unit. *Dimens Crit Care Nurs* 2007;26:194–198.

Question 18.3

Mrs. Kulkarni is a 53-year-old Indian-born, non-English-speaking immigrant with widespread metastatic breast cancer involving liver, lung, brain, and bone. She has been told that she is not a candidate for additional chemotherapy and that her life expectancy is limited. You plan to discuss goals of care with her and recommend hospice care and “do not resuscitate” status. Today, she presents to the supportive care clinic with her husband of 20 years and her three daughter. One of the daughters speaks fluent English and has volunteered to interpret for the family.

All of the following statements are true regarding the use of medical interpreters *except*:

- A. Family members can serve as interpreters for a non-English-proficient patient.
- B. The gold standard is use of medical interpreters.
- C. The interpreter should not influence the opinion or action of the patient.
- D. Medical interpreters serve as cultural brokers and translate the concept and meaning from patients language to English.

Answer 18.3

The correct answer is (A)

Family members, patients' friends, or other health care providers should not serve as interpreters to a non-English-proficient patient. The gold standard is use of medical interpreters who can not only serve as cultural brokers and translate the concepts and meanings from the patient's language to English but also interpret the physician's explanations and proposed interventions for the patient and family.

Further Reading

Karliner LS, Jacobs EA, Chen AH, Mutha S. Do professional interpreters improve clinical care for patients with limited English proficiency? A systematic review of the literature. *Health Serv Res.* 2007;42(2):727–754. doi:10.1111/j.1475-6773.2006.00629.x

Question 18.4

Mrs. Sarah is a 66-year-old Malaysian woman with pancreatic cancer who presents for the first time to the supportive care clinic for back pain and severe itching. Her cancer is locally advanced and unresectable. She is receiving experimental chemotherapy. Recent imaging shows tumor progression with intra- and extrahepatic ductal dilation. On physical exam, she has new jaundice and scleral icterus. Labs reveal a total bilirubin of 13. The patient is proficient in English but defers the medical decisions to her daughter, who accompanies her. Prior to meeting with the patient, the patient's daughter takes you aside in the clinic hallway and specifically tells you not to inform her mother that she has cancer.

All of the following are appropriate responses to the daughter *except*:

- A. It would be unethical not to disclose the cancer diagnosis to your mother.
- B. Why do you want me to withhold the information?
- C. What are you concerned about?
- D. What would happen if your mother were to hear the truth?

Answer 18.4

The correct answer is (A)

In some cultures, family may request nondisclosure so as to prevent the patient from “losing hope and just give up and die” after becoming aware of the diagnosis and/or prognosis. Use of an explanatory model of open-ended questions is appropriate to elicit the family’s concerns. The patient may decline the right to know the diagnosis and can defer to his or her family members. This is ethically acceptable based on the principle of autonomy.

Further Reading

Johnson KS, Kuchibhatla M, Tulsky JA. What explains racial differences in the use of advance directives and attitudes toward hospice care? *J Am Geriatr Soc.* 2008;56(10):1953–1958.

Smith AK, McCarthy EP, Paulk E, et al. Racial and ethnic differences in advance care planning among patients with cancer: Impact of terminal illness acknowledgment, religiousness, and treatment preferences. *J Clin Oncol.* 2008;26(25):4131–4137.

Question 18.5

Mr. Jay is a 62-year-old Filipino male with metastatic cholangiocarcinoma who presents to the supportive care clinic for uncontrolled pain and lack of appetite. The patient is being considered for an experimental trial. In addition to symptom control, you discuss advance care planning with the patient and his spouse. Your discussion includes various aspects of his disease, treatment, and advance care planning. You are surprised to learn from the conversation that the goal of the patient is to get rid of his cancer and that he believes his cancer is curable.

All of the following statements regarding prognostic awareness are true *except*:

- A. Patients who report that they are terminally ill have worse quality of life and mood.
- B. There is a high frequency of inaccurate perception of curability among advanced cancer patients receiving palliative care.
- C. The perception of curability significantly differs by gender, education, performance status, and country of origin.
- D. All of the above.

Answer 18.5

The correct answer is (D)

Prognostic information and patients' understanding of illness are a critical component of informed shared decision-making. A recent multicenter study found that inaccurate perception of curability of cancer is common (up to 55%) and is significantly associated with gender, education, performance status, status, and culture. A study by Nipp et al. of early advanced lung and colorectal cancer patients found that patients' cancer treatment goal of "to cure my cancer" was significantly associated with better quality of life and less anxiety.

Further Reading

Nipp RD, Greer JA, El-Jawahri A, et al. Coping and prognostic awareness in patients with advanced cancer. *J Clin Oncol.* 2017;35(22):2551–2557.

Yennu S., Shamieh OM, Rodrigues LF, et al. Perception of curability in an international cohort of advanced cancer patients receiving palliative care. *J Clin Oncol.* 2016;34(26 Suppl.):5.

19

Psychosocial and Spiritual Issues in Palliative Care

MARVIN OMAR DELGADO GUAY
AND SRIRAM YENNURAJALINGAM

Question 19.1

Mrs. Sanders is a 54-year-old female with hepatocellular cancer and is bedbound with increasing fatigue.

Which of the following questions by Mrs. Sanders suggests spiritual suffering?

- A. "Why is this happening to me?"
- B. "How will I pay for my care?"
- C. "What is likely to happen next?"
- D. "Will I suffocate?"

Answer 19.1

The correct answer is (A)

The words patients use to communicate the perceptions of their end-of-life needs reveal how important it is to assess the dynamics of patient–clinician communication. Suffering is a biopsychosocial, multidimensional construct that includes physical, emotional, as well as spiritual pain. Many questions can arise from the spiritual suffering because there can be a loss of relationship between oneself, with others, and with the divine.

Further Reading

Pargament KI, Koenig HG, Tarakeshwar N, Hahn J. Religious coping methods as predictors of psychological, physical and spiritual outcomes among medically ill elderly patients: A two year longitudinal study. *J Health Psychol.* 2004;9:713–730.

Question 19.2

Mrs. Peters is a 72-year-old former cleaning woman with refractory chronic lymphocytic leukemia, poorly controlled diabetes mellitus and consequent peripheral neuropathy, renal insufficiency, and coronary artery disease. She has advanced congestive heart failure that is not responding well to medical therapy. Her daughter asks you not to talk to her mother about the cancer because it “would take away all hope.” She wants you to give chemotherapy but tell the patient it is “strong antibiotics.”

Which of the following is your best response?

- A. Agree and wait for a future opportune time.
- B. Ask the daughter what kind of hope she would like her mother to have.
- C. Disagree and tell the patient the truth.
- D. Tell the daughter you have to tell the patient the truth.

Answer 19.2

The correct answer is (B)

Because the social context of illness may be involved in requests for “everything,” exploring family dynamics is sometimes key to unlocking the underlying meaning and importance of these requests.

Further Reading

King DA, Quill T. Working with families in palliative care: One size does not fit all. *J Palliat Med.* 2006;9:704–715.

Quill TE, Arnold R, Back AL. Discussing treatment preferences with patients who want “everything.” *Ann Intern Med.* 2009;151:345–349.

Question 19.3

Mr. Smith is a 55-year-old male with advanced colon carcinoma s/p chemotherapy. He presents to you with a complaint of feeling “bummed out” for the past 3 months. His wife died 4 months ago. He is not working anymore. He does not have anxiety or a change in appetite or psychomotor retardation. He has a mild change in sleep habits. His colostomy has been working well. He expressed some meaning in his life.

Which of the following is the most likely diagnosis?

- A. Schizophrenia
- B. Anxiety disorder
- C. Manic–depressive disorder
- D. Adjustment disorder with depressed mood
- E. Major depressive episode

Answer 19.3

The correct answer is (D)

Adjustment disorder with mixed mood seems to be similar to the disorder with depressed mood. A comparison between subjects with adjustment disorder, those with specific psychiatric disorder, and those who are not ill indicates that subjects with adjustment disorder differ from the other two groups in the severity of symptoms, psychosocial adaptation, and number and intensity of stressors. A comparison between adjustment disorder with depressed mood and other mood disorders shows that adjustment disorder with depressed mood is a moderate form of depression in terms of both severity of symptoms and degree of social repercussions of the illness. This moderate form of depression is associated with the presence of stressors judged to be severe in younger and better adapted patients likely to display emotional instability in the form of violent behavior, impulsivity, abuse of toxic substances, and even personality disorders with, at the very least, interpersonal problems. The identification and diagnosis of adjustment disorder is not straightforward, but it is important because many of these patients will benefit from counseling.

Further Reading

- Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, hematological, and palliative-care settings: A meta-analysis of 94 interview-based studies. *Lancet Oncol.* 2011;12:160–174.
- Rayner L, Price A, Hotopf M, Higginson IJ. The development of evidence-based European guidelines on the management of depression in palliative cancer care. *Eur J Cancer.* 2011;47:702–712.

Question 19.4

Mr. Troy is a 45-year-old male who has advanced AIDS and Kaposi sarcoma. He has been nonadherent with highly active antiretroviral therapy (HAART) and has a multiple-resistance strain of HIV. He has lost weight and reports a poor appetite. He sleeps poorly. He reports a lack of energy and spends most of his time at home. During a visit to his physician, he reports not having interest in anything in his life. He is comfortable talking about the fact that he will die.

A clinical suspicion of major depression is most supported by which of the following?

- A. Changes in appetite and sleep patterns
- B. Feelings of hopelessness and helplessness
- C. Lack of energy
- D. Comfort in talking about the prospect of death

Answer 19.4

The correct answer is (B)

Persistent low mood, loss of interest in everyday activities, feelings of hopelessness, worthlessness, or guilt, and suicidal ideation are key symptoms of depression in palliative care. It is also important to be aware of nonverbal cues indicative of depression, such as slumped posture, lack of movement, flat affect, and reduced emotional reactivity. Somatic symptoms commonly associated with depression (e.g., appetite change, fatigue, sleep disturbance, psychomotor slowing, and loss of libido) may be due to physical disease or treatment and are therefore less useful in making a diagnosis of depression in palliative care.

Further Reading

- Noorani NH, Montagnini M. Recognizing depression in palliative care patients. *J Palliat Med.* 2007;10:458–464.
- Rayner L, Lee W, Price A, et al. The clinical epidemiology of depression in palliative care and the predictive value of somatic symptoms: Cross-sectional survey with 4-week follow-up. *Palliat Med.* 2011;25(3):229–241.
- Rayner L, Loge JH, Wasteson E, Higginson IJ. The detection of depression in palliative care. *Curr Opin Support Palliat Care.* 2009;3:55–60.

Question 19.5

Mr. Taylor is a 52-year-old male with metastatic renal cell carcinoma s/p nephrectomy and chemotherapy. He has a post-operative pain syndrome with formation of a neuroma with neuropathic pain. Although he is an airline pilot, he has been unable to work for the past year.

This patient might be expected to be suffering in which sphere?

- A. Emotional
- B. Practical
- C. Spiritual
- D. All of the above
- E. None of the above

Answer 19.5

The correct answer is (D)

Suffering is a biopsychosocial, multidimensional construct that includes physical, emotional, as well as spiritual pain. The spirituality and religiosity field is important to consider when evaluating patients with advanced and terminal illness because it can influence coping strategies and quality of life.

Further Reading

Delgado-Guay MO, Hui D, Parsons HA, et al. Spirituality, religiosity, and spiritual pain in advanced cancer patients. *J Pain Symptom Manage.* 2011;41(6):986–994.

Pargament KI, Koenig HG, Tarakeshwar N, Hahn J. Religious coping methods as predictors of psychological, physical and spiritual outcomes among medically ill elderly patients: A two year longitudinal study. *J Health Psychol.* 2004;9:713–730.

Question 19.6

Mr. Ward is a 61-year-old farmer with non-small cell lung cancer metastatic to liver and bone. In talking about the future course of his illness, he begins to cry. His wife is also tearful.

Besides having facial tissues available, what is the next best approach?

- A. Continue with the discussion
- B. Reassure him
- C. Be silent
- D. Tell them to stop crying

Answer 19.6

The correct answer is (C)

There is evidence that open, effective communication promotes coping and psychological adjustment to advanced disease. Skills such as active listening, patient-centered consulting, open-ended questioning, and appropriate response to cues have been found to increase the ability of palliative care professionals to elicit emotional concerns and detect distress before depression develops.

Further Reading

- Lewin SA, Skea ZC, Entwistle V, Zwarenstein M, Dick J. Interventions for providers to promote a patient-centered approach in clinical consultations. *Cochrane Database Syst Rev.* 2001;2001(5):CD003267.
- Ryan H, Schofield P, Cockburn J, et al. How to recognize and manage psychological distress in cancer patients. *Eur J Cancer Care (Engl).* 2005;14:7–15.

Question 19.7

Dr. McDonald is a 74-year-old obstetrician/gynecologist with chronic myelogenous leukemia that recurred after treatment with imatinib and interferon. His counts are controlled with cyclophosphamide. After an office visit, he asks you to help him commit suicide.

You should respond by saying which of the following?

- A. "Tell me more about what you have in mind."
- B. "I would never do that."
- C. "Are you having trouble sleeping?"
- D. "Where do you have pain?"

Answer 19.7

The correct answer is (A)

It has been observed that physicians respond to requests to die by focusing predominantly on determination of the patient's decision-making capacity. It is important to recognize that there is inadequate attention to the underlying meaning and importance of these requests. Exploring what is behind the request is the most appropriate option to pursue. Although competent patients have the right to refuse life-sustaining treatment (and in Oregon and Washington, as well as in Belgium, Luxembourg, and Switzerland, they may request physician-assisted suicide), a compassionate and comprehensive psychiatric evaluation can help clarify both the patient's concerns and the ethically permissible medical options.

Further Reading

Muskin PR. The request to die. *JAMA*. 1998;279:323–328.

Rodin G, Zimmermann C, Rydall A, et al. The desire for hastened death in patients with metastatic cancer. *J Pain Symptom Manage*. 2007;33:661–675.

Walker J, Waters RA, Murray G, et al. Better off dead: Suicidal thoughts in cancer patients. *J Clin Oncol*. 2008;26:4725–4730.

Question 19.8

A 35-year-old male has a history of suicide attempts and has recently been diagnosed with advanced melanoma. Today when you examine him in your office, he seems more depressed than usual. He recently lost his job and has been having marital problems. You ask him if he has suicidal thoughts, and he says that he has on one occasion in the past few days. He says he is “OK” right now, but yesterday he made a plan to shoot himself.

Based on the history, which of the following should you do at this point?

- A. Voluntary hospitalization unless he refuses; then institute involuntary commitment.
- B. Keep him at your office for 3 or 4 hours and observe; if he is OK, then send him home with close follow-up.
- C. Because he is not acutely suicidal in your office, arrange for a visiting nurse to check on him.
- D. Because he is not acutely suicidal in your office, arrange for outpatient follow-up tomorrow.
- E. Voluntary hospitalization; if he refuses, then arrange appropriate follow-up tomorrow.

Answer 19.8

The correct answer is (A)

Evaluation and treatment of a suicidal patient are challenging tasks for the physician. Because no validated predictive tools exist, clinical judgment guides the decision-making process. Although there is insufficient evidence to support routine screening, evidence shows that asking high-risk patients about suicidal intent leads to better outcomes and does not increase the risk of suicide. Important elements of the history that permit evaluation of the seriousness of suicidal ideation include the intent, plan, and means; the availability of social support; previous suicide attempts; and the presence of comorbid psychiatric illness or substance abuse. After intent has been established, inpatient and outpatient management should include ensuring patient safety and medical stabilization, activating support networks, and initiating therapy for psychiatric diseases. Care plans for patients with chronic suicidal ideation include these same steps, as well as referral for specialty care.

Further Reading

Norris D, Clark MS. Evaluation and treatment of the suicidal patient. *Am Fam Physician*. 2012;85(6):602–605.

Question 19.9

Ms. Caroline is a 27-year-old female with advanced breast cancer s/p chemotherapy who is brought in by her husband. He says that she has become a worrywart. She is always worried about her job. She worries about her parents who live 50 miles away. She sometimes worries about her marriage and that her husband does not love her. She worries that they do not have enough money to make it through the month. She has had some episodes of hyperventilation. She does not relate any sleep disturbances or appetite changes. She says she has been worried “all her life.” You diagnose her with generalized anxiety disorder.

In addition to behavioral therapy, which of the following is the best treatment for this disorder?

- A. Haloperidol
- B. Lithium
- C. Clonazepam
- D. Monoamine oxidase inhibitor
- E. Buspirone or similar agent

Answer 19.9

The correct answer is (E)

Bupirone is non-addictive and non-sedating. It is useful in generalized anxiety disorder.

Further Reading

Rayner L, Price A, Hotopf M, Higginson IJ. The development of evidence-based European guidelines on the management of depression in palliative cancer care. *Eur J Cancer*. 2011;47:702–712.

Question 19.10

Ms. Cooper is a 36-year-old female with metastatic breast cancer with metastases to lung and bone who presents with an attack of severe shortness of breath, palpitations, shaking, diffuse numbness, and an intense fear of dying. These attacks are not precipitated by any known factor or event. She is not on any medications and does not consume alcohol. In addition, she is particularly afraid to leave her house unless she can go with someone. Her physical examination is completely normal. A whole “battery” of tests, including thyroid functions, electrolytes, electrocardiogram (ECG), computed tomography of the chest, and ECG Holter monitoring, has been normal.

In addition to cognitive–behavioral therapy, which of the following is the best initial therapy for this woman?

- A. Diazepam
- B. Lithium
- C. Flurazepam
- D. Fluphenazine
- E. Paroxetine

Answer 19.10

The correct answer is (E)

The selective serotonin reuptake inhibitors are the best initial medical therapy for panic attacks/disorders.

Further Reading

Rayner L, Price A, Hotopf M, Higginson IJ. The development of evidence-based European guidelines on the management of depression in palliative cancer care. *Eur J Cancer*. 2011;47:702–712.

20

**Palliative Care in the
Last Hours of Life**

AHSAN AZHAR

Question 20.1

A 63-year-old female with adenocarcinoma of endometrium is admitted to the intensive care unit (ICU) with septic shock. She is in multi-organ failure. After 5 days of aggressive ICU management, the patient's family decides to pursue the palliative care route. Following goals of care discussions with the ICU team, the decision is made to withhold further aggressive management and focus on comfort. The patient is transferred to the acute palliative care unit (APCU). In the APCU, she receives IV fluids at a rate of 42 ml/hr and is on supplemental oxygen. She is minimally responsive with occasional rapid, shallow breathing with groaning. The family members request to know how long the patient will live because they need to inform out-of-state family so they may visit and pay their last respects and also so that the family can prepare for the funeral.

Which of the following is not a predictor of impending death in cancer patients in the last days of life?

- A. Low blood pressure
- B. Nonreactive pupils
- C. Drooping of nasolabial folds
- D. Hyperextension of neck
- E. Grunting of vocal cords

Answer 20.1

The correct answer is (A)

Eight highly specific physical signs that may inform the diagnosis of impending death within 3 days among cancer patients were identified by Hui et al. Signs of impending death, including nonreactive pupils, inability to close eyelids, a decreased response to verbal stimuli, a decreased response to visual stimuli, drooping of nasolabial folds, peripheral cyanosis, pulselessness of the radial artery, and respiration with mandibular movement, were documented more frequently in expected deaths compared to unexpected deaths.

Further Reading

- Bruera S, Chisholm G, Dos Santos R, Bruera E, Hui D. Frequency and factors associated with unexpected death in an acute palliative care unit: Expect the unexpected. *J Pain Symptom Manage*. 2015;49(5):822–827.
- Hui D, Dos Santos R, Chisholm G, et al. Bedside clinical signs associated with impending death in patients with advanced cancer: Preliminary findings of a prospective, longitudinal cohort study. *Cancer*. 2015;121(6):960–967.

Question 20.2

A 54-year-old male with renal cell cancer metastatic to bone has been admitted to the hospital for mental status changes during the past several days. Delirium continues to worsen despite medical management. The palliative care team is consulted to evaluate care options for the patient and provide necessary education to the family regarding end-of-life care. As you enter the room, gurgling and rattling noises are audible from the patient. The patient's wife and other family members are present at the bedside and are visibly distressed. They request information regarding when they may take him home.

Which of the following statements is true regarding terminal secretions?

- A. Terminal secretions are a manifestation of volume overload and pulmonary edema.
- B. Treatment with the anticholinergic atropine is associated with a shorter survival compared with other commonly used anticholinergic agents.
- C. The median survival after the development of terminal secretions is 24 hours.
- D. Terminal secretions are not an objective sign of imminent death.

Answer 20.2

The correct answer is (C)

Terminal secretions are associated with imminent death, with an average life expectancy of 24 hours. In the dying process, patients lose their ability to swallow and clear oral secretions, which then pool in the oropharynx and bronchi. The airflow through these secretions results in the gurgling noise that is referred to as a “death rattle.” It is vital that families be educated about this phenomenon because the noise can be quite distressing for them. Families should be informed that this does not cause any distress for patients per se and is a predictor of death (hours to days, with median survival being less than 24 hours). The maneuver that can provide immediate relief at home by the family is repositioning of the head of the patient to one side. It is simple and avoids the use of muscarinic acetylcholine receptor blockers (anticholinergic drugs) to dry the secretions. Commonly used anticholinergic drugs include glycopyrrolate, scopolamine, atropine, and hyoscyamine. All these drugs have varying degrees of side effects.

Further Reading

- Mercadante S, Villari P, Ferrera P. Refractory death rattle: Deep aspiration facilitates the effects of antisecretory agents. *J Pain Symptom Manage.* 2011;41(3):637–639.
- Morita T, Ichiki T, Tsunoda J, Inoue S, Chihara S. A prospective study on the dying process in terminally ill cancer patients. *Am J Hosp Palliat Care.* 1998;15(4):217–222.
- Wildiers H, Dhaenekint C, Demeulenaere P, et al. Atropine, hyoscyne butylbromide, or scopolamine are equally effective for the treatment of death rattle in terminal care. *J Pain Symptom Manage.* 2009;38(1):124–133.

Question 20.3

The palliative care team at a hospital is participating in the care of a 67-year-old male with end-stage renal disease who stopped dialysis treatments 5 days ago after being on hemodialysis for years. The patient is somnolent except for brief periods of arousal, during which he is increasingly confused. He has an even respiratory pattern and no audible oropharyngeal secretions. His radial pulse remains palpable, and he has faint mottling on his knees. There is a small amount of urine output (<200 ml daily). During a family care conference, his daughter asks how long the dying process will continue.

Which of the following is most accurate regarding the patient's prognosis?

- A. 2 days
- B. 5 days
- C. 10 days
- D. 20 days
- E. Unknown

Answer 20.3

The correct answer is (B)

The median survival for patients after discontinuation of dialysis is 10 days. Prognostication near end of life remains a challenging domain, but nonetheless it is vital to help prepare the family, especially after withdrawal of life-sustaining treatments such as dialysis. Studies indicate that the time to death for patients with chronic kidney disease after discontinuation of hemodialysis ranges from 8 to 12 days, with a median survival of 10 days.

Further Reading

- Cohen LM, Germain MJ, Poppel DM, et al. Dying well after discontinuing the life-support treatment of dialysis. *Arch Intern Med.* 2000;160(16):2513–2518.
- Hirsch DJ. Death from dialysis termination. *Nephrol Dial Transplant.* 1989;4(1):41–44.
- O'Connor NR, Dougherty M, Harris PS, Casarett DJ, et al. Survival after dialysis discontinuation and hospice enrollment for ESRD. *Clin J Am Soc Nephrol.* 2013;8(12):2117–2122.

Question 20.4

An 82-year-old male with a history of chronic obstructive pulmonary disease, end-stage congestive heart failure, and renal impairment has been receiving treatment at his home. His condition rapidly declined over the past few weeks, and the family enrolled the patient in hospice care. The hospice nurse comes for her first visit to enroll the patient on hospice care. While evaluating the patient and discussing hospice benefits and care with the patient and family, his automatic implantable cardioverter–defibrillator (AICD) starts firing rapidly. He is awake, complaining of acute pain, and is noted to be in distress. The family requests to “stop it” and make him comfortable.

What is the immediate step to provide optimal symptom control?

- A. Re-evaluate the patient after the AICD stops firing
- B. Call the AICD manufacturer and request the company send a representative to deactivate the device
- C. Use a magnet and place it over the chest
- D. Administer lorazepam IV stat
- E. Administer morphine IV stat

Answer 20.4

The correct answer is (D)

AICD deactivation must be discussed with patients as part of routine advanced care planning. If the AICD is not deactivated, it may fire and cause extreme distress and pain to the patient. If this occurs, the priority is to provide immediate symptom relief (especially if the patient is awake and in acute distress) with stat benzodiazepine administration while at the same time placing a magnet over the patient's chest, which can temporarily deactivate the AICD feature. Company representative must be contacted thereafter, for technician to make a visit for permanent de-activation of the device to prevent future distress.

Further Reading

- Beets MT, Forringer E. Urgent implantable cardioverter defibrillator deactivation by unconventional means. *J Pain Symptom Manage.* 2011;42(6):941–945.
- Goldstein N, Carlson M, Livote E, Kutner JS. Brief communication: Management of implantable cardioverter-defibrillators in hospice: A nationwide survey. *Ann Intern Med.* 2010;152:296–299.
- Kirk TW. Deactivation of automatic implantable cardioverter-defibrillators in hospice and home care patients at the end of life. *Home Healthc Nurse.* 2008;26(7):431–437.

Question 20.5

A 46-year-old male was diagnosed with glioblastoma multiforme (GBM) 12 months ago. The GBM remains refractory to all treatment. The patient is currently at home under hospice care, unable to swallow, receiving end-of-life care. He develops acute-onset seizures. The continuous care hospice nurse is at the bedside.

What is the best approach to control the seizures?

- A. Midazolam intranasal
- B. Lorazepam sublingual
- C. Diazepam rectal
- D. Morphine subcutaneous

Answer 20.5

The correct answer is (A)

Seizures near the end of life can be extremely distressing not only for the patients but also for the family members. Standard of care is stat benzodiazepine administration. Midazolam intranasal is the fastest acting benzodiazepine available to control intractable and distressing symptoms by rapidly controlling the seizures. Midazolam intranasal can be easily and safely administered by the family at home, compared to a subcutaneous, intravenous, or rectal administration. Further studies are needed to assess the ease of use and efficacy.

Further Reading

- Haut SR, Seinfeld S, Pellock J. Benzodiazepine use in seizure emergencies: A systematic review. *Epilepsy Behav.* 2016;63:109–117.
- Jain P, Sharma S, Dua T, et al. Efficacy and safety of anti-epileptic drugs in patients with active convulsive seizures when no IV access is available: Systematic review and meta-analysis. *Epilepsy Res.* 2016;122:47–55.
- Koekkoek JA, Postma TJ, Heimans JJ, Reijneveld JC, Taphoorn MJ. Antiepileptic drug treatment in the end-of-life phase of glioma patients: A feasibility study. *Support Care Cancer.* 2016;24(4):1633–1638.
- Zelcer M, Goldman RD. Intranasal midazolam for seizure cessation in the community setting. *Can Fam Physician.* 2016;62(7):559–561.

Question 20.6

A 46-year-old male with advanced refractory pancreatic cancer is being treated in an inpatient hospice facility. His symptoms of pain and shortness of breath due to lung metastasis and massive malignant ascites have been well managed with morphine via a continuous infusion using a patient-controlled analgesia (PCA). Over the course of the past 3 days, his urine output has continued to decline and he is more somnolent. Last night, he had episodes of agitation that required additional doses of haloperidol. Foley catheter insertion revealed only 50 ml of dark brown urine. His family is noticing generalized jerking movements of the body and reports that he is having increasing pain not relieved by additional boluses of morphine. He is extremely agitated, crying in pain, and restless.

What is the immediate next step to provide adequate comfort to the patient?

- A. Increase basal rate of morphine on the PCA
- B. Administer chlorpromazine because haloperidol is not working
- C. Administer lorazepam IV stat to provide immediate control of myoclonus
- D. Write orders for opioid rotation to discontinue morphine and initiate fentanyl infusion
- E. Start normal saline at a rate of 100 ml/hr

Answer 20.6

The correct answer is (C)

Renal failure near end of life will lead to accumulation of opioid metabolites normally excreted by the kidneys. In the case of morphine, the metabolite morphine-3-glucuronoid (M3G), which is believed to have no antinociceptive properties, exerts neuroexcitatory effects. Its accumulation leads to opioid-induced neurotoxicity (OIN), including excessive somnolence, agitation, restlessness, myoclonic jerking, and severe agitated delirium with hallucinations, as well as opioid-induced hyperalgesia. Prevention should be practiced, however. In the case of acute OIN features, immediately stop the opioid infusion; prescribe stat benzodiazepine to abate the symptoms; and perform opioid rotation to an opioid not metabolized/cleared by the kidneys, such as fentanyl or methadone. Hydration should be considered but weighed against the risk of worsening the edema, anasarca, or ascites, leading to further distressing symptoms such as dyspnea, especially if the patient has entered the oliguric or anuric phase.

Further Reading

Mercadante S. Pathophysiology and treatment of opioid-related myoclonus in cancer patients. *Pain*. 1998;74(1):5–9.

Mercadante S. Opioid rotation for cancer pain: Rationale and clinical aspects. *Cancer*. 1999;86(9):1856–1866.

Question 20.7

A 46-year-old male with advanced refractory pancreatic cancer is being treated in an inpatient hospice facility. His family has noticed generalized jerking movements of the body and reports that the patient has increasing pain not relieved by additional boluses of morphine. He is extremely agitated, crying in pain, and restless.

What is the next best step?

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- D. Write orders for opioid rotation to discontinue morphine and initiate fentanyl infusion
- E. Start normal saline at a rate of 100 ml/hr

Answer 20.7

The correct answer is (D)

Renal failure near end of life will lead to the accumulation of opioid metabolites normally excreted by the kidneys. In the case of morphine, the metabolite M3G, which is believed to have no antinociceptive properties, exerts neuroexcitatory effects. Its accumulation leads to OIN, including excessive somnolence, agitation, restlessness, myoclonic jerking, and severe agitated delirium with hallucinations, as well as opioid-induced hyperalgesia. Prevention should be practiced, however. In the case of acute OIN features, immediately stop the opioid infusion; prescribe stat benzodiazepine to abate the symptoms; and perform opioid rotation to an opioid not metabolized/cleared by the kidneys, such as fentanyl or methadone. Hydration should be considered but weighed against the risk of worsening the edema, anasarca, or ascites, leading to further distressing symptoms such as dyspnea, especially if the patient has entered the oliguric or anuric phase.

Question 20.8

A 67-year-old female with terminal ovarian cancer is being taken care of at home under hospice care. She complains of increasing thirst. Family is asking about providing hydration. She has poor IV access, and home infusion of IV fluids was not previously recommended due to ascites and shortness of breath. An intraperitoneal catheter has aided the removal of excess ascites, and her shortness of breath has been better. However, she continues to complain of increasing thirst but chokes when attempting to drink water. She also reports distressing hallucinations and periods of confusion. There is occasional myoclonus. In addition to regular mouth care and stopping drugs that may potentiate xerostomia, the hospice nurse calls you, the hospice medical director, to discuss initiation of fluids to provide comfort and relief of symptoms at end of life.

What route will you advise the nurse to use for administration of fluids?

- A. Intravenous; transfer patient to local emergency center for peripherally inserted central catheter line insertion
- B. Subcutaneous (hypodermoclysis)
- C. Rectal (proctoclysis)
- D. Enteral; insert nasogastric tube

Answer 20.8

The correct answer is (B)

Dehydration near end of life can aggravate symptoms such as fatigue, delirium, and myoclonus. However, hydration near end of life has been controversial. In a multicenter study involving patients at end of life, researchers did not find any benefit of giving hydration at 1 l/day in terms of improving symptoms, quality of life, or survival compared with placebo. In summary, matching the daily losses including insensible losses is a guideline that most follow. Another concern with fluid administration is the route of delivery. The enteral route is always preferred, but oral intake universally decreases near end of life, and particularly in cases of intractable nausea, vomiting, or odyno/dysphagia, the parenteral route needs to be considered. Intravenous hydration can be costly as well as logistically challenging. Subcutaneous injections or infusion (hypodermoclysis) of fluids and certain comfort care medications (including opioids, dexamethasone, metoclopramide, and haloperidol) can easily be accomplished by trained family members and avoids attempts to gain IV access, especially when these patients already have poor/fragile veins.

Further Reading

- Bruera E, Hui D, Dalal S, et al. Parenteral hydration in patients with advanced cancer: A multicenter, double-blind, placebo-controlled randomized trial. *J Clin Oncol*. 2013;31(1):111–118.
- Hui D, Dev R, Bruera E. The last days of life: Symptom burden and impact on nutrition and hydration in cancer patients. *Curr Opin Support Palliat Care*. 2015;9(4):346–354.
- Vidal M, Hui D, Williams J, Bruera E. A prospective study of hypodermoclysis performed by caregivers in the home setting. *J Pain Symptom Manage*. 2016;52(4):570–574.

21

Palliative Sedation

PAUL W. WALKER

Question 21.1

A 39-year-old male with advanced lung cancer is admitted to the palliative care unit during your rotation on that service. When you are rounding, he calmly tells you that he wants to be sedated because he has heard that it is a service that the palliative care team provides.

What is palliative sedation?

- A. A treatment of last resort
- B. A treatment used for refractory symptoms
- C. An ethical and legally acceptable treatment
- D. All of the above

Answer 21.1

The correct answer is (D)

Palliative sedation is a treatment of last resort for severe symptoms that are refractory to the management of physicians who specialize in end-of-life care. It implies that physicians expert in symptom management be involved with the assessment and care of the patient. It is a legally and ethically acceptable treatment and is distinct from euthanasia. The goal is to relieve suffering by inducing a decrease in or absence of awareness—a reduction in consciousness—by administering sedating medications.

Further Reading

Cherny HI, Radbruch L. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med.* 2009;23(7):581–593.

Walker PW. Clinical aspects of palliative sedation for refractory symptoms. In: Taboada P, ed. *Sedation at the End-of-Life: An Interdisciplinary Approach*. Dordrecht, the Netherlands: Springer; 2015:27–40.

Question 21.2

After visiting with the patient, the interdisciplinary team discusses his request and considers whether it is reasonable. The charge nurse reports that there are four requirements that are necessary to consider the situation appropriate for performing palliative sedation. One is that the patient must be suffering from a refractory symptom, defined as a symptom that “cannot be adequately controlled despite aggressive efforts to identify a tolerable therapy that does not compromise consciousness.”

Other requirements include which of the following?

- A. A terminal illness must be present.
- B. Death must be imminent (within days).
- C. A do-not-resuscitate order must be in effect.
- D. All of the above.

Answer 21.2

The correct answer is (D)

In addition to having a refractory symptom, the patient must have a terminal illness with death imminent and a do not resuscitate (DNR) in place to be considered appropriate for administration of palliative sedation. This makes it very clear that this treatment is specific to the end of life with the goal to relieve distress via sedation when no other treatments are effective in managing the intractable symptom.

Further Reading

- Braun TC, Hagen NA, Clark A. Development of a clinical practice guideline for palliative sedation. *J Palliat Med.* 2003;6(3):345–350.
- Cherny NI. Palliative sedation. In: Bruera E, Higginson JJ, Ripamonti C, von Gunten C., eds. *Textbook of Palliative Medicine*. Oxford, UK: Hodder Arnold; 2006:976–987.
- Cherny NI, Portney RK. Sedation in the management of refractory symptoms: Guidelines for evaluation and treatment. *J Palliat Care.* 1994;10(2):31–38.

Question 21.3

Before the end of the day, you discuss further with the patient his request to be sedated. He says that he is interested in what is available to help him should he become more short of breath because he has had episodes of breathlessness previously and admits to a fear of suffocating due to his cancer. Currently, he is managing with a low level of dyspnea, and he is relieved by the effectiveness of his opioid regimen as well as your reassurance that he will not be allowed to “suffocate.”

What is the most common refractory symptom for which palliative sedation is used?

- A. Dyspnea
- B. Pain
- C. Delirium
- D. Existential distress

Answer 21.3

The correct answer is (C)

Reasons for sedation vary by country and setting of care, but agitated delirium is by far the most common reason for administration of palliative sedation. This is not surprising given the high incidence of delirium at the end of life. Treatment of refractory dyspnea is the second most common reason. Other conditions include terminal hemorrhage, intractable seizures, uncontrolled pain, and existential distress. Currently, existential distress is controversial, with various arguments present both for and against. Those who advocate for using palliative sedation as treatment for refractory existential distress have outlined that extra measures be considered to ensure that palliative sedation is necessary and administered only for a limited time initially. The patient in this case appears to have his concerns relieved by your discussion and is much less anxious.

Further Reading

Elsayem A, Curry E, Boohene J, et al. Use of palliative sedation for intractable symptoms in the palliative care unit of a comprehensive cancer center. *Support Care Cancer*. 2009;17(1):53–59.

Rousseau P. Existential suffering and palliative sedation: A brief commentary with a proposal for clinical guidelines. *Am J Hosp Palliat Care*. 2001;18(3):151–153.

Question 21.4

The next day on morning rounds, you learn that another of your patients is in severe distress. A 65-year-old female with renal cell carcinoma and brain metastasis has become more confused and agitated overnight. Despite increasing doses of haloperidol and chlorpromazine, she is still climbing out of bed, and she even punched her nurse. Both the family and the nursing staff are very concerned because nothing so far has controlled the situation. You can find no reversible cause for this patient's delirium. You consider that palliative sedation is indicated in this patient's situation because she meets all the criteria for palliative sedation.

What is the next step you should take?

- A. Ask the nurse to set up a midazolam infusion
- B. Talk to the family members about the need for palliative sedation
- C. Ask for a psychiatric consultation
- D. All of the above

Answer 21.4

The correct answer is (B)

Before initiating palliative sedation, it is important that the family understand and agree to the plan of care. They need to understand that the goal of the treatment is to relieve intractable suffering and not to end the patient's life prematurely. They may have questions about whether this treatment is precipitous and should be delayed or whether the sedation will directly or indirectly hasten death. Many serious misunderstandings can be presumed when physicians are required to sedate patients at the end of life. As much as possible, it is important to have open and clear communication with family members and caregivers so that all understand the necessity and goals of treatment. It is then important to document these discussions in the medical record. Checking with the nursing staff to be sure they understand the situation is also appropriate because nurses new to palliative/hospice care may not be familiar with palliative sedation and misconstrue the intent.

Further Reading

- Cherny HI, Radbruch L. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med.* 2009;23(7):581–593.
- Walker PW. Clinical aspects of palliative sedation for refractory symptoms. In: Taboada P, ed. *Sedation at the End-of-Life: An Interdisciplinary Approach*. Dordrecht, the Netherlands: Springer; 2015:27–40.

Question 21.5

After appropriate communication, you place your medication orders for palliative sedation to be administered.

What in your understanding does palliative sedation not include?

- A. Proportional sedation, meaning that the lightest sedation be utilized that will control the refractory symptom
- B. Intermittent, continuous, as well as respite sedation
- C. The primary goal that the patient be sedated until unresponsive.
- D. Light, moderate, or deep sedation

Answer 21.5

The correct answer is (C)

It is a common misconception that there is only one type of palliative sedation—that of deep continuous sedation. Palliative sedation is a heterogeneous collection of sedation types ranging from light to deep sedation and intermittent (including respite sedation) through to continuous. Proportionate sedation is the guiding principle, with the goal being administration of the least amount of sedation possible to achieve control of the patient's suffering due to the refractory symptom.

Further Reading

- Cherny NI. Palliative sedation. In: Bruera E, Higginson IJ, Ripamonti C, von Gunten C., eds. *Textbook of Palliative Medicine*. Oxford, UK: Hodder Arnold; 2006:976–987.
- Cherny HI, Radbruch L. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med*. 2009;23(7):581–593.
- Krakaure E, Quinn T. Sedation in palliative medicine. In: Hanks G, Cherny NI, Christakis NA, et al., eds. *Oxford Textbook of Palliative Medicine*. Oxford, UK: Oxford University Press; 2010:1560–1568.

Question 21.6

Many sedating drugs are available in the pharmacopeia.

Which of the following medications is inappropriate as an agent used for palliative sedation?

- A. Morphine.
- B. Midazolam
- C. Propofol
- D. Chlorpromazine

Answer 21.6

The correct answer is (A)

Use of opioids as sedating agents is not appropriate because sedation is a possible side effect only of a drug for which the primary effect is to provide analgesia. Some patients can tolerate quite high doses of opioid medications without becoming sedated. Other toxicity may occur from the opioid, such as opioid-induced neurotoxicity. It is preferable to use drugs for which the primary effect is sedation, such as drugs from the benzodiazepine class (midazolam is the most common agent used for palliative sedation worldwide), neuroleptics (haloperidol, chlorpromazine, and methotrimeprazine/levopromazine), anesthetic agents (propofol), and barbiturates (phenobarbital, thiopental, pentobarbital, and amobarbital—all used less often now for this indication). In the case of midazolam, an infusion of 1 mg/hr is often used as a starting dose, with titration and bolus doses administered depending on individual response. It is important to monitor the control of the refractory symptom carefully. A tool such as the Richmond Agitation–Sedation Scale helps reliably report the patient’s level of sedation based on responses to verbal and physical stimulation.

Further Reading

- Cherny HI, Radbruch L. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med.* 2009;23(7):581–593.
- Walker PW. Clinical aspects of palliative sedation for refractory symptoms. In: Taboada P, ed. *Sedation at the End-of-Life: An Interdisciplinary Approach*. Dordrecht, the Netherlands: Springer; 2015:27–40.

Question 21.7

Your patient's wife appears uneasy and quietly takes you aside and asks you if the midazolam infusion that has calmed her husband's restlessness and allowed him to rest peacefully will have the effect of shortening his life.

What do you tell her about what the medical literature reports on palliative sedation and its risk for hastening death?

- A. Palliative sedation has been shown in multiple studies not to hasten death.
- B. Palliative sedation hastens death by causing respiratory depression.
- C. Palliative sedation hastens death by increasing the risk of aspiration.
- D. Palliative sedation hastens death by causing hemodynamic compromise.

Answer 21.7

The correct answer is (A)

For many years, it was presumed that palliative sedation shortened the life of patients by causing respiratory depression, aspiration, or hemodynamic compromise. It was considered that this was an acceptable trade-off for symptom control. A plethora of trials (14 to date) have not shown this to be the case. These trials show no significant difference in survival between palliative/hospice patients who receive palliative sedation and those who do not, even with propensity score adjustment. One may speculate that with proper proportional use of these sedating agents, the already significant risk of death in these terminally ill patients may be rather minimally altered. Fortunately, this finding may now remove a possible burden of guilt that clinicians and family members may have had to endure previously.

Further Reading

- Beller EM, van Driel ML, McGregor L, Truong S, Michell G. Palliative pharmacological sedation for terminally ill adults. *Cochrane Database Syst Rev.* 2015;2015(1):CD010206.
- Maeda I, Morita T, Yamaguchi T, et al. Effect of continuous deep sedation on survival in patients with advanced cancer (J-Proval): A propensity score-weighted analysis of a prospective cohort study. *Lancet Oncol.* 2016;17(1):115–122.

22

**Grief and
Bereavement**

RONY DEV

Question 22.1

Which of the following negative feelings during the stages of grief is the most frequent?

- A. Acceptance
- B. Yearning
- C. Depression
- D. Anger
- E. Disbelief

Answer 22.1

The correct answer is (B)

A study examining the stage theory of grief reported a high degree of acceptance among grieving individuals. Yearning was the most frequent negative emotion among grievers, followed by depression, anger, and disbelief. Acceptance was noted in a high degree of individuals, but because it is a positive emotion, it is not the correct response. Depressed mood was noted to peak at 6 months and gradually decrease in frequency. The emotions, in general, did follow the sequence proposed by Kubler-Ross and others (i.e., denial followed by anger, bargaining, depression, and acceptance), but variability in individuals was still noted.

Further Reading

Maciejewski PK, Zhang B, Block SD, Prigerson HG. An empirical examination of the stage theory of grief. *JAMA*. 2007;297(7):716–723.

Question 22.2

Which emotional reaction in an acutely grieving individual would *not* be considered part of a “normal” grief response?

- A. Brief episodes of breathlessness
- B. Ruminating thoughts of the deceased
- C. Fatigue and insomnia
- D. Fleeting thoughts of not wanting to live
- E. Calm acceptance
- F. Loss of appetite

Answer 22.2

The correct answer is (E)

In 1994, Erich Lindemann, after working with bereaved individuals who lost loved ones in a tragic fire in a nightclub, published the first systematic study examining the symptoms of an acute grief response. He found that the normal grief response involved somatic distress, preoccupation with sad memories of a loved one, and feelings of guilt and anger. Emotional distress often presented in waves and was often dominated by reminiscing of the deceased. Grieving individuals would also present with a physical response that could include restlessness, breathlessness, numbness, tremors, sleep disturbances, loss of appetite, fatigue, and somatic aches and pains. Calm acceptance is an unusual response and may indicate a complicated grief disorder.

Further Reading

Lindemann E. Symptomatology and management of acute grief 1944. *Am J Psychiatry*. 1994;151(6 Suppl.):155–160. (Original work published 1994)

Question 22.3

Which of the following is *least* likely to predict a person at risk for persistent complex bereavement disorder (a.k.a. prolonged grief disorder)?

- A. A person's previous grief response
- B. The nature of a person's attachment to the deceased
- C. A person's support network of family and friends
- D. The location and nature of death

Answer 22.3

The correct answer is (A)

Prolonged complex bereavement disorder affects approximately 10%–20% of bereaving individuals. Critical clinical findings include symptoms of grief that disrupt normal function of an individual and persist 6 months or longer after the death of a loved one. Often, the grief reaction is complicated adjustment disorder, clinical depression, anxiety, and substance abuse. An individual's previous response is least likely to predict his or her risk for persistent complex bereavement disorder. Risk factors for persistent complex grief disorder include a person's attachment to an individual, a history of psychiatric disorders or substance abuse, concurrent stressors, and the place of death.

Further Reading

Kissane DW. Bereavement. In: Doyle D, Hanks G, Cherny N, Calman K, eds. *Oxford Textbook of Palliative Medicine*. 3rd ed. New York, NY: Oxford University Press; 2004:1135.

Prigerson HG, Horowitz MJ, Jacobs SC, et al. Prolonged grief disorder: Psychometric validation of criteria proposed for DSM-V and ICD-11. *PLoS Med*. 2009;6(8):e1000121.

Question 22.4

Which of the following would distinguish major depression from anticipatory grief in a cancer patient at the end of life?

- A. Anorexia with cancer cachexia
- B. Persistent thoughts of ending one's life and suicidal ideation
- C. Fatigue and insomnia
- D. Anger and irritability

Answer 22.4

The correct answer is (B)

In patients with terminal illness, symptoms of anticipatory grief present prior to death. Common symptoms such as appetite changes, fatigue, and sleep disturbance may be attributed to the underlying illness and may not distinguish an anticipatory grief response in a patient. Anticipatory grief is a normal process associated with dying and can be difficult to distinguish from clinical depression. In terminally ill patients, anticipatory grief is distinguished by waxing and waning moods, fleeting suicidal thoughts, and anxiety about death. In patients with clinical depression, persistent suicidal ideation, active desire for an early death, anhedonia, and feelings of worthlessness, excessive guilt or hopelessness dominate. Of the choices, persistent thoughts of ending one's life are the strongest indicators of clinical depression.

Further Reading

Birholz G, Gibson JM, Clements PT. Dying patients' thoughts of ending their lives: A pilot study of rural New Mexico. *J Psychosoc Nurs Ment Health Serv.* 2004;42(8):34–44.

Jacobsen JC, Zhang B, Block SK, et al. Distinguishing symptoms of grief and depression in a cohort of advanced cancer patients. *Death Stud.* 2010;34(3):257–273.

Question 22.5

A Native American patient with terminal lung cancer, under your care in hospice, passes away peacefully. The patient caregivers are unsure about proper burial customs and ask your advice.

Which of the following is the most appropriate response?

- A. Arrange a cremation
- B. Leave the deceased on the ground for wild animals to devour
- C. Arrange a mass burial with furs and ornaments
- D. Place the deceased in a canoe fastened to a pole
- E. Obtain counsel from the tribal leader before proceeding with burial

Answer 22.5

The correct answer is (E)

Native American people have various death customs and beliefs that help them cope with the experience of death. Individual tribes maintain their own unique burial customs. Tribes in the Arctic leave the deceased on frozen ground for wild animals to consume. Tribes in the upper Midwest place the deceased in lavish tombs. Because burial customs varied among the different tribes, the most appropriate answer is to obtain counsel from the tribal leader before proceeding with burial.

Further Reading

Native American religion. <http://www.deathreference.com/Me-Nu/Native-American-Religion.html>. Accessed 2017.

Question 22.6

Which of the following is *not* a symptom proposed for the diagnostic criteria for persistent complex bereavement disorder?

- A. Persistent yearning for the deceased
- B. Emotional pain attributed to the death of a loved one
- C. Preoccupation with the deceased
- D. Feeling alone or detached from other people since the death
- E. Trouble sleeping
- F. Bitterness or anger related to the loss

Answer 22.6

The correct answer is (E)

The proposed criteria for persistent complex bereavement disorder include the following:

A. Death of a close other.

B. Since the death, at least one of the following on most days to a clinically significant degree for at least 12 months after the death: (1) persistent yearning for the deceased, (2) intense sorrow and emotional pain in response to death, (3) preoccupation with the deceased, and (4) preoccupation with the circumstance of the death.

C. Since the death, at least six of the following on most days to a clinically significant degree for at least 12 months after the death: (1) marked difficulty accepting the death, (2) disbelief or emotional numbness over the loss, (3) difficulty with positive reminiscing about the deceased, (4) bitterness or anger related to the loss, (5) maladaptive appraisal about oneself in relation to the deceased or the death (e.g., self-blame), (6) excessive avoidance of reminders of the loss, (7) a desire to die to be with the deceased, (8) difficulty trusting other people since the death, (9) feeling alone or detached from other people since the death, (10) feeling that life is meaningless or empty without the deceased or the belief that one cannot function without the deceased, (11) confusion about one's role in life or a diminished sense of one's identity, and (12) difficulty or reluctance to pursue interests or to plan for the future since the loss.

D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

E. The bereavement reaction must be out of proportion or inconsistent with cultural or religious norms.

Further Reading

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Publishing; 2013.

Question 22.7

Members of which of the following religious faiths would avoid medications, such as opioids, in order to remain mindful at the time of death?

- A. Hinduism
- B. Christianity
- C. Buddhism
- D. Islam

Answer 22.7

The correct answer is (C)

Individuals of the Buddhist faith may refuse pain medications or sedatives as they approach death in order to remain mindful. In addition, they may request a shrine or statue of Buddha and prefer an ordained monk or spiritual teacher to chant over them during the dying process. Ideally, the dying process should take place in an environment that is peaceful and calm.

Further Reading

The Buddhist Society. Buddhist funerals. <http://www.thebuddhistsociety.org/page/buddhist-funerals>. Accessed 2017.

23

**Communication
and Teamwork**

EDUARDO BRUERA

Question 23.1

Why is an interdisciplinary team necessary in palliative care?

- A. Multiple clinical situations can be addressed in a much more efficient way when all members of the team conduct assessments and share their findings in real time.
- B. Palliative care interdisciplinary teams have demonstrated the superiority of an established team compared to individual disciplines in improving patients' reported quality of life.
- C. Both A and B.
- D. None of the above.

Answer 23.1

The correct answer is (C)

Palliative care addresses physical, psychosocial, and spiritual dimensions of patients and families. The care is focused on the person rather than on the disease. Although these patients could be seen separately by individuals from various disciplines, that would increase the complexity and the cost of care compared to an interdisciplinary team approach.

The palliative care interdisciplinary team approach in settings such as the acute palliative care unit and the outpatient center has demonstrated the superiority of an established team compared to a non-team approach with individuals from various disciplines.

A patient may complain of pain 10/10 and also give very high scores for most other symptoms on the Edmonton Symptom Assessment Scale. This may be due to severe tumor burden, but it also may be due to somatization of the patient's emotional distress as physical symptoms, delirium generating disinhibition and high expression of symptoms, or it may be related to chemical coping and the need to obtain opioids for another member of the family. An interdisciplinary team is able to interpret the patient-reported symptoms and to generate a joint strategy. A non-team approach might result in the palliative care physician diagnosing a significant component of chemical coping, the counselor diagnosing a significant amount of nociceptive pain, the pharmacist diagnosing inappropriate dosing of opioids, and the rehabilitation and spiritual clinicians perceiving that they should not interact with this patient due to high symptom burden.

Further Reading

Macmillan K, Kashuba L, Emery B. Organization and support of the interdisciplinary team. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine and Supportive Care*. 2nd ed. Boca Raton, FL: CRC Press; 2016:251–256.

Question 23.2

Which of the following are members of the interdisciplinary team?

- A. Palliative care physician
- B. Palliative care nurse
- C. Social workers
- D. Both A and B
- E. All of the above

Answer 23.2

The correct answer is (E)

A palliative care physician and a palliative care nurse are the core members of the interdisciplinary team. However, other team members are needed to provide successful care, including pharmacists, physical and occupational therapists, chaplains, psychologists, social workers, dietitians, integrative medicine practitioners, art therapists, and volunteers.

Most teams have a core group of members from four or five disciplines who see all patients, and members from other disciplines are recruited for the care of patients and/or family members according to the findings of the core group. The composition of the team may change according to patient characteristics. For example, a team delivering care to a large number of patients with end-stage lung disease or lung cancer will frequently have a respiratory therapist as part of the core team.

Further Reading

Macmillan K, Kashuba L, Emery B. Organization and support of the interdisciplinary team. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine and Supportive Care*. 2nd ed. Boca Raton, FL: CRC Press; 2016:251–256.

Question 23.3

Which of the following is the best approach for team members to interact with each other?

- A. Daily interdisciplinary team clinical case discussions
- B. Weekly interdisciplinary team meetings
- C. Family meetings
- D. Both A and B

Answer 23.3

The correct answer is (D)

Most interdisciplinary palliative care team members are in regular contact regarding specific patients. This regular contact involves electronic or in-person discussion of clinical findings and proposed course of action in the ambulatory or consult team areas. It also may include joint visits to patients and families by individuals from multiple disciplines in acute palliative care units, family conferences, or in particularly difficult situations such as those associated with aberrant opioid use or conflict between the patient and the family. In addition, most teams have a weekly 1-hour meeting to discuss particularly difficult patient cases with the purpose of planning care but also to support team members and educate each other on what can be done differently from each discipline's perspective. These meetings also allow for discussion of logistic issues regarding the team functions.

Further Reading

Macmillan K, Kashuba L, Emery B. Organization and support of the interdisciplinary team. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine and Supportive Care*. 2nd ed. Boca Raton, FL: CRC Press; 2016:251–256.

Question 23.4

Which of the following is the best leadership arrangement for interdisciplinary teams?

- A. The program management approach
- B. The vertical management approach
- C. Neither A nor B
- D. Both A and B

Answer 23.4

The correct answer is (A)

A program management approach is ideal for interdisciplinary palliative care teams. As opposed to a vertical approach in which each member of the different disciplines reports to his or her own discipline leader (e.g., Director of Pharmacy, Director of Social Services, Director of Chaplaincy, Director of Rehabilitation Services, and Director of Nursing), program management supports horizontal structures of colleagues working together to deliver care to specific patient populations. The program management approach promotes trust, efficiency, and team identity, and it allows for changes in logistic arrangements to accompany clinic needs rather than the needs of vertical leaders.

Unfortunately, in the majority of cases, the program management approach is difficult to implement because it threatens the power of the vertical structures. Most palliative care interdisciplinary teams work with a combination of vertical and horizontal arrangements. Financial issues are frequently important in determining organizational structure and leadership because some of the interdisciplinary team members, such as physicians and psychologists, are able to bill for their services, whereas others are part of a core global budget of an institution. A large body of evidence supports the major financial savings resulting from the use of interdisciplinary palliative care teams, and this evidence should be used in negotiating program leadership with institutional executives.

Further Reading

Macmillan K, Kashuba L, Emery B. Organization and support of the interdisciplinary team. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine and Supportive Care*. 2nd ed. Boca Raton, FL: CRC Press; 2016:251–256.

24

Family Conference in Palliative Care

MARGARET L. ISAAC
AND J. RANDALL CURTIS

Question 24.1

Ms. C is an 87-year-old female with advanced dementia who is intubated in the intensive care unit (ICU) for the treatment of sepsis. She has two sons and a daughter who speak Cantonese and are not fluent in English. The primary ICU team and palliative care consultation team plan to set up a family conference to address goals of care.

Which of the following is true?

- A. Family members with limited English proficiency (LEP) have been shown to receive similar levels of information and statements of support as English-speaking family members during family conferences.
- B. More explanation by physicians and a correspondingly lower percentage of family speech during family conferences are associated with greater family satisfaction.
- C. Statements of non-abandonment by clinicians have little effect on family members.
- D. Explicit expressions of support for medical decisions are helpful for families.
- E. None of the above.

Answer 24.1

The correct answer is (D)

Explicit expressions of support for medical decisions, including withdrawal of life support, are helpful for families. Family members with LEP actually receive less information and fewer statements of emotional support from clinicians during family conferences. A higher percentage of family speech is associated with greater satisfaction. Statements of non-abandonment, as well as the use of empathic statements and support for medical decisions by surrogates, including the decision to withdraw life support, are associated with increased satisfaction.

Critical aspects of family conferences

Family conferences are among the more complex communication challenges that clinicians navigate. A variety of strategies and approaches are associated with improved outcomes (family satisfaction), including, but not limited to, the following:

- The use of empathic statements
- Explicit support by clinicians for decisions made by surrogates, including the decision to withdraw life support
- Increased percentage of family speech (as opposed to clinician speech)
- Expressions of non-abandonment
- Clarity in provider roles and consistent information and messages delivered by all members of the health care team
- Clinician accessibility and continuity of care

Further Reading

McDonagh JR, Elliott TB, Engelberg RA, et al. Family satisfaction with family conferences about end-of-life care in the ICU: Increased proportion of family speech is associated with increased satisfaction. *Crit Care Med*. 2004;32:1484–1488.

Selph RB, Shiang J, Engelberg RA, Curtis JR, White DB. Empathy and life support decisions in intensive care units. *J Gen Int Med*. 2008;23:1311–1317.

Question 24.2

Mr. B is a 62-year-old male with ischemic cardiomyopathy and metastatic colon cancer who is admitted to the ICU with respiratory failure. His family has been present at the bedside.

Which of the following statements is false?

- A. Utilizing a proactive communication strategy with family members in the ICU can decrease post-traumatic stress disorder-related symptoms and symptoms of anxiety and depression among family members.
- B. Printed communication materials have been shown to improve satisfaction but do not improve family comprehension.
- C. Family members appreciate very complete information from ICU clinicians and are more satisfied when a larger proportion of the family conference is composed of clinician speech.
- D. Pre-meeting is an important strategy to ensure clinician goals and messages are aligned.
- E. Family members of critically ill patients who participate in medical decision-making are at increased risk of post-traumatic stress symptoms.

Answer 24.2

The correct answer is (B)

The use of printed informational materials has been shown to improve family comprehension in the ICU setting. Pre-meeting has been advocated as an important step in family conferences to ensure consistent messaging and goals, particularly when multiple clinicians and teams may be involved. Also, multiple studies have illustrated the difficulties and complications that family members experience during and after a patient's critical illness.

Proactive communication strategies in the ICU

The following steps have been proposed to guide family conferences:

1. Pre-meet—discuss agenda, roles, and desired outcome
2. Introduce—names and roles of participants, agenda setting
3. Assess—solicit family understanding of/perspective on medical situation
4. Update—share information/updates/recommendations, end with the “big picture”
5. Empathize—acknowledge and support emotions
6. Prioritize—elicit the family's perspective on the patient's values/goals and prior statements about treatment preferences
7. Align—bring care plan and patient's values into alignment, discuss next steps

Further Reading

Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. *N Engl J Med*. 2007;356:469–478.

Question 24.3

Ms. D is a 23-year-old female who was in a motor vehicle accident. She sustaining multiple fractures, splenic and liver lacerations, rib fractures and left-sided pneumothorax, and an intracranial hemorrhage. Her parents, brother, and partner have been at the bedside and have been visibly distressed during the two family conferences that have already occurred.

Which of the following has been shown to improve the experience of families/surrogate decision-makers in the ICU setting?

- A. Patient navigators to facilitate communication in the ICU
- B. Shorter length of ICU stay
- C. Involvement of spiritual care services
- D. Restrictions in visiting hours to allow family members opportunities for rest and self-care out of the hospital
- E. Both A and C

Answer 24.3

The correct answer is (E)

The involvement of patient navigators has been shown to decrease depression symptoms in family members. In addition, patients and families who are satisfied with how their spiritual needs are met are more satisfied overall with their care. Longer length of ICU stay is actually associated with greater family satisfaction, perhaps suggesting that having more time to make decisions about goals of care may be beneficial. Open visiting hours and flexible family presence at the bedside are associated with increased family satisfaction.

Patient navigators and communication facilitators to reduce family distress

Communication facilitators/patient navigators are health care workers (commonly nurses or social workers) trained to act as a liaison between critical care teams and families in the ICU. They have expertise in effective clinician–family communication, attachment theory, mediation, and conflict resolution. Use of communication facilitators may improve later mental health outcomes for family members and has been shown to decrease health care costs and ICU length of stay, particularly for patients who die in the ICU.

Further Reading

- Curtis JR, Treece PD, Nielsen EL, et al. Randomized trial of communication facilitators to reduce family distress and intensity of end-of-life care. *Am J Respir Crit Care Med*. 2016;193:154–162.
- Torke AM, Wocial LD, Johns SA, et al. The family navigator: A pilot intervention to support intensive care unit family surrogates. *Am J Crit Care*. 2016;25:498–507.
- White DB, Cua SM, Walk R, et al. Nurse-led intervention to improve surrogate decision making for patients with advanced critical illness. *Am J Crit Care*. 2012;21:396–409.

Question 24.4

Mr. W is a 57-year-old male with morbid obesity, obesity hypoventilation syndrome, pulmonary hypertension, and right-sided heart failure. He is currently admitted to the ICU, where he is being treated for recurrent pneumonia and respiratory failure. He is being ventilated through a tracheostomy, which was placed 2 years ago after multiple ICU admissions requiring intubation and mechanical ventilation. The patient is a high school graduate who previously worked as an airplane mechanic and has been on disability for the past 8 years. His primary care doctor has had multiple conversations with him about goals of care, and he has been consistent in stating that he continues to want any intervention that might prolong his life. He has also been evaluated by the inpatient palliative care consultation team during this admission.

Which of the following statements is true?

- A. End-of-life care preferences are most stable in patients without severe illness.
- B. In-hospital advance care planning may decrease health care costs at the end of life.
- C. End-of-life care preferences are most stable in patients with lower educational attainment.
- D. Advance care planning is associated with an increase in the rate of ICU admissions and ICU length of stay.
- E. Surrogate decision-makers have been shown to have a high degree of accuracy in predicting the care preferences of patients.

Answer 24.4

The correct answer is (B)

End-of-life care preferences have been shown, in a systematic review, to be most stable in inpatients and seriously ill outpatients, in patients with higher educational levels, and among those who participated in advance care planning. Advance care planning is associated with a decrease in the rate of ICU admissions and length of stay. Surrogate decision-makers (both durable power of attorney for health care (DPOA-HC) and legal next of kin) have been found to be incorrect in predicting care preferences one-third of the time.

Advance care planning and end-of-life decision-making

Advance care planning is an important part of the outpatient and inpatient care of chronically and critically ill patients. Although studies have shown that care preferences may not be stable over time in all patients, they tend to be more stable in patients who have serious illnesses. Health care directives are an important tool that can decrease the burden on surrogate decision-makers, many of whom are not able to accurately predict the wishes of their loved one. Inpatient palliative care with advance care planning has been shown to decrease ICU utilization and length of stay and, correspondingly, may also decrease ICU costs. Most important, advance care planning has the promise of allowing patients to be the determining voice in shaping their care at the end of life.

Further Reading

- Aurriemma CL, Nguyen CA, Bronheim R, et al. Stability of end-of-life preferences: A systematic review of the evidence. *JAMA Intern Med.* 2014;174(7):1085–1092.
- Khandelwal N, Benkeser DC, Coe NB, Curtis JR. Potential influence of advance care planning and palliative care consultation on ICU costs for patients with chronic and serious illness. *Crit Care Med.* 2016;44:1474–1481.

Question 24.5

Ms. H is a 52-year-old female with widely metastatic cancer. Her oncologist now believes that further chemotherapy and other cancer-directed therapies would confer more risk than benefit. She has been enrolled in hospice. She indicates during a family conference that she continues to want cardio-pulmonary resuscitation (CPR) and “everything done” should she have a cardiac arrest. The hospice registered nurse asks you, the primary care doctor, to readdress code status with the patient. When the patient is asked about her hopes for the end of her life, she says she would like to die at home, without pain, with her daughter at her side.

Which of the following statements is true?

- A. The personal resuscitation preferences of physicians for their patients differ from those of patients.
- B. Patients typically overestimate the likelihood of survival following resuscitation.
- C. Providing numerical estimates of resuscitation survival has been shown to impact code status preferences.
- D. Framing discussion of resuscitation as part of a larger conversation about goals, hopes, and fears can be an effective strategy.
- E. All of the above are true.

Answer 24.5

The correct answer is (E)

Discussing resuscitation is a critical skill set for outpatient and inpatient clinicians alike because the manner in which code status is addressed with patients impacts the decisions that they make. Physicians are less likely to choose CPR in the setting of life-limiting illness than are patients, and patients, on average, substantially overestimate the likelihood of CPR survival. Evidence suggests that presenting survival estimates can impact the decisions patients make about code status. Often, patients choose to be “full code,” not knowing the likelihood of survival or the degree of dependence and functional limitation that might follow a successful resuscitation. Understanding a patient’s goals, hopes, and fears about the end of his or her life can allow resuscitation preferences to be situated in a larger, more meaningful context. Phrases that might be useful in these conversations include the following:

- “Are there any circumstances in which you think that life would not be worth living? Some patients tell me that if they were so sick that they couldn’t interact with friends and family long term, or if they couldn’t care for themselves and were dependent on others long term, that life wouldn’t be worth living for them. How do you feel?”
- “When you think about the end of your life, what do you hope for?”
- “Have you seen anyone in your life that has had a ‘good death’? A ‘bad death’?”
- “If you should die despite all of our efforts, do you want us to use CPR or other aggressive interventions, or should we allow you to have a natural death?”

Further Reading

Periyakoil VS, Neri E, Fong A, Kraemer H. Do unto others: Doctors’ personal end-of-life resuscitation preferences and their attitudes toward advance directives. *PLoS One*. 2014;9:e98246.

25

Caregiver-Related Concerns

KATHRIN MILBURY

Question 25.1

Mrs. S is overwhelmed by the recurrence of her husband's disease. She feels inadequate to care for him and generally feels helpless. She is anxious about the uncertainty of her husband's disease trajectory.

Which of the following caregiving interventions may be most efficacious in reducing Mrs. S's anxiety?

- A. Information and education
- B. Counseling and psychotherapy
- C. Home care services for the cancer patient
- D. Family meeting
- E. Psychoeducation

Answer 25.1

The correct answer is (A)

Accurate information helps reduce uncertainty and empowers caregivers by giving them a sense of control. Caregivers report wanting information about the cancer, symptom etiology, what to expect in the future, treatment side effects, and how to manage medical emergencies. Information is particularly important at the time of diagnosis, hospitalization, start of new treatments, recurrence, and during the dying phase.

Importantly, across the illness trajectory, due to the wide range of tasks that need to be mastered, caregivers' information needs change over time. In one survey, caregivers indicated they desired symptom management information in the area of pain, weakness, and fatigue as well as resources to facilitate patient care.

Further Reading

- Given BA, Given CW, Kozachik S. Family support in advanced cancer. *CA Cancer J Clin.* 2001;51(4):213–231.
- McCorkle R, Pasacreta JV. Enhancing caregiver outcomes in palliative care. *Cancer Control.* 2001;8(1):36–45.
- Nijboer C, Tempelaar R, Triemstra M, et al. The role of social and psychologic resources in caregiving of cancer patients. *Cancer.* 2001;91(5):1029–1039.
- Wong RK, Franssen E, Szumacher E, et al. What do patients living with advanced cancer and their carers want to know? A needs assessment. *Support Care Cancer.* 2002;10(5):408–415.

Question 25.2

Mrs. G is hospitalized and decisions have to be made about her treatment and care. Her adult children have taken over the role of treatment decision-makers, but you believe there is conflict about priorities and goals. You also sense a discrepancy between the desires of Mrs. G and those of her family.

What instrument might be helpful to assess the situation?

- A. Caregiver Reaction Assessment (CRA)
- B. Caregiver Strain Index (CSI)
- C. Center for Epidemiologic Studies–Depression Scale (CES-D)
- D. Cancer Communication Assessment Tool for Patients and Families (CCAT-PF)

Answer 25.2

The correct answer is (D)

The CCAT-PF is an instrument that assesses congruence in patient–caregiver communication and identifies specific areas of conflict that may be targeted by interventions. Treatment disagreement is problematic because it can complicate decisions-making, leading to poor treatment choices. It is also associated with greater patient depression, higher perceived family conflict and lower family cohesion, and lower patient and caregiver well-being.

The CRA and CSI are validated tools to assess areas of caregiver burden. The CES-D assesses depressive symptoms, and a score of 16 or greater denotes the clinical cut-off for “caseness” warranting further psychological assessment.

Further Reading

- Given CW, Given B, Stommel M, et al. The Caregiver Reaction Assessment (CRA) for caregivers to persons with chronic physical and mental impairments. *Res Nurs Health*. 1992;15(4):271–283.
- Radloff L. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Measure*. 1977;1(3):385–401.
- Robinson BC. Validation of a caregiver strain index. *J Gerontol*. 1983;38(3):344–348.
- Siminoff LA, Rose JH, Zhang A, et al. Measuring discord in treatment decision-making: Progress toward development of a cancer communication and decision-making assessment tool. *Psychooncology*. 2006;15(6):528–540.

Question 25.3

Mrs. M has progressive disease and experiences increasing functional decline.

In which of the following ways would you offer optimal care and support to Mrs. M's family members given the stage of her disease?

- A. Encourage out-of-town family to visit; refer caregivers to disease-specific support groups or counseling; regularly ask about health, well-being, and practical needs of caregivers; offer resources for respite care; after death, send a bereavement card and call after 1 or 2 weeks; screen for complicated bereavement
- B. Inform the patient and family about support groups; ask about practical support needs (e.g., transportation, prescription drug coverage, respite care, and personal care); listen to concerns
- C. Encourage support or counseling for family caregivers; ensure that caregivers have information about practical resources, stress, depression, and adequacy of medical care; identify respite and practical support resources; recommend help from family and friends; raise the possibility of hospice and discuss its benefits; listen to concerns

Answer 25.3

The correct answer is (C)

The family needs practical and emotional support. Option A is best suited for family caregivers of patients with late-stage disease. Option B is best suited for family caregivers of patients with early stage disease at the time of diagnosis.

Further Reading

Morrison RS, Meier DE. Clinical practice: Palliative care. *N Engl J Med*. 2004;350(25):2582–2590.

Question 25.4

Mrs. F is worried about her husband's pain.

When providing education regarding pharmacological pain management, it is important for her to understand which of the following?

- A. Which medications to use for pain relief and when to give a medication
- B. How to assess the efficacy of pain control
- C. How to monitor for side effects
- D. All of the above

Answer 25.4

The correct answer is (D)

Instructing family caregivers on pharmacological issues and medication instructions is important to ensure patient pain management and caregiver efficacy. A caregiver who is afraid of causing addiction, overdosing, or side effects may limit its use or undermedicate the patient. Education regarding appropriate dose and symptom management is important to increase treatment adherence.

Further Reading

Ferrell BR, Grant M, Chan J, et al. The impact of cancer pain education on family caregivers of elderly patients. *Oncol Nurs Forum*. 1995;22(8):1211–1218.

Juarez G, Ferrell BR. Family and caregiver involvement in pain management. *Clin Geriatr Med*. 1996;12(3):531–547.

Question 25.5

Mr. J's disease has progressed, and he is experiencing increasing functional declines. His family is not a tight-knit unit, and family members do not appear to communicate with each other. However, they are very concerned about Mr. J's symptom management and survival, and they are seeking information from the treating physician.

Which of the following interventions may be most efficacious in communicating with the family?

- A. Appointing a family spokesperson
- B. Convening a family meeting
- C. Recommending family therapy
- D. Asking social work to communicate with the family

Answer 25.5

The correct answer is (B)

The family meeting is ideal for eliciting caregiver concerns, providing clear information about treatment, facilitating end-of-life care decisions, and reassuring caregivers that symptoms will be adequately managed and patient preferences will be respected. Family meetings are most effective when the agenda is transparent; a clearly designated staff person leads the meeting; and family members are given the opportunity to ask questions, express concerns, and confront painful emotions with the help of trained and compassionate professionals.

Option A, appointing a family spokesperson, may be best suited for families who are cohesive and harmonious. Option C, family therapy, may be beyond the scope of the oncology team to resolve long-standing family conflict. Regarding option D, asking social work to communicate with the family, it is ideal for family meetings to include a social worker or psychologist to assist with follow-up and support. However, communications with mental health professionals are not intended to substitute for those with treating physicians. One study found that caregivers' burden and distress were reduced if they believed that the treating physician listened to their needs and opinions.

Further Reading

- Azoulay E. The end-of-life family conference: Communication empowers. *Am J Respir Crit Care Med.* 2005;171(8):803–804.
- Emanuel EJ, Fairclough DL, Slutsman J, et al. Assistance from family members, friends, paid care givers, and volunteers in the care of terminally ill patients. *N Engl J Med.* 1999;341(13):956–963.
- Gueguen JA, Bylund CL, Brown RF, et al. Conducting family meetings in palliative care: Themes, techniques, and preliminary evaluation of a communication skills module. *Palliat Support Care.* 2009;7(2):171–179.

26

Ethical and Legal Decision-Making

DONNA S. ZHUKOVSKY,
COLLEEN M. GALLAGHER,
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Question 26.1

Ms. PT is a 63-year-old female with widely metastatic breast cancer who is admitted to the hospital with severe pain and rapidly becomes delirious. She does not have advance directives and has not seen her husband for 15 years. Her significant other, with whom she has lived for the past 10 years, has accompanied her to all medical appointments, as have many of her siblings. Her children visit once or twice a year. Her father is deceased and her mother is a nursing home resident due to extensive care needs.

Who is (are) Ms. PT's appropriate surrogate decision-maker(s)?

- A. The majority of the patient's reasonably available adult children
- B. Her domestic partner
- C. Her husband
- D. Her mother
- E. Her oldest child
- F. As designated by state law or statute

Answer 26.1

The correct answer is (F)

When patients are unable to speak for themselves, clinicians need to turn to individuals familiar with the patients' values to make treatment decisions. This is consistent with the principle of autonomy. There are often multiple parties, including friends and family members, who may be a suitable surrogate decision-maker. Fortunately, many states have passed legislation establishing a hierarchy for appropriate decision-makers. The order of priority varies from state to state, so clinicians must familiarize themselves with the applicable statutes in their jurisdiction. Most statutes will prioritize spouses, adult children, and parents of patients, followed by siblings and other close family members. If the highest ranking individual is unable or unwilling to serve as decision-maker, or after reasonable efforts to contact the individual he or she is unavailable, clinicians must work their way down the list until a willing and able decision-maker can be found. In many states, when the patient does not have a medical power of attorney (MPOA), also known as a durable power of attorney for health care or the equivalent, it is typically a family member or close acquaintance who knows the patient well. Because this varies by geographic location, it is important for clinicians to know the laws and statutes for the state in which they are providing care.

Further Reading

- Beauchamp TL, Childress JF. A framework of standards for surrogate decision making. In: *Principles of Biomedical Ethics*. 6th ed. New York, NY: Oxford University Press; 2008:135–140.
- Chaet DH. The AMA Code of Medical Ethics' opinions on patient decision-making capacity and competence and surrogate decision making. *AMA J Ethics*. 2016;18:601–603.
- Jonsen AR, Siegler M, Winslade WJ. Surrogate decision makers. In: *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine*. 7th ed. New York, NY: McGraw-Hill; 2006:87–90.

Question 26.2

Ms. TM, critically ill from advanced cancer, is sedated and receiving mechanical ventilation in the intensive care unit (ICU). She is separated from her husband, who cannot be located after diligent efforts by your team's social worker. You and the social worker meet with Ms. TM's family and significant other to discuss goals of care. After helping them understand that the patient is unlikely to survive this hospitalization, Ms. TM's mother states that she "wants everything done because she cannot bear to lose her baby." Ms. TM's daughter states that her mother has always been a fighter and would want every opportunity to survive. Her partner tells you that when Ms. TM's father died after a prolonged trial of mechanical ventilation in the ICU last year, she told him that she would never want to live like that.

Whose opinion fits best with commonly accepted bioethical standards of decision-making?

- A. Her mother's
- B. Her daughter's
- C. Her domestic partner's
- D. Her oncologist's

Answer 26.2

The correct answer is (C)

The domestic partner's opinion fits best with commonly accepted bioethical standards of decision-making because he is representing the patient's recently expressed wishes. There are traditionally three standards for surrogate decision-making (SDM). Pure autonomy "applies exclusively to formerly autonomous, now-incompetent patients who expressed a relevant, autonomous treatment preference" that may have been expressed in writing (i.e., in an advance directive) or orally. When expressed wishes are not available, substituted judgment may be used. This standard attempts to construct the patient's preferences based on the surrogate's knowledge of the patient's goals and values. When patients have never had capacity (e.g., children and individuals with cognitive disabilities) or when preferences are unknown, best interests, whereby decisions are made to promote the person's well-being and minimize suffering, may be used. It is important that health care professionals encourage patients to appoint an MPOA, also known as a durable power of attorney for health care, and discuss their goals and values with their MPOA and surrogates so that if SDM becomes necessary, the surrogates have knowledge of patient wishes.

Further Reading

- Beauchamp TL, Childress JF. A framework of standards for surrogate decision making. In: *Principles of Biomedical Ethics*. 6th ed. New York, NY: Oxford University Press; 2008:135–140.
- Berlinger N, Jennings B, Wolf SM. Guidelines for the decision-making process. In: *The Hastings Center Guidelines for Decisions on Life-Sustaining Treatment and Care Near the End of Life*. 2nd ed. New York, NY: Oxford University Press; 2013:43–66.
- Chaet DH. The AMA Code of Medical Ethics' opinions on patient decision-making capacity and competence and surrogate decision making. *AMA J Ethics*. 2016;18:601–603.
- Jonsen AR, Siegler M, Winslade WJ. Surrogate decision makers. In: *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine*. 7th ed. New York, NY: McGraw-Hill; 2010:87–90.
- Sulmasy DP, Snyder L. Substituted interests and best judgments: An integrated model of surrogate decision making. *JAMA*. 2010;304:1946–1947.

Question 26.3

You are the attending physician for a patient with lung cancer who has been admitted for end-of-life care. Prior to admission, he had not used any opioids other than the occasional tablet of hydrocodone/acetaminophen. He denies pain but reports he became severely dyspneic this morning. He does not want any diagnostic studies or interventions other than medications titrated to comfort. You ask the nurse to give him morphine 2 mg IV right away. A new graduate, she comes to you quite distressed 15 minutes later because the patient has died.

This represents an example of which of the following?

- A. Physician-assisted suicide (a.k.a. physician-assisted death)
- B. Euthanasia
- C. The principle of double effect
- D. Sedation for refractory symptoms (a.k.a. palliative sedation)

Answer 26.3

The correct answer is (C)

The clinicians' actions were motivated by a desire to diminish the patient's suffering by lowering his awareness of his dyspnea. Their intention was not to bring about his death (nor was the patient's death a result of medical error). It was entirely foreseeable that administering morphine could result in respiratory depression that would accelerate the patient's death. Nevertheless, the clinician orders morphine to alleviate the patient's suffering despite the risk of death. This decision can be justified under the principle of double effect. When invoking the principle of double effect, the intent is to provide a beneficial outcome while acknowledging that there may be undesirable side effects. The key to the beneficial effect is not by way of the foreseen undesirable effect. Furthermore, the benefits associated with the "good" effect must outweigh the harm that would result in the "bad" effect. For this patient, the intent of using morphine was to relieve dyspnea by altering his perception of dyspnea, not by respiratory depression to accelerate his demise. With physician-assisted death, the intent is to end suffering by providing the patient with the means to end his or her life. Similarly, with euthanasia, the intent is to eliminate suffering by causing death. With sedation for refractory symptoms, the intent is to diminish suffering by lowering awareness.

Further Reading

Berlinger N, Jennings B, Wolf SM. Introduction. In: *The Hastings Center Guidelines for Decisions on Life-Sustaining Treatment and Care Near the End of Life*. 2nd ed. New York, NY: Oxford University Press; 2013:1–8.

Sulmasy DP, Pellegrino ED. The rule of double effect: Clearing up the double talk. *Arch Intern Med*. 1999;159:545–550.

Tulsky JA. Ethics in the practice of palliative care. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine*. 2nd ed. Boca Raton, FL: CRC Press; 2015:119–126.

Question 26.4

Mr. PT is a 44-year-old high school physics teacher who suddenly collapses while teaching class. He is rushed to the local emergency room, where computed tomography scan reveals a massive subdural hematoma. Four weeks later, he still shows no sign of recognizing family or friends, does not have intelligible speech, and cannot follow simple commands. He intermittently opens his eyes and appears to be awake, but he does not consistently track his wife's voice. The attending neurologist performs a comprehensive evaluation and concludes that the patient has brainstem function.

The findings in this patient are consistent with a diagnosis of which of the following?

- A. Locked-in syndrome
- B. Brain death
- C. Persistent vegetative state
- D. Minimally conscious state

Answer 26.4

The correct answer is (D)

Persistent vegetative state (PVS), also termed *unresponsive wakefulness syndrome* by the European Task Force on Disorders of Consciousness, is defined by persistent unconsciousness with intermittent periods of wakefulness. There are no signs of cognitively mediated behavior. Mr. PT does not have locked-in syndrome because he does not have intact cognition. Individuals with locked-in syndrome have intact cognition but are quadriplegic and unable to speak due to lack of motor function required for speech. He is not comatose because he has periods of wakefulness. A diagnosis of coma requires absence of arousal (periods of wakefulness or vigilance) and of awareness (cognition). There is no voluntary eye opening and no purposeful movement. He is not brain dead because he is not in a coma and is spontaneously breathing. Brain death implies absence of cerebral and brainstem function, including absence of brainstem reflexes and apnea. Some states have legal statutes defining clinical states such as brain death that the practitioner should be aware of if involved in such determinations. Individuals with a diagnosis of minimally conscious state may appear similar to those with PVS, but they have definite, albeit minimal, evidence of awareness. Awareness may be of self or of the environment. Demonstration of awareness requires clear and reproducible evidence of one or more of the following: simple command following, gestural or verbal yes/no responses, and intelligible verbalization.

Further Reading

- Bruno MA, Vanhau denhuys e A, Thibaut A, Moonen G, Laureys S. From unresponsive wakefulness to minimally conscious PLUS and functional locked-in syndromes: Recent advances in our understanding of disorders of consciousness. *J Neurol*. 2011;258:1373–1384.
- Seel RT, Sherer M, Whyte J, et al. Assessment scales for disorders of consciousness: Evidence-based recommendations for clinical practice and research. *Arch Phys Med Rehabil*. 2010;91:1795–1813.
- Young GB. Neurologic prognosis after cardiac arrest. *N Engl J Med*. 2009;361:605–611.

Question 26.5

Bobby is a 17-year-old male who has multiply relapsed acute leukemia. Of late, he has had several hospitalizations for respiratory failure due to pneumonia that have resulted in ICU stays, the administration of pressor support, and mechanical ventilation. He tells you, his primary physician, that he does not want to be intubated again and does not want to return to the hospital.

Which of the following do you do now?

- A. Write an out-of-hospital do not resuscitate (OOH DNR) order
- B. Tell him he is not of legal age so that the decisions are not his to make
- C. Request a psychiatry consultation to evaluate him for depression
- D. Explore his understanding of his disease status and ask him to tell you why he made these choices
- E. Both A and C

Answer 26.5

The correct answer is (D)

Decision-making by and for adolescents poses numerous challenges. Unless a mature or emancipated minor, a patient younger than age 18 years is not of legal age to make his or her own medical decisions. For this reason, you cannot automatically give effect to Bobby's treatment preferences by writing an OOH DNR without gathering more information. Option A is therefore incorrect. However, Bobby is 17 years old and may possess the psychological maturity necessary to make treatment decisions for himself. Depending on the patient's diagnosis, prognosis, as well as the likely benefits and burdens of proposed treatment (and with the active involvement of the patient's parent or legal guardian), clinicians may honor the treatment preferences of a mature minor who has demonstrated a clear understanding of the consequences of his or her treatment decisions. For this reason, option B is an inaccurate statement. Deciding to consult psychiatry in evaluation of depression (option C) may be appropriate, but not enough detail is provided in the vignette to make this the single best choice. In this situation, you should engage with the patient to assess his maturity and his level of comprehension of his disease in order to determine whether the patient possesses the insight required to make such a serious decision about his health.

Further Reading

American Medical Association. Opinions on consent, communication and decision making. In: *Code of Medical Ethics*. <https://www.ama-assn.org/sites/default/files/media-browser/code-of-medical-ethics-chapter-2.pdf>. Published 2001. Updated June 2016. Accessed October 5, 2016.

Berlinger N, Jennings B, Wolf SM. Guidelines concerning neonates, infants, children, and adolescents. In: *The Hastings Center Guidelines for Decisions on Life-Sustaining Treatment and Care Near the End of Life*. 2nd ed. New York, NY: Oxford University Press; 2013:67–87.

Question 26.6

KL is a 36-year-old mother of four young children. She has breast cancer metastatic to bone and peritoneum, diagnosed soon after the birth of her youngest child. She has been receiving total parenteral nutrition (TPN) for short bowel syndrome related to Crohn's disease for the past 5 years. She now has multilevel malignant bowel obstruction, with an albumin level of 1.9. She has been advised to discontinue TPN because she has recently had multiple hospital admissions for sepsis related to her TPN line. She states, "I can't give up TPN. It is my source of life."

You do which of the following?

- A. Agree with her and continue TPN
- B. Discuss the changing burdens and benefits of TPN for her in the context of her current medical situation
- C. Discuss with her what would be her most important goals during the next few weeks to months, given the recent decline in her medical condition
- D. Both B and C

Answer 26.6

The correct answer is (D)

TPN has been life-saving for this patient during the past several years but is not any longer, given the change in her medical circumstances. The advanced nature of the cancer and her poor nutritional status, as demonstrated by her low albumin level, are indications of change in efficacy of the TPN, and the frequent hospitalizations related to potentially life-threatening sepsis are indications of increased burden. Option A is not correct because TPN is no longer providing adequate nutritional support and is putting her at increased risk of death from infection. By helping her understand the changing benefits and burdens of TPN in her situation and developing an understanding of her values, goals, and preferences at this time in her life, you participate in shared decision-making to develop a plan that reflects her values, goals, and preferences based on a mutual understanding of her medical circumstances and appropriate care options.

Further Reading

- Ganzini L. Artificial nutrition and hydration at the end of life: Ethics and evidence. *Palliat Support Care*. 2006;4:135–143.
- Geppert CM, Andrews MR, Druyan ME. Ethical issues in artificial nutrition and hydration: A review. *JPEN J Parenter Enteral Nutr*. 2010;34:79–88.
- Hospice and Palliative Nurses Association. Artificial nutrition and hydration in advanced illness. *J Hosp Palliat Nurs*. 2012;14:173–176.
- Institute of Medicine. Clinician–patient communication and advance care planning. In: *Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life*. Washington, DC: National Academies Press; 2015:117–216.

Question 26.7

Mr. SK is an 82-year-old male with metastatic colon cancer who emigrated to the United States several years ago from China and who has progressed through third-line chemotherapy. You have been his physician for the past 2 years, during which time he has repeatedly told you that he does not want treatments that will make him feel ill. You meet with him and his sons to explain that any additional treatment is unlikely to be of benefit but has a high likelihood of toxicity. You recommend hospice care. His sons want him to have additional chemotherapy, to which he agrees.

You do which of the following?

- A. Tell the sons that it is their father's right to make his own medical decisions
- B. Ask the social worker to explore his home situation to determine if there are concerns of abuse
- C. Refer the patient to psychiatry to determine if he has the capacity for medical decision-making
- D. Ask the patient what values are most important to his decision-making

Answer 26.7

The correct answer is (D)

The principle of autonomy presumes that competent individuals are rational moral agents capable of making decisions concerning their own current and future selves based on their own values and interests. In the United States, most competent patients are perceived as prioritizing their own treatment preferences when making medical decisions for themselves. In some cultures, decisions are made more communally, incorporating preferences of friends and family members. Although the value is unfamiliar to some, voluntary subordination of one's own preferences to the preferences of friends and family members is a valid expression of autonomy. Mr. SK may place more value on having his sons decide for him than he does on receiving the care he prefers. Understanding the perspectives of the involved stakeholders will often defuse potential conflicts. Although clinicians should be sensitive and appropriately deferential to value systems different from their own, they should be aware of the possibility of coercion. It is inconsistent with the principle of autonomy for others to *force* the patient into a given course of action. The difference between voluntary subordination and coercion is not always clear, and if concerned, you may wish to consult the psychosocial resources in your institution.

Further Reading

- Furst CJ, Ekblad S. Transcultural palliative care. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine*. 2nd ed. Boca Raton, FL: CRC Press; 2015:137–143.
- Singer PA, Viens AM. Religious and cultural perspectives in bioethics [Section IX]. In: Singer PA, Viens AM, eds. *The Cambridge Textbook of Bioethics*. Cambridge, UK: Cambridge University Press; 2009:379–462.
- Tulsky JA. Ethics in the practice of palliative care. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine*. 2nd ed. Boca Raton, FL: CRC Press; 2015:119–126.

Question 26.8

When obtaining informed consent, which of the following conditions is not necessary?

- A. Disclosure of possible side effects and complications
- B. A formal mental status exam
- C. Freedom from coercion
- D. Knowledge of alternative treatments and their possible outcomes
- E. Both A and B

Answer 26.8

The correct answer is (B)

Informed consent and informed refusal require (1) that the patient have decision-making capacity; (2) disclosure of risks that a *reasonable* person would want to know in deciding whether to receive the particular treatment; (3) comprehension of the disclosed risks and benefits; and (4) voluntariness, meaning the patient is free from coercion by friends, family, or clinicians. Informed consent does not require disclosure of *all* possible side effects and complications of a proposed intervention. A reasonable patient would want to know his or her diagnosis; the nature, risks, benefits, and likelihood of success of the proposed intervention; the nature, risks, benefits, and likelihood of success of alternative treatments; and the likely results of no treatment. Although decision-making capacity is a prerequisite of informed consent, a formal mental status exam is not required every time informed consent is sought from a patient. A formal mental status exam is only necessary if there is reason to suspect that the patient lacks decision-making capacity. The informed consent conversation and the patient's or surrogate's (as appropriate) decision should be documented in the medical record. If written consent is provided, that should also be included in the medical record.

Further Reading

American Medical Association. Opinions on consent, communication and decision making. In: *Code of Medical Ethics*. <https://www.ama-assn.org/sites/default/files/media-browser/code-of-medical-ethics-chapter-2.pdf>. Published 2001. Updated June 2016. Accessed October 5, 2016.

Berlinger N, Jennings B, Wolf SM. Guidelines for the decision-making process. In: *The Hastings Center Guidelines for Decisions on Life-Sustaining Treatment and Care Near the End of Life*. 2nd ed. New York, NY: Oxford University Press; 2013:43–66.

Canterbury v. Spence (464 F.2d 772) 1972. (Court case)

Murray B. Informed consent: What must a physician disclose to a patient? *AMA J Ethics*. 2012;14:563–566.

Question 26.9

Physicians have a moral obligation to not abandon their patients.

Which of the following situations constitutes abandonment?

- A. The physician is not an approved provider for the patient's insurance plan.
- B. The physician does not call the parents of a child who died in the hospital of a chronic illness, even though the physician had spent much time with the family in the hospital.
- C. Without discussing the reasons why with the patient, the physician will not schedule a follow-up appointment with a nonadherent patient.
- D. The physician will not schedule a follow-up appointment with a patient who has been violent in the office on multiple occasions despite explicit discussion of acceptable behavior.
- E. Both C and D.

Answer 26.9

The correct answer is (C)

One of the most fundamental duties is to provide a continuum of care, often referred to as non-abandonment. Option A is incorrect because there is not an established relationship. Option B is incorrect because the physician provided care throughout the child's course, including coverage during periods of absence. Many caring clinicians lose touch with bereaved families for a variety of reasons, including the misperception that contact will cause additional distress for families. However, most families value this contact. Option C is abandonment because before terminating the relationship, the physician must explore reasons for the patient's nonadherence, offer support, and provide explicit conditions for terminating the relationship in advance. Option D is not abandonment because the patient continues to exhibit violent behavior despite prior explanations of what constitutes acceptable behavior in the care setting. For finer nuances about abandonment, clinicians should familiarize themselves with the laws of the state(s) in which they practice.

Further Reading

Jonsen AR, Siegler M, Winslade WJ. Pediatric notes. In: *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine*. 7th ed. New York, NY: McGraw-Hill;2006:99–100.

Question 26.10

When concerned about a patient's capacity for medical decision-making, all of the following are required components of the capacity assessment *except*:

- A. Call psychiatry for a formal mental status evaluation.
- B. Ask the patient to explain what will happen to him or her with and without the proposed treatment.
- C. Ask the patient to tell you about other treatment options.
- D. Ask for the patient's understanding of his or her diagnosis.

Answer 26.10

The correct answer is (A)

Psychiatric consultation can be requested for determination of capacity for medical decision-making, but it is not required. Any physician can assess capacity for medical decision-making. The evaluation should demonstrate if the patient can communicate choices, understand relevant information, appreciate the situation and its consequences relative to him- or herself, manipulate the information rationally, and communicate his or her decision. Clinical tools such as the MacCAT-T can help clinicians make this assessment. Capacity for medical decision-making relates to the specific health care question at hand and may fluctuate over time. In contrast, competency is a legal determination made by a judge that encompasses a broader array of decisions than health care.

Further Reading

American Medical Association. Opinions on consent, communication and decision making. In: *Code of Medical Ethics*. <https://www.ama-assn.org/sites/default/files/media-browser/code-of-medical-ethics-chapter-2.pdf>. Published 2001. Updated June 2016. Accessed October 5, 2016.

Ganzini L, Volicer L, Nelson WA, Fox E, Derse AR. Ten myths about decision-making capacity. *J Am Med Directors Assoc*. 2004;5:263–297. Available at http://www.ethics.va.gov/docs/necrpts/nec_report_20020201_ten_myths_about_dmc.pdf

Grisso TA, Appelbaum PS, Hill-Fotouhi C. The MacCAT-T: A clinical tool to assess patient's capacities to make treatment decisions. *Psychiatr Serv*. 1997;48:1415–1419.

Question 26.11

You are a staff nurse on a hospital unit where one of your neighbors is receiving care. She is a single mother, and you are worried that her 15-year-old twins are on their own during her hospitalization. When you talk with her about your concerns, she says they know how to take care of themselves and will be fine during her hospital stay. She does not see the need for any additional involvement because she has left them alone overnight in the past.

You do which of the following?

- A. Ask other neighbors to keep an eye on them
- B. Tell her that you will let her church community know so they can help
- C. Ask the social worker to meet with her to evaluate the home situation
- D. Call Child Protective Services

Answer 26.11

The correct answer is (C)

Among patients' rights are privacy, confidentiality, treatment refusal, and safety. In the United States, the confidentiality of patient's protected health information is regulated by the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, HIPAA states that a covered entity, including physicians, may not disclose individually identifiable health information about a patient without the patient's consent, unless the disclosure is for a purpose permitted under HIPAA. Permitted purposes include (but are not limited to) treatment, payment, and health care operations. Options A and B are incorrect because disclosing personal health information should be restricted to other health care personnel for the purpose of providing care; to appropriate authorities when disclosure is required by law; and/or when, in the clinician's judgment, the patient is at significant risk of harm to self or others. Otherwise, information should be disclosed only with patient consent. It is acceptable to ask the social worker to meet with the patient to evaluate the home situation to determine if the children are at risk for harm and, if so, to initiate a report to Child Protective Services.

Further Reading

American Medical Association. Opinions on consent, communication and decision making. In: *Code of Medical Ethics*. <https://www.ama-assn.org/sites/default/files/media-browser/code-of-medical-ethics-chapter-2.pdf>. Published 2001. Updated June 2016. Accessed October 5, 2016.

American Medical Association. Opinions on privacy, confidentiality and medical records. In: *Code of Medical Ethics*. <https://www.ama-assn.org/sites/default/files/media-browser/code-of-medical-ethics-chapter-3.pdf>. Published 2001. Updated June 2016. Accessed October 5, 2016.

Berlinger N, Jennings B, Wolf SM. Guidelines for the decision-making process. In: *The Hastings Center Guidelines for Decisions on Life-Sustaining Treatment and Care Near the End of Life*. 2nd ed. New York, NY: Oxford University Press; 2013:43–66.

Question 26.12

You are in the process of admitting a patient from another country to your hospice service. You are just about to ask her to sign consent when her husband asks to sign the consent in her place because he does not want her to know that her life expectancy is 6 months or less, if her cancer follows its natural course. He tells you quite emphatically that in their culture, people are not told when they are dying so that they do not give up hope.

You do which of the following?

- A. Ask the patient to sign consent because she lives in the United States now
- B. Tell the husband that without her knowledge of prognosis, you cannot admit her to hospice care
- C. Ask the patient to tell you about her medical situation and how she likes to make decisions about her health care
- D. Inform the referring physician that she is not a good candidate for hospice

Answer 26.12

The correct answer is (C)

By asking the patient what she understands about her situation and how she likes to make decisions about her care, you are allowing her to exercise her autonomy by prioritizing her values. Although she is from another culture, one cannot automatically assume that she holds the values that predominate in her culture of origin. By asking the patient how she would like treatment decisions to be made, you are treating her as an individual with her own values and goals rather than as a member of a cultural group that may or may not reflect her true beliefs. Option A is incorrect because it demonstrates an imposition of your own values without regard to her preferences. Similarly, option B is incorrect because it signals to the husband that his values are not worthy of respect. Option D is incorrect because she is medically appropriate for hospice care and without further discussion with her, you do not know if her goals fit with the goals of hospice care.

Further Reading

- Beauchamp TL, Childress JF. Veracity. In: *Principles of Biomedical Ethics*. 6th ed. New York, NY: Oxford University Press; 2008:288–295.
- Furst CJ, Ekblad S. Transcultural palliative care. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine*. 2nd ed. Boca Raton, FL: CRC Press; 2015:137–143.
- Herbert PC, Hoffmaster B, Glass KC. Truth telling. In: Singer PA, Viens AM, eds. *The Cambridge Textbook of Bioethics*. New York, NY: Cambridge University Press; 2008:36–42.
- Tulsky JA. Ethics in the practice of palliative care. In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine*. 2nd ed. Boca Raton, FL: CRC Press; 2015:119–126.

27

Prognosis

ROMINA ROSSI, EMANUELA SCARPI,
AND MARCO MALTONI

Question 27.1

Mr. Rossi, a 45-year-old male suffering from glioblastoma, underwent surgery and adjuvant radiochemotherapy. After 3 months, he was diagnosed with relapse, so he underwent second-line chemotherapy. At the same time, the oncologist required a palliative care consultant for supportive care. The patient and his family were followed for 8 months by a palliative care team. During that time, the patient underwent radiosurgery, was an inpatient in hospice for 1 month, and a psychological support was implemented. When he died, the patient was at home with palliative care service, the symptoms were controlled, and the caregiver did not feel alone.

Which of the following is the correct conclusion from this case?

- A. The oncologist got prognostication and communication wrong.
- B. Early palliative care may be useful for good quality of care.
- C. Palliative care is necessary only for end-of-life care.
- D. The referral criteria for palliative care are only cancer trajectory and performance status.

Answer 27.1

The correct answer is (B)

Most health care professionals equate palliative care with end-of-life care. In current clinical practice, palliative care is predominantly offered through hospice care or inpatient consultation only after active treatment has failed or if the oncologist believes that the situation is too complex to manage alone. However, recent studies have shown positive impacts on clinical outcomes, quality of life outcomes, and cost of care by integration of palliative care with anticancer treatment.

In 2010, a pivotal study on the subject by Temel et al. showed an advantage in early palliative care (EPC) with regard to quality of life, depression, and survival in a population of lung cancer patients. A recent study by an Italian group, which examined a population of patients with pancreatic cancer in the metastatic or locally advanced unresectable phase, showed that a systematic EPC approach added to standard cancer care was associated with improved quality of life, mainly on the physical subscale.

A recent review found that there are six major categories for referral criteria in the outpatient palliative care clinic: cancer trajectory, prognosis, physical symptoms, performance status, psychosocial distress, and end-of-life care planning.

Further Reading

Hui D, Meng YC, Bruera S, et al. Referral criteria for outpatient palliative cancer care: A systematic review. *Oncologist*. 2016;21:895–901.

Maltoni M, Scarpi E, Dall'Agata M, et al.; Early Palliative Care Italian Study Group. Systematic versus on-demand early palliative care: Results from a multicentre, randomized clinical trial. *Eur J Cancer*. 2016;65:61–68.

Temel JS, Greer JA, Muzikansky A, et al.; Early palliative care for patients with metastatic non-smallcell lung cancer. *N Engl J Med*. 2010;363:733–742.

Question 27.2

Mrs. Rossi, a 67-year-old female, is suffering from local recurrence of renal liposarcoma and kidney failure (stage IV). On admission to the hospital, Karnofsky Performance Scale was 30% and Palliative Prognostic Score (PaP) was 16.5. At the palliative care consultation, the patient was agitated, dyspneic, and with initial peripheral cyanosis. Urine output was low. The physician communicated the serious prognosis to the husband, but he did not believe it and asked that his wife be admitted to hospice for the best supportive care.

Which of the following clinical signs indicate that a patient's death is imminent?

- A. Dyspnea and agitation
- B. Peripheral cyanosis
- C. Peripheral cyanosis and decreased urine output
- D. Peripheral cyanosis and dyspnea

Answer 27.2

The correct answer is (C)

As patients approach the last days of their lives, they experience a multitude of physiological changes affecting their neurocognitive, cardiovascular, respiratory, and muscular functions. Prior studies suggest that the following are highly diagnostic of impending death in days—the so-called late signs: apnea period, Cheyne–Stokes breathing, death rattle, respiration with mandibular movement, peripheral cyanosis, pulselessness of radial artery, and decreased urine output. Recently, a prospective observational study systematically examined another comprehensive list of signs that represent multiple organ systems and identified eight additional highly specific physical signs of impending death: nonreactive pupils, decreased response to verbal stimuli, decreased response to visual stimuli, inability to close eyelids, drooping of the nasolabial fold, hyperextension of the neck, grunting of the vocal cords, and upper gastrointestinal bleed. The decreased response to verbal stimuli and drooping of nasolabial fold were independently significant in the final multivariate model. All of the late signs occurred only in the last days of life at relatively low frequencies, so their absence cannot rule out imminent death but their presence may be highly predictive.

Further Reading

Hui D, Dos Santos R, Chisholm G, et al. Bedside clinical signs associated with impending death in patients with advanced cancer: Preliminary findings of a prospective longitudinal color study. *Cancer*. 2015;121:960–967.

Question 27.3

Mr. Smith is a 52-year-old male who has locally advanced pancreatic cancer with liver metastases. He has completed two lines of chemotherapy and now has disease progression.

How can life expectancy be prognosticated more accurately?

- A. Clinical prediction of survival (CPS)
- B. Prognostic score
- C. Biological factors
- D. Cancer stage

Answer 27.3

The correct answer is (B)

In advanced phases of the disease, prognostication cannot be based on the same information as in early stages, when it is typically based on tumor stage, histology type/grading, and molecular assessment. On the other hand, if the patient is not near death, there will be no clinical signs of impending death.

A recent review of evidence-based recommendations on the use of prognostic factors in advanced cancer patients suggested that the median survival of the population who underwent palliative care was less than 90 days. The available data showed with strong evidence that prognostic factors of life expectancy in advanced cancer patients are the CPS, performance status, clinical symptoms of cancer anorexia–cachexia syndrome (anorexia, weight loss, dysphagia, and xerostomia), dyspnea, some biological factors (leukocytosis, lymphocytopenia, and C-reactive protein level), and prognostic scores.

Although CPS is a valid and quick tool, the accuracy varies between 20% and 30% because clinicians significantly overestimate survival.

Various validated prognostic scores, such as the PaP score, the Palliative Prognostic Index (PPI), the Palliative Performance Scale (PPS), and the Prognosis in Palliative Care Study (PiPS), are available. In the PaP and its revised version, the D-PaP, delirium is as an additional predictor. The PPI identifies five variables (oral intake, the presence or absence of edema, dyspnea at rest, delirium, and PPS) that are independently predictive of survival. The PPS is a modification of the Karnofsky Performance Scale in which ambulation, activity, self-care, intake, and conscious level are considered. The PiPS predicts whether advanced cancer patients are likely to survive for 14 or 56 days.

Further Reading

Maltoni M, Scarpi E, Pittureri C, et al. Prospective comparison of prognostic scores in palliative care cancer populations. *Oncologist*. 2012;17:446–454.

Question 27.4

Mr. Brown is an 80-year-old male suffering from chronic obstructive pulmonary disease, heart failure, and increased dementia, and he lives at home. After a fall, he became less active, started eating less, and had repeated infections. His family asked the doctor, “What can we do for him? Is he likely to die?”

How can the prognosis in non-cancer chronic illnesses be predicted?

- A. Performance status.
- B. It depends on the type of chronic illness.
- C. Based on the same score used for cancer patients.
- D. There are general indicators, specific clinical indicators, and a negative answer to the “surprise question.”

Answer 27.4

The correct answer is (D)

Prognostication is a clinical challenge in non-cancer chronic illnesses. The trajectory of functional decline in chronic illnesses is different from the end of life in cancer patients. The clinical care pathway in these patients starts with the answer to the “surprise question”: “Would you be surprised if this patient were to die in the next few months, weeks, days?” The answer to this question combines a range of clinical, comorbid, social, and other factors that give a whole picture of deterioration. However, the surprise question alone has a weak prognostic accuracy (slightly more than 50%).

The second requirement to predict the end stage in a chronic illness is the presence of general indicators of decline—general physical decline and increasing need of support, decreasing activity, comorbidity (which is regarded as the major predictive indicator of mortality and morbidity), malnutrition with progressive weight loss, decreasing response to treatment, repeated unplanned/crisis admission, and the occurrence of sentinel events (e.g., a serious fall and bereavement). The following functional assessments should be employed: performance status (the Karnofsky Performance Scale or the Eastern Cooperative Oncology Group scale); the Barthel Index, which describes the basic activities of daily living as “core” to the functional assessment (e.g., feeding, bathing, grooming, dressing, continence, toileting, transfer, mobility, and coping with stairs); and the PULSE screening assessment that take in consideration the Psychological condition, Upper limb function, Lower limb function, Sensory and Environment.

The third requirement of prediction is the presence of specific clinical indicators in advanced non-cancer illnesses that are associated with poor prognosis.

Further Reading

Salpeter SR, Luo EJ, Malter DS, Stuart B. Systematic review of noncancer presentation with a median survival of 6 months or less. *Am J Med.* 2012;125:512.e1–6.

Question 27.5

A 71-year-old male patient has a plurimetastatic squamous cell carcinoma. He has just terminated second-line chemotherapy. He had a Karnofsky Performance Scale of 60%, dyspnea (numerical rating scale = 5), and anorexia.

Which other prognostic factors are necessary to estimate prognosis by PaP score?

- A. Clinical Prediction of Survival (CPS) and percentage of red blood cells
- B. CPS, lymphocyte percentage, and total white blood cell count
- C. CPS
- D. Pain and delirium measurement

Answer 27.5

The correct answer is (B)

The PaP score is used to predict overall survival in advanced cancer patients. The score was obtained from a Weibull multivariate regression model including Karnofsky Performance Status score, CPS in weeks, anorexia, dyspnea, total white blood cell count, and lymphocyte percentage. These variables were chosen after a backward selection procedure from a set of 34 biological and clinical factors. The sum of partial scores of each of the six variables gave the PaP score. Total scores are in the range of 0 to 17.5, and patients are assigned to three different risk groups according to a “30-day survival probability”: group A probability, >70%; group B probability, 30%–70%; and group C probability, <30%. According to the PaP score, the median survival times are 64 days in group A (30-day survival probability, 82.0%), 32 days in group B (30-day survival probability, 52.7%), and 11 days in group C (30-day survival probability, 9.6%).

The PaP score was successfully validated on an independent case series and has only recently been used in clinical practice.

The weakness of this score is that CPS is a subjective assessment, and it is known that clinicians overestimate survival. Moreover, another drawback is the heavy weight that is attributed to the CPS. Less criticized is the necessity of blood sample.

Further Reading

- Glare P, Virik K. Independent prospective validation of the Pap score in terminally ill patients referred to a hospital-based palliative medicine consultation service. *J Pain Symptom Manage.* 2001;5:891–898.
- Maltoni M, Nanni O, Pirovano M, et al. Successful validation of the Palliative Prognostic Score in terminally ill cancer patients: Italian Multicenter Study Group on Palliative Care. *J Pain Symptom Manage.* 1999;17:240–247.

Question 27.6

The purpose of a risk prediction model is to provide an estimate of an individual's risk of developing an outcome. The estimate can then be used to guide interventions to prevent the outcome. A good risk prediction model will predict these risks accurately. There are three commonly used methods to assess the accuracy for predicting clinical outcomes: discrimination, calibration, and reclassification.

Which of the following is the most appropriate method for assessing discrimination in survival analysis?

- A. Hosmer–Lemeshow statistic
- B. Area under the receiver operator curve (AUC ROC)
- C. Harrell's C-index
- D. Net reclassification improvement

Answer 27.6

The correct answer is (C)

Discrimination measures how well a prognostic model distinguishes (discriminates) individuals with and without the outcome of interest (dead/alive, event/non-event). It is commonly assessed by Harrell's C-index. The C-index is the probability that a randomly selected patient with the event will have a higher predicted risk than a randomly selected patient without the event. A value of 0.5 indicates no predictive discrimination and a value of 1.0 indicates perfect separation of patients with different outcomes. To be statistically significant, the C-index should have a 95% Confidence Interval not including 0.5. For example, in a hypothetical experiment in which we randomly select pairs of patients with and without the event of interest, we obtain a C-index of 0.64 (95% Confidence Interval 0.25-1.00). Because the 95% Confidence Interval includes 0.5, the C-index is not statistically significant and therefore the prognostic model does not distinguish the status of interest well.

Limitation of C-index is that it may be insensitive to clinically important risk differences because it assess risk rankings and does not take into account relative differences in risk magnitude. Moreover, it is less sensitive to the addition to a novel prognostic marker to an existing model and other statistics should be used to assess the degree of improvement with addition of the new factor (for example, Integrated Discrimination Improvement, based on integrated sensitivity and specificity).

Further Reading

Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker: From area under the ROC curve to reclassification and beyond. *Stat Med*. 2008;27:157-172.

Question 27.7

An existing and validated prognostic score predicts survival in terminally ill cancer patients. This prognostic score assigns patients to three different risk groups according to a 30-day survival probability. Suppose that the prognostic index would be improved by incorporating a new important prognostic factor.

How to estimate the validity of the new revised prognostic index?

- A. Akaike Information Criteria
- B. “calibration by validation” method
- C. sensitivity and specificity
- D. Area under the receiver operating characteristic curve (AUC ROC)

Answer 27.7

The correct answer is (B)

A prognostic index is usually derived from a regression model as a weighted means of the covariates (prognostic factors), with weights (partial scores) proportional to the parameter estimates.

The “calibration by validation” method, proposed by Van Houwelingen and adapted by Miceli et al. for establishing a prognostic index for classification purposes, allows the revision of an existing prognostic index by introducing a new covariate in the model.

The score revision is performed by including the original prognostic index and the new prognostic factor in a multivariable model. The model parameter estimates are used to calculate the partial score for the new prognostic factor and the revised cut-offs to define the prognostic groups in such a way as to leave the partial scores for the variables originally contributing to the prognostic index unchanged.

The revised prognostic index is obtained by summing the original prognostic index and the partial score of the newly included prognostic factor without affecting the partial scores of the original tool.

With this method, the validation and revision will not necessarily affect the original prognostic index but can be handled by suitably modifying the cut-off values used to define the prognostic groups.

Further Reading

Miceli R, Lusa L, Mariani L. Revising a prognostic index developed for classification purpose: an application to gastric cancer. *Tumori*. 2005;91:221–226.

Scarpi E, Maltoni M, Miceli R, et al. Survival prediction for terminally ill cancer patients: Revision of the Palliative Prognostic Score with incorporation of delirium. *Oncologist*. 2011;16:1793–1799.

Van Houwelingen HC. Validation, calibration, revision and combination of prognostic survival models. *Stat Med*. 2000;19:3401–3415.

28

**Challenging
Conversations
in Palliative Care**

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Question 28.1

A 49-year-old male with cerebral hemorrhage was admitted to the intensive care unit 3 days ago. A family conference was arranged to determine goals of care with the attending physician, resident physician, registered nurse, and the patient's spouse and adult children. The family members are anxious to learn about his condition and prognosis. The physician discusses the patient's case, sometimes deferring to the resident physician and nurse, who have more knowledge of the patient's day-to-day status.

The family members' satisfaction with the conference is most likely to be associated with which of the following?

- A. Experience of the attending physician
- B. Length of the meeting
- C. Percentage of time the nurse spoke
- D. Percentage of time the family members spoke

Answer 28.1

The correct answer is (D)

The percentage of time family members speak during a family conference has been shown to be significantly associated with improved family satisfaction with the meeting. In addition, the greater percentage of time family members speak significantly decreases the family's perception of conflict between the family and the physician.

Further Reading

McDonagh JR, Elliott TB, Engleberg RA, et al. Family satisfaction with family conferences about end-of-life care in the intensive care unit: Increased proportion of family speech is associated with increased satisfaction. *Crit Care Med.* 2004;32:1484–1488.

Question 28.2

A 76-year-old female with advanced dementia on enteral tube feeding who developed aspiration pneumonia is admitted to hospice. She is nonverbal and is accompanied by her husband. Religious items were found bedside. As goals of care were being discussed, her husband mentioned that it is not appropriate to make any plans because God decides when people die.

Which of the following interventions is the most appropriate initial step?

- A. Ask the chaplain in the hospital to visit with the husband.
- B. Offer to arrange a meeting with the husband and the family's pastor.
- C. Reassure the patient's husband that everything will be done for his wife.
- D. Clarify the husband's spiritual beliefs with regard to end-of-life care.

Answer 28.2

The correct answer is (D)

When a patient or family member raises a spiritual or religious issue, the most appropriate first response is to take a spiritual history. In this case, clarification of the husband's comment is safe and provides the physician a better understanding of the context of the conversation and background of the husband. Such an exploration can also be a validation of the husband and his spiritual beliefs—a validation that may enhance the husband's trust of the physician. An understanding of the husband's spiritual position will allow the physician to discuss the situation in terms relevant to the husband and highlight which interventions and services may be helpful.

Further Reading

Okon TR. Spiritual, religious, and existential aspects of palliative care. *J Palliat Med.* 2005;8(2):392–414.

Question 28.3

A 77-year-old male with metastatic prostate cancer is being admitted to hospice. You are doing a home visit, and you notice religious cards and crucifixes in his house. He seems depressed, and upon asking about his mood, he states, “I don’t know why this is happening. I’ve believed in God and lived in faith all my life, and now that I am in this condition, I’m not sure if I believe anymore.” Your religious beliefs are different from those of the patient.

What is the best response right now?

- A. Offer to pray with the patient.
- B. Counsel the patient that God is still present in his life.
- C. Ask the patient to speak more about his concerns and provide supportive listening.
- D. Apologize to the patient that you are not able to address his religious concern and ask the chaplain to visit.

Answer 28.3

The correct answer is (C)

Many patients raise spiritual or religious concerns at the end of life. Palliative physicians are not experts in spiritual care but should develop the skill of taking a basic spiritual history and be able to provide a listening presence to the patient who wants to discuss spiritual or religious concerns. Some techniques that physicians can use to investigate religious or spiritual concerns with patients include asking open-ended questions, asking the patient to say more, using empathic comments, and asking about emotional concerns. In this case, as the physician, you might respond to the patient by saying, “It must be really hard to feel that way” and then ask an open-ended question, such as “Tell me more about the role of God and the church in your life.” Some pitfalls for the physician to avoid include offering answers or solutions to the patient’s spiritual dilemma, imposing the physician’s own beliefs on the patient, and providing premature reassurance.

Further Reading

- Lo B, Ruston D, Kates LW, et al. Discussing religious and spiritual issues at the end of life: A practical guide for physicians. *JAMA*. 2002;287(6):749–754.
- Sulmasy DP. Spirituality, religion, and clinical care. *Chest*. 2009;135(6):1634–1642.

Question 28.4

A 65-year-old female diagnosed with metastatic lung cancer presents to your clinic after deciding not to pursue chemotherapy and to instead focus on quality of life. She hopes to make it to her granddaughter's wedding in 12 months, but given her poor performance status, you estimate her prognosis to be less than 6 months. She mentions that she believes in positive thinking and prayer and that "hope is all I can reach for." During the visit, the patient and her family ask you for an estimate of her prognosis. After exploring this request, you find that they all want explicit information.

How can you best meet this request but also support the patient's hope?

- A. Tell the patient and her family that you do not know what lies ahead but you will support them no matter what happens.
- B. Tell the patient that you do not know what lies ahead but you will support her no matter what happens, and then separately discuss the prognosis with her family members so they can help make decisions.
- C. Disclose the bad news about her realistic prognosis in a straightforward but compassionate way to the patient and her family.
- D. Disclose only the most optimistic estimates of prognosis to support hope.

Answer 28.4

The correct answer is (C)

Although hope is an important construct for many patients, including the woman in this case, who was clear about wanting explicit information about her prognosis, data suggest that withholding the prognosis is not viewed as an acceptable way of maintaining hope for most patients. Patients and families state that prognostic information helps them make emotional and logistic preparations for death. There is also the suggestion in the literature that patients and surrogates turn to other sources of hope besides their physician. Hope-giving characteristics in a physician include offering the most up-to-date treatment, appearing knowledgeable, telling patients that pain will be controlled, discussing all treatment options, and appropriately using humor.

Further Reading

Apatira L, Boyd EA, Malvar G, et al. Hope, truth, and preparing for death: Perspectives of surrogate decision makers. *Ann Intern Med.* 2008;149(12):861–868.

Question 28.5

A 70-year-old Chinese woman has had progressive weakness on her right side for the past month. Her daughter is her primary caregiver and medical power of attorney. The patient does not speak English. Her family members, who speak to her in Mandarin, state that she appears to be intermittently confused. She denies pain, but they notice that her facial expressions and grunts indicate otherwise. Magnetic resonance imaging of the brain showed a large mass in the left hemisphere. She had told her family previously that she can handle anything except cancer. For this reason, her family would like to withhold this information from her. They tell her instead that she had a stroke, and they decline further testing and radiotherapy.

What is the next best step to take in the care of this patient?

- A. Avoid the term “cancer” in discussions with the patient.
- B. Discuss with the family members their concerns and follow with a discussion of the process of decision-making with the patient and family using an interpreter.
- C. Speak to the patient without the family present using a Mandarin interpreter.
- D. Evaluate the patient’s decision-making capacity with a family member translating.

Answer 28.5

The correct answer is (B)

Cross-cultural issues are particularly challenging at the end of life. These challenges have to do with both language issues and decision-making issues. In most cultures, decisions are not made solely by the individual but, rather, by family consensus or even by a community. Even in Anglo-Saxon cultures, in which individual autonomy is treasured, patients rarely make decisions in a vacuum without consideration of their family. Involvement of the family in the decision-making process is consistent with the palliative care approach of treating the patient and family as the unit of care. Discussions on how decisions should be made and who should participate do not require disclosure of medical information. If this patient cannot or does not want to participate in the decision, then medical information does not need to be provided to her.

Further Reading

Hallenbeck J, Arnold R. A request for nondisclosure: Don't tell mother. *J Clin Oncol.* 2007;25:5030–5034.

Question 28.6

A 7-year-old male is under the care of the home hospice team secondary to medulloblastoma. He has a 4-year-old sister, who is witnessing her brother's physical and cognitive decline and also her parents' stress and sorrow. Her parents ask for advice about how to address their daughter's concerns.

What is the best recommendation for the parents?

- A. Make sure she is present when her brother dies.
- B. Discourage the sister from seeing her brother in his last days.
- C. Use euphemisms to describe death.
- D. Encourage her to attend the funeral.

Answer 28.6

The correct answer is (D)

Children as young as age 2 years are beginning to develop a concept of death, and participation in death rituals can assist in helping young children grieve in a healthy manner. Strong emotions should be allowed but not necessarily expected because many young children express their feelings of sorrow and fear through play rather than more “adult” expressions of grief. Children will often “self-titrate” their expressions of emotions based on what they feel ready to experience. Expecting tears or discouraging laughter can interrupt this important self-regulation of grief. Providing the foundation and support regarding the loss and grief is most helpful.

Further Reading

Himmelstein BP. Palliative care for infants, children, adolescents, and their families. *J Palliat Med.* 2006;9(1):163–181.

Himmelstein BP, Hilden JM, Boldt AM, Weissman D. Pediatric palliative care. *N Engl J Med.* 2004;350:1752–1762.

Question 28.7

A 40-year-old female with end-stage recurrent breast cancer with brain metastases is now somnolent in the palliative care unit. As her palliative care physician, you are asked by her husband for advice about how he should address the grief and bereavement needs of the couple's 4-year-old daughter.

Which of the following recommendations is best supported by evidence?

- A. Wait for the child to ask questions, and answer in an age-appropriate manner.
- B. Refer the child to a child psychologist for cognitive-behavioral therapy.
- C. Refer the child to a child play therapy expert.
- D. Maintain daily routines to help the child feel secure.

Answer 28.7

The correct answer is (C)

Child play therapy can be used for children as young as 2 or 3 years. It involves activities such as drawing pictures or molding clay, playing with puppets or sand, and therapeutic storytelling. Sessions typically last 30–45 minutes and provide a venue in which children can be coached on strategies to cope with difficulties they may be encountering in their lives. Child play therapy has been shown through research to be an effective intervention in improving outcomes for children who are bereaved or traumatized by the illness or death of a beloved adult or sibling.

Further Reading

Dowdney L. Childhood bereavement following parental death. *J Child Psychol Psychiatry*. 2000;41(7):819–830.

Kaduson HG, Schaefer CE. *Contemporary Play Therapy: Theory, Research and Practice*. New York, NY: Guilford; 2007.

29

**Pediatric
Palliative Care**

KEVIN MADDEN

Question 29.1

Kate is a 16-year-old female with metastatic gastric adenocarcinoma. Dr. Jones, her pediatric oncologist, tells you that her cancer has been unresponsive to chemotherapy and there are no further disease-directed therapies. Kate's parents understand that she can no longer be cured. During your consultation, Kate's parents request that you not tell her about her poor prognosis.

Which of the following is the best *initial* response to Kate's parents?

- A. "I know how you must feel. I of course will not share any information you do not want me to with her."
- B. "I am sure that Dr. Jones has some other therapies that may give you hope."
- C. "Can you tell me more about why you do not want to tell Kate?"
- D. "I may be able to find another physician who can enroll her in a Phase I trial if you'd like."
- E. "Research shows that parents who do not tell their child that they are dying often regret this decision."

Answer 29.1

The correct answer is (C)

Health care professionals tend to comply with parents' well-intentioned, but potentially harmful, requests for nondisclosure out of respect for parental decision-making authority. Uncertainty and fear often drive the parental request, and so the first step is to explore the parents' fears about telling their child. Guidelines stress the importance of age- and developmentally appropriate communication with the child, including discussions about health care decision-making from the beginning.

Although option E is true, it should not be your *initial* response to the parents' request. Research has shown that no parent whose child died regretted being honest with the child about his or her diagnosis, whereas up to 25% of parents who did not disclose information regretted the decision after the child's death.

Further Reading

Freyer DR. Care of the dying adolescent: Special considerations. *Pediatrics*. 2004;113(2):381–388.

Goldberg A, Frader J. Holding on and letting go: Ethical issues regarding the care of children with cancer. *Cancer Treat Res*. 2008;140:173–194.

Kreicbergs U, Valdimarsdottir U, Onelov E, Henter JI, Steineck G.

Talking about death with children who have severe malignant disease. *N Engl J Med*. 2004;351(12):1175–1186.

Question 29.2

The following day, Kate is in significant pain. Dr. Jones confides in you that the parents are asking for increased doses of morphine, but she is concerned that they are “trying to move things along.”

Which of the following is the best response?

- A. “It sounds like her parents want to shield their daughter from knowing what is really going on.”
- B. “Don’t worry; it is a myth that opioids hasten death at the end of life.”
- C. “It is not uncommon for parents to have thoughts of hastening a child’s death, but it almost always signals significant emotional distress in the parent.”
- D. “It sounds like we should consider palliative sedation.”

Answer 29.2

The correct answer is (C)

It is almost unbearable for a parent to bear witness to the death of his or her child. In fact, in one study, approximately one out of every three parents would have considered hastening death for their child under certain circumstances, with uncontrolled pain being the most likely reason.

Option A is incorrect because it is speculative, as is the statement that the parents are “trying to move things along.” Option B is incorrect because it is not only factually not true but also dismissive of the real conflict that Dr. Jones is encountering. Option D is incorrect because palliative sedation would only be considered when the pain is refractory to standard opioid therapy.

Further Reading

Dussel V, Joffe S, Hilden JM, et al. Considerations about hastening death among parents of children who die of cancer. *Arch Pediatr Adolesc Med.* 2010;164(3):231–237.

Question 29.3

A few days later, Kate's clinical condition worsens. She has worsening dyspnea due to metastatic disease. With your guidance and support, her parents have lovingly and compassionately explained to her that she is dying. Kate worries that she will have tremendous suffering and suffocate. She Googled "sedation at the end of life" and asks whether she would be a candidate.

Which of the following is the most accurate statement about palliative sedation in children?

- A. Rapid titration of opioids is initiated until the patient becomes apneic.
- B. It cannot be done in children because they are minors.
- C. It cannot be done in children because it is euthanasia.
- D. It is an ethical intervention for children who have symptoms that are refractory to standard therapy.

Answer 29.3

The correct answer is (D)

Palliative sedation is an ethical intervention for both children and adults for the treatment of symptoms that are refractory. Cherny and Portenoy's definition of refractory has three crucial components:

1. Intensive efforts short of sedation fail to provide relief.
2. Additional invasive or non-invasive treatments are incapable of providing relief.
3. Additional therapies are associated with excessive or unacceptable morbidity, or they are unlikely to provide relief within a reasonable time frame.

Option C is incorrect because palliative sedation is not the same as euthanasia. Death may occur during palliative sedation, but the *principle of double effect* provides the ethical foundation to justify the practice:

- The nature of the act is itself good, or at least morally neutral.
- The agent intends the good effect and not the bad either as a means to the good or as an end itself.
- The good effect outweighs the bad effect in circumstances sufficiently grave to justify causing the bad effect and the agent exercises due diligence to minimize the harm.

Option A is incorrect because this would be euthanasia. Option B is incorrect because palliative sedation can be performed in both children and adults.

Further Reading

Cavanaugh TA. *Double-Effect Reasoning: Doing Good and Avoiding Evil*. New York, NY: Oxford University Press; 2006.

Cherny NI, Portenoy RK. Sedation in the management of refractory symptoms: Guidelines for evaluation and treatment. *J Palliat Care*. 1994;10(2):31–38.

Question 29.4

John is a previously healthy 10-year-old male brought to the emergency department with fever, cough, and rhinorrhea. Last week, his 7-year-old sister, Lauren, was diagnosed with a viral upper respiratory infection. While receiving an albuterol treatment, he loses consciousness. Cardiopulmonary resuscitation is unsuccessful and he dies.

Which of the following statements is true?

- A. His parents will likely have emotional closure within 6 months to 1 year.
- B. The risk of anxiety and depression in fathers is greater if the child is older than age 8 years.
- C. The risk of overwhelming grief is equal for both the mother and the father.
- D. The incidence of separation or divorce is higher in couples whose child has died.
- E. All of the above.

Answer 29.4

The correct answer is (B)

The risk of anxiety and depression in fathers of deceased children is twice as high if the child was older than age 8 years at the time of death.

The death of a child is one of life's most stressful events. Studies suggest it may take 4–6 years to “work through” the death of a child.

In most families, the mother is the primary caregiver. Thus, mothers experience overwhelming grief more frequently than do fathers.

Contrary to popular belief, parents are *less likely* to separate or divorce following the death of a child.

Further Reading

Barrera M, D'Agostino NM, Schneiderman G, et al. Patterns of parental bereavement following the loss of a child and related factors. *Omega*. 2007;55(2):145–167.

Eilegard A, Kreicbergs U. Risk of parental dissolution of partnership following the loss of a child to cancer: A population-based long-term follow-up. *Arch Pediatr Adolesc Med*. 2010;164(1):100–101.

Kreicbergs U, Valdimarsdottir U, Onelov E, Henter JI, Steineck G. Anxiety and depression in parents 4–9 years after the loss of a child owing to a malignancy: A population-based follow-up. *Psychol Med*. 2004;34(8):1431–1441.

Kreicbergs UC, Lannen P, Onelov E, Wolfe J. Parental grief after losing a child to cancer: Impact of professional and social support on long-term outcomes. *J Clin Oncol*. 2007;25(22):3307–3312.

Question 29.5

With respect to John's sister Lauren and grief, which of the following statements is normal for a sibling of a child who has died?

- A. Lauren studies extra hard because John was a straight A student.
- B. Lauren takes a stuffed animal from John's room and sleeps with it every night.
- C. Lauren feels guilty about John's death because when she was sick, she wished it were him instead of her.
- D. Lauren is worried that she will die the next time she gets a cold.
- E. All of the above.

Answer 29.5

The correct answer is (E)

It is normal in the bereavement process of siblings to assume some of the deceased child's "identity." They will often take on an important or defining characteristic of the deceased child, such as being "the smart one," "the funny one," or "the athletic one." It is crucial to help guide parents to reassure surviving children that they are loved for being themselves. It is also normal for bereaved siblings to hold on to memories or personal objects that represent their dead sibling.

It is common for siblings of the deceased to misunderstand the circumstances of their sibling's death, and they will often assume some personal responsibility. Just as children can perceive their own illness as a punishment, bereaved siblings remarkably show a similar tendency and can feel that their sibling's death is a punishment for their own "bad behavior." It is absolutely crucial to provide concrete and age-appropriate information because this can mollify underlying anxiety and fear about their sibling's death.

Further Reading

Davies B. *Shadows in the Sun: The Experiences of Sibling Bereavement in Childhood*. Philadelphia, PA: Brunner/Mazel; 1999.

Nolbris M, Hellstrom AL. Siblings' needs and issues when a brother or sister dies of cancer. *J Pediatr Oncol Nurs*. 2005;22(4):227–233.

Question 29.6

Jimmy is a 7-year-old male who has left leg pain from newly diagnosed osteosarcoma. He has been taking acetaminophen with codeine, but it has not provided sufficient pain relief. He is referred to you for pain management, and you recommend discontinuing the acetaminophen with codeine.

Which of the following is the reason(s) for discontinuing acetaminophen with codeine?

- A. Up to 35% of children lack the enzyme to convert codeine to morphine.
- B. The child may develop hepatotoxicity from excessive acetaminophen.
- C. Some children are “ultra-rapid metabolizers” and convert codeine to morphine in higher than normal amounts, placing them at risk for respiratory insufficiency.
- D. Both A and B.
- E. Both A and C.
- F. Both B and C.
- G. All of the above.

Answer 29.6

The correct answer is (E)

Acetaminophen with codeine continues to be the most prescribed opioid for children with pain despite the fact that almost one-third of patients cannot metabolize codeine to morphine and so only receive pain relief from acetaminophen. In addition, some children are “ultra-rapid metabolizers” and convert codeine to morphine rapidly, producing extremely elevated plasma levels of morphine causing respiratory insufficiency and sometimes death. For these two reasons, acetaminophen with codeine is infrequently prescribed by pediatric palliative care providers with extensive experience in pain management.

Hepatotoxicity is always a possibility when administering acetaminophen, but it is unlikely to occur in children when using acetaminophen with codeine at accepted dosages. The current recommendation is a maximum of 75 mg/kg/day, not to exceed 4 g daily.

Further Reading

American Pain Society. *Principles of Analgesic Use*. 7th ed. Glenview, IL: American Pain Society; 2016.

Sullivan JE, Farrar HC; the Section on Clinical Pharmacology Therapeutics, Committee on Drugs. Fever and antipyretic use in children. *Pediatrics*. 2011;127(3):580–587.

30

Geriatric Issues in Palliative Care

MARVIN OMAR DELGADO GUAY
AND SRIRAM YENNURAJALINGAM

Question 30.1

Mrs. Smith is a 91-year-old female diagnosed with end-stage dementia who was recently admitted to hospice. The past few weeks were very challenging because she had worsening of her agitation, but this is now better controlled as a result of adjustments to her medications. Her primary caregiver is her 70-year-old daughter, who has her own medical issues. You discuss caregiver burnout with the daughter and recommend for her mother to be admitted for inpatient respite care.

Which of the following is the most appropriate goal for the admission?

- A. Provide rest for the patient
- B. Streamline the patient's drug regimen to make it less complicated
- C. Provide rest for the caregivers
- D. Provide rest for the hospice home care team

Answer 30.1

The correct answer is (B)

In this case, the goal of admission to the inpatient hospice facility is to give the family or other persons caring for the patient some rest from their caregiving duties. Respite care is short-term inpatient care provided by hospice for this purpose. Other reasons for admission to a hospice inpatient facility include adjustments in medication for the purpose of improving symptoms and when patients may be near death and families and/or the patient prefer that the patient die in the facility, especially in the case of patients with significant symptom burden. Admissions to provide rest for the hospice home team or for revision of plan of care are inappropriate.

In general, hospice provides the following levels of care depending on the needs of the patient and the family:

Routine home care: The patient is at home and is not receiving continuous care. The patient may reside in a private residence, assisted living, residential care facility, or skilled nursing facility.

Continuous home care: The patient is receiving continuous nursing care at home for brief periods of crisis in order to maintain the patient at home. The patient may reside in a private residence, assisted living, residential care facility, or skilled nursing facility.

Inpatient respite care: The patient is in a facility on a short-term basis to provide relief to family members.

General inpatient care: The patient is in an inpatient facility for pain control or acute or chronic symptom management that cannot be managed in other settings.

Further Reading

Connor SR. U.S. hospice benefits. *J Pain Symptom Manage* 2009;38(1):105–109.

Question 30.2

A 78-year-old female who is residing in a nursing home has progressive dementia. Since your last evaluation, the patient has lost 10 pounds, and the daughter is very concerned that her mother is going to starve to death. The nurses report that the patient sometimes chokes on her food. The daughter asks about placing a feeding tube.

Which of the following is the most appropriate next step for this patient?

- A. Tell the daughter that a feeding tube is inappropriate because it will not prevent weight loss in a patient with dementia
- B. Get a nutritionist involved by measuring the patient's daily caloric intake
- C. Explain to the daughter that a decrease in food intake is part of the natural process of dying
- D. Request for a swallowing evaluation

Answer 30.2

The correct answer is (D)

It is known that weight loss and progressive dysphagia are prognostic indicators of end-stage dementia. However, simple changes in the texture and consistency of food and the manner of feeding may improve the patient's oral intake, and this is a reasonable option even in patients with advanced dementia. A swallowing evaluation would have both prognostic and diagnostic value in this case. Placing a feeding tube is not a sound option, but these kinds of conversations are emotionally laden and should be undertaken with care after all other non-invasive options have been tried. In addition, although a decrease in food does occur near the end of life, diet modification should be tried before such a conclusion is discussed. Computation of the caloric intake has little value at this time because it only confirms the information that is already known and will not change the management.

Further Reading

- Hanson LC, Ersek M, Gilliam R, Carey TS. Oral feeding options for people with dementia: A systematic review. *J Am Geriatr Soc.* 2011;59(3):463–472.
- Mitchell SL. Clinical practice: Advanced dementia. *N Engl J Med.* 2015;372(26):2533–2540.

Question 30.3

A 92-year-old female who is residing in a nursing home has progressive dementia. You are asked to discuss possible admission to hospice care with the daughter.

Patients with dementia may be eligible for hospice if they meet which of the following criteria of the Functional Assessment Staging (FAST) scale?

- A. Inability to handle the mechanics of toileting
- B. Cannot sit up without assistance
- C. Decreased ability to perform complex tasks
- D. Urinary incontinence

Answer 30.3

The correct answer is (B)

Hospice eligibility criteria for patients with dementia states that the patient should have stage 7C or beyond on the FAST scale along with evidence of one or more of the following conditions in the past 12 months: aspiration pneumonia, pyelonephritis, recurrent fever, multiple pressure ulcers, the presence of other condition that suggests limited prognosis, and 10% weight loss in the past 6 months.

The FAST scale is as follows:

1. No difficulties
2. Subjective forgetfulness
3. Decreased job functioning and organizational capacity
4. Difficulty with complex tasks, instrumental activities of daily living (ADLs)
5. Requires supervision with ADLs
6. Impaired ADLs, with incontinence
- 7A. Ability to speak limited to six words
- 7B. Ability to speak limited to single word
- 7C. Loss of ambulation
- 7D. Inability to sit
- 7E. Inability to smile
- 7F. Inability to hold head up

Further Reading

Jayes RL, Arnold RM, Fromme EK. Does this dementia patient meet the prognosis eligibility requirements for hospice enrollment? *J Pain Symptom Manage.* 2012;44(5):750–756.

Mitchell SL, Kiely DK, Hamel MB, et al. Estimating prognosis for nursing home residents with advanced dementia. *JAMA.* 2004;291(22):2734–2740.

Question 30.4

You are evaluating an 86-year-old female with moderate dementia and a history of wandering and paranoia. Her family reports that it has been difficult to cope with her delusions that they are all trying to harm her. She has called the police several times to report that one of her sons, who lives in Australia, is trying to kill her.

Which of the following pharmacologic interventions is appropriate to manage the patient's symptom?

- A. Valproic acid
- B. Seroquel
- C. Lorazepam
- D. Citalopram

Answer 30.4

The correct answer is (B)

For patients with dementia, treatment includes drugs that have been shown to slow the decline in cognition, including acetylcholinesterase inhibitors (donepezil, rivastigmine, and galantamine) and NMDA antagonists (memantine). Other pharmacologic interventions under investigation include ginkgo biloba, caffeine, nonsteroidal anti-inflammatory drugs (NSAIDs), and methylphenidate. For patients with behavioral issues, the use of antipsychotics such as Quetiapine has been recommended. The US Food and Drug Administration has issued a black box warning after studies have shown increased risk of death in patients with dementia-related psychosis. Valproic acid is a mood stabilizer that is used as a second-line treatment in patients with dementia-related psychosis. Benzodiazepines are not used to treat psychosis in patients with dementia because they may cause delirium in these patients. Selective serotonin reuptake inhibitors are generally used for patients with depression and not those with psychosis.

Further Reading

- Maust DT, Kim HM, Seyfried LS, et al. Antipsychotics, other psychotropics, and the risk of death in patients with dementia: Number needed to harm. *JAMA Psychiatry*. 2015;72:438.
- Rossum RC, Rector TS, Lederle FA, Dysken MW. Are all commonly prescribed antipsychotics associated with greater mortality in elderly male veterans with dementia? *J Am Geriatr Soc*. 2010;58:1027.

Question 30.5

An 86-year-old female with advanced dementia has been refusing her food and sometimes chokes. She has had significant weight loss, and her daughter is concerned about starvation. She discusses the appropriateness of a feeding tube with you.

In patients with advanced dementia, which of the following outcomes has been shown to be present?

- A. Increase in life expectancy
- B. Improved healing of decubitus ulcers
- C. Reduced risk of aspiration
- D. Increased use of restraints

Answer 30.5

The correct answer is (B)

Patients with dementia often try to pull out their feeding tubes, and this is often the cause of increased restraint use in nursing homes. In previous studies, placement of feeding tubes has not been shown to improve quality of life or improve functional status in patients with terminal illness, including those with advanced dementia. There is no reduction in aspiration pneumonia or improvement in the healing of decubitus ulcers. The use of feeding tubes has been recommended in select patient populations for whom it may be life-prolonging, such as the following:

- Patients with proximal gastrointestinal obstruction secondary to malignancy but with good functional status
- Patients with head and neck cancers receiving active chemotherapy
- Selected patients with HIV
- Patients with amyotrophic lateral sclerosis

Further Reading

Hanson LC, Ersek M, Gilliam R, Carey TS. Oral feeding options for people with dementia: A systematic review. *J Am Geriatr Soc.* 2011;59(3):463–472.

Question 30.6

An 80-year-old female with advanced dementia has been reported to be more agitated during the past few days. Her daughter, who is her primary caregiver, reported that she has refused to eat and has become very combative. She used to ambulate with the help of an aide, but has not done so in the past few days. When you examine the patient, you note that the right knee is warm with moderate effusion. The patient grimaces when you palpate the area.

What is the most appropriate next step?

- A. Give the patient Tylenol as needed for her pain
- B. Send the patient to a rheumatologist for a diagnostic and therapeutic tap of the knee joint
- C. Recommend bed rest
- D. Proceed to get more details in the history from caregivers

Answer 30.6

The correct answer is (D)

This case illustrates one of the difficulties that clinicians encounter when taking care of patients with dementia. Evaluation for the presence and severity of symptoms is often difficult in patients who are not able to express and quantify them. Often, clinicians must rely on a good history as well as careful observation of the patient to make the most appropriate diagnosis and treatment plan. Giving a pain medication, although it may be part of the treatment plan, is not the best next step. With single joint involvement, you may want to rule out other conditions, such as trauma and septic joint, with a good history and physical exam. Referral to a rheumatologist may not be the best option unless the diagnosis is clear. Bed rest will cause deconditioning in a frail elderly patient and is not a good choice.

Further Reading

- Helme RD, Gibson SJ. The epidemiology of pain in elderly people. *Clin Geriatr Med.* 2001;17:417.
- Murphy E, Froggatt K, Connolly S, et al. Palliative care interventions in advanced dementia. *Cochrane Database Syst Rev.* 2016;2016(12):CD011513.
- Volicer L, Hurley AC, Blasi ZV. Scales for evaluation of end-of-life care in dementia. *Alzheimer Dis Assoc Disord.* 2001;15:194.

31

**Palliative Care
in Long-Term Care
Settings**

SRIRAM YENNURAJALINGAM

Question 31.1

A 28-year-old male is transferred from a nursing facility in a persistent vegetative state with his third episode of urosepsis. He has a stage 4 pressure ulcer on his coccyx and severe contractures. During each hospitalization, he had to be admitted to the intensive care unit (ICU) and put on vasopressors and a mechanical ventilator for 1 or 2 weeks. The ICU team members believe that they have tried everything to convince the family that this care is futile. Still, the family persists in their hope for a miracle. When you sit down with the patient's mother, she tells you that she is frustrated by the endless meetings and that she wants "everything done to help him." She says that she feels like the ICU doctors do not care about her son, and she resents having to talk to you ("Do they make you talk to everyone?"). She says, "I cannot give up. I have faith that God will give me a miracle and bring my son back."

Which of the following would be the most appropriate response?

- A. "Given how long your son has been asleep, it is very unlikely he will ever awaken."
- B. "Maybe God has a different plan for your son."
- C. "Have you thought about what we should do if you do not get a miracle?"
- D. "Why do you think your son will be the one to get a miracle?"
- E. "I can see how important a miracle is to you."

Answer 31.1

The correct answer is (E)

Given the level of distrust and discord with the family, the proper goal in this meeting is to begin to rebuild a relationship. A simple reflective statement shows that you are trying to understand the mother's point of view. The statement allows you to join with her (although it is neutral about your belief about whether a miracle is going to occur). Moreover, this statement is likely to encourage the mother to talk more about her feelings about miracles so you can better understand her beliefs, hopes, and goals for her son.

The other answers are likely to evoke more resistance and not promote your goal of developing a better relationship with the patient's family. A family may attempt to engage you in a theological discussion, and you may proceed if you believe you have developed appropriate rapport and you feel comfortable discussing religious or spiritual issues. Otherwise, asking if the patient and family would like to talk to a chaplain or clergy member may be more appropriate.

Further Reading

Back AL, Arnold RM, Tulsky JA. *Mastering Communication with Seriously Ill Patients: Balancing Honesty with Empathy and Hope*. Cambridge, UK: Cambridge University Press; 2009.

DeLisser HM. A practical approach to the family that expects a miracle. *Chest*. 2009;135(6):1643–1647.

Question 31.2

An 85-year-old African American male with moderate to severe dementia has been in a nursing home for the past 6 months and now is referred to hospice care by his daughter. The floor nurse is concerned about his worsening constipation. He needed to go to the emergency center for disimpaction last week. His daughter continues to give him his medications, including multiple antihypertensive medications. Recent decline in his condition has led to near normal blood pressure. While visiting you in the clinic, his daughter states that she is concerned about a drop in blood pressure.

Which of the following antihypertensive drugs is most appropriate to discontinue?

- A. Terazosin
- B. Furosemide
- C. Fosinopril
- D. Verapamil

Answer 31.2

The correct answer is (D)

Of the agents listed, verapamil has the strongest association with constipation. This adverse effect has been noted in multiple studies and appears to be dose dependent. In a recent study that pooled adverse event data from seven double-blind, randomized trials with a total of approximately 2,000 patients, the incidence of constipation was 15% in the verapamil group compared to 3% in the placebo group. Although furosemide (option B) has been associated with constipation, this effect does not appear to be pronounced. In a cohort study of nursing home patients, furosemide was found to be less constipating than verapamil. Terazosin and fosinopril (options A and C, respectively) are not typically associated with constipation.

Further Reading

- Schuster BG, Kosar L, Kamrul R. Constipation in older adults: Stepwise approach to keep things moving. *Can Fam Physician*. 2015;61(2):152–158.
- White WB, Johnson MF, Anders RJ, Elliot WJ, Black HR. Safety of controlled-onset extended-release verapamil in middle-aged and older patients with hypertension and coronary artery disease. *Am Heart J*. 2001;142:1010–1015.

Question 31.3

An 85-year-old male who has advanced heart failure is admitted to the general medicine service for declining performance status, urinary incontinence, and lower abdominal/suprapubic pain. He began to wear an adult undergarment after these episodes started; on initial exam, the garment was fully soaked with urine. During the next 5 hours, he continued to have lower abdominal fullness and pain and no urine output. Urinalysis from the emergency room was negative. He had a normal blood urea nitrogen:creatinine ratio. You are consulted to assist with pain management. From your history, the patient notes that he lives with his son and has 24-hour private care. His current medications include amitriptyline, terbutaline, atorvastatin, dicyclomine, and, more recently, an over-the-counter cough/cold medicine with diphenhydramine and pseudoephedrine for upper respiratory infection symptoms during the past 3 days.

Which of the following tests will likely provide the diagnosis?

- A. Repeat urinalysis and obtain a urine culture
- B. Obtain a bedside bladder scan
- C. Monitor strict input/output for 12 hours
- D. Check serial serum creatinine q6 hours
- E. Order an urgent renal ultrasound

Answer 31.3

The correct answer is (B)

Acute urinary retention (AUR) generally presents as an inability to pass urine. It is typically associated with lower abdominal and/or suprapubic discomfort. Affected patients are often restless and may appear to be in considerable distress. Chronic urinary retention is often painless. Acute-on-chronic urinary retention may present with overflow incontinence. Patients may complain of incontinence rather than the inability to pass urine. Multiple medications are implicated as a cause of urinary retention; most common among these are the anticholinergic and sympathomimetic drugs. This patient is taking multiple culpable medications, including amitriptyline, terbutaline, and the recently begun pseudoephedrine/diphenhydramine combination, all of which are pharmacologic agents associated with urinary retention. Medications lead to AUR through a variety of mechanisms. Patients taking opioids and anticholinergic medications are at higher risk for AUR due to decreased bladder sensation. Anticholinergic medications also reduce detrusor contractility. Nasal decongestants that contain sympathomimetic agents increase smooth muscle tone in the region of the bladder neck.

Further Reading

Acute urinary retention. UpToDate website. <https://www.uptodate.com/contents/acute-urinary-retention>. Accessed May 18, 2017.

Question 31.4

A 91-year-old patient is a nursing home resident with worsening memory and cognition and performance status during the past 2 years. She is typically a pleasant woman, but this afternoon she started yelling and cursing and hitting anyone who came near her. This episode lasted approximately 40 minutes before she was finally able to be redirected. She reported people stealing things from her room and spying on her. Just 10 minutes ago, she became agitated again.

Which of the following medications is your first choice for treating this patient's mental condition?

- A. Amitriptyline
- B. Memantine
- C. Lexapro
- D. Lorazepam
- E. Haloperidol

Answer 31.4

The correct answer is (E)

Haloperidol is a common antipsychotic and is generally considered the first-line treatment for delirium. Lorazepam and amitriptyline can both precipitate or worsen delirium in this patient population. If the patient has clear signs of opioid-induced neurotoxicity with myoclonus and perhaps seizures as part of the agitated state, then benzodiazepines have a role.

Further Reading

Young J, Inouye SK. Delirium in older people. *BMJ*. 2007;334:842–846.

Question 31.5

In recent years, advance care planning (ACP) interventions for nursing home residents have been tested to facilitate completion of advance directives, improve resident satisfaction with health care, and reduce inappropriate health care utilization cost.

Which of the following statements is true?

- A. ACP interventions decrease hospitalization rates and health care costs.
- B. Residents who receive ACP intervention are likely to have their preferences for various end-of-life therapies documented in the medical record and to receive care that is concordant with their preferences.
- C. Resident/family satisfaction is significantly better compared to that of a control group in residents who receive ACP intervention.
- D. All of the above.
- E. Both A and B.

Answer 31.5

The correct answer is (E)

Recently, two randomized controlled studies used different approaches to identify and document residents' and families' preferences for end-of-life treatments. Morrison et al. tested an intervention that targeted social workers who received education and support in conducting ACP discussions with residents and families. Compared to the usual care control group, residents in the intervention were significantly more likely to have their preferences for various end-of-life therapies documented in the medical record and to receive care that was concordant with their preferences. Molloy et al. conducted a large multisite trial involving six nursing homes and 1,292 nursing home residents/proxies to test an advance directive program called Let Me Decide. The outcomes included satisfaction with health care and health care utilization. Intervention sites reported fewer hospitalizations per resident and lower health care costs compared to control sites. Resident/family satisfaction was not significantly different in the two groups.

Further Reading

Molloy DW, Guyatt GH, Russo R, et al. Systematic implementation of an advance directive program in nursing homes: A randomized controlled trial. *JAMA*. 2000;283:1437–1444.

Morrison RS, Chichin E, Carter J, et al. The effect of a social work intervention to enhance advance care planning documentation in the nursing home. *J Am Geriatr Soc*. 2005;53:290–294.

Question 31.6

Which of the following statements regarding pain and symptom management in patients with advanced dementia in a nursing home is true?

- A. The number of symptoms correlates directly with age.
- B. Pain is undertreated due to concerns of addiction, fear of tolerance, and underreporting.
- C. Pain, dyspnea, and agitation are the three commonly reported symptoms in the last 3 months of life.
- D. All of the above.

Answer 31.6

The correct answer is (D)

Patients with advanced dementia in a nursing home usually underreport and are also undertreated. The number of symptoms correlates directly with age (5.7 symptoms in patients younger than age 65 years and 7.4 in those older than 85 years). Pain and related symptoms in advanced dementia are common. In the CASCADE study of more than 300 nursing home patients with advanced dementia, nearly 25% of patients were reported to be in pain, 30% had dyspnea, and 30% had agitation in the last 3 months of life.

Further Reading

Mitchell SL, Teno JM, Kiely DK, et al. The clinical course of advanced dementia. *N Engl J Med*. 2009;361(16):1529.

32

**Palliative Care
in End-Stage
Heart Failure**

LINH MY THI NGUYEN

Question 32.1

Mr. A is an 80-year-old male with ischemic cardiomyopathy with an ejection fraction of 20% who is hospitalized for treatment of acute advanced heart failure. His team optimizes his cardiac medications and determines he is not a candidate for surgical procedures. He cannot carry on any physical activity, and when he tries to get out of bed, his discomfort is increased.

In addition to having New York Heart Association (NYHA) class IV symptoms, which of the following is required for the patient to be eligible for hospice?

- A. Documented ejection fraction $\leq 20\%$
- B. Treatment-resistant symptomatic supraventricular or ventricular arrhythmia
- C. History of cardiac arrest or resuscitation
- D. Not a candidate for surgical procedures

Answer 32.1

The correct answer is (D)

Option D is a required for patients to be considered in the terminal stage of heart disease (life expectancy of 6 months or less). Options A–C are supporting factors but not required to establish eligibility for hospice care.

Hospice referral for heart disease

Patients are considered to have a prognosis of 6 months or less if Nos. 1 and 2 are present; factors from No. 3 add supporting documentation:

1. Optimally treated for heart disease (angiotensin-converting enzyme (ACE) inhibitors and diuretics; vasodilators including nitroglycerin, nitroprusside, and nesiritide or patients not on vasodilators have a reason for not being on these drugs, such as hypotension or renal disease; beta-blockers, aldosterone antagonists, and device therapies), or not a candidate for surgical procedures, or the patient declines these procedures.
2. NYHA class IV (symptoms at rest): Significant failure may be documented with an ejection fraction $\leq 20\%$ but is not required if not available.
3. Supporting factors but not required: treatment-resistant symptomatic supraventricular or ventricular arrhythmias, history of cardiac arrest or resuscitation, history of unexplained syncope, brain embolism of cardiac origin, or concomitant HIV disease.

Further Reading

Local coverage determination (LCD) for hospice determining terminal status (L33393). Centers for Medicare & Medicaid Services website. http://www.highpeakshospice.org/files/public/pdf/Local_Coverage_Determination_for_Hospice_-_Determining_Terminal_Status_L33393.pdf. Accessed December 29, 2016.

Stuart B. The NHO medical guidelines for non-cancer disease and local medical review policy: Hospice access for patients with diseases other than cancer. *Hosp J.* 1999;14(3–4):139–154.

Question 32.2

Ms. B is an 85-year-old female with heart failure with an ejection fraction of 25% who has had an implantable cardiac defibrillator (ICD) for several years. During this hospitalization, she had a detailed discussion with her team and decided to forgo further device therapies, changed her code status to do not resuscitate (DNR), and agreed to a referral for home hospice.

Which of the following statements is true regarding the use of ICD therapy for this patient?

- A. The patient's decision-making capacity should be evaluated with a psychiatric consultation.
- B. The patient is not imminently dying; therefore, the team should wait and send a representative from the device manufacturer to the patient's house when she is closer to death.
- C. The DNR order is inconsistent with the functioning of an ICD because the ICD will shock the patient back into a life-sustaining rhythm.
- D. Deactivation of the ICD is required for hospice enrollment.

Answer 32.2

The correct answer is (C)

The patient has no evidence of impaired decision-making capacity. Although imminent death is an indication for deactivation of ICD therapy, this patient currently has other indications, including the inconsistency of the ICD with the patient's goal of comfort and DNR. Option B is incorrect because device manufacturers will not send representatives to patients' home. Option D is incorrect because deactivation of an ICD is not a requirement and, therefore, should not be a barrier to hospice enrollment.

Discontinuing implantable cardiac defibrillator therapy

Indications for discontinuation include a change in the goals of care or the ICD is inconsistent with the goals of care (e.g., DNR order, forgoing further device therapies, and desire for comfort), withdrawal of anti-arrhythmic medications, or imminent death. In urgent or emergent situations in which the patient is incessantly shocked by the ICD, a magnet should be placed over the ICD.

Further Reading

Allen L. Palliative care for patients with advanced heart failure.

UpToDate website. https://www.uptodate.com/contents/palliative-care-for-patients-with-advanced-heart-failure-decision-support-symptom-management-and-psychosocial-assistance?search=GoodIn&source=search_result&selectedTitle=2~2. Accessed December 30, 2016.

Garlitski AC. Management of cardiac implantable electronic devices in patients receiving palliative care. UpToDate website. <https://www.uptodate.com/contents/management-of-cardiac-implantable-electronic-devices-in-patients-receiving-palliative-care>. Accessed December 30, 2016.

Question 32.3

Mr. C is a 75-year-old male with chronic heart failure with reduced ejection fraction. He is receiving a left ventricular assist device (LVAD) but has symptoms of dyspnea with minimal activity.

What is his functional classification according to the NYHA and American College of Cardiology Foundation/American Heart Association (ACC/AHA) staging for heart failure?

- A. NYHA class II, ACC/AHA stage C
- B. NYHA class III, ACC/AHA stage D
- C. NYHA class III, ACC/AHA stage D
- D. NYHA class II, ACC/AHA stage C

Answer 32.3

The correct answer is (B)

The patient has NYHA class III because he has symptoms with minimal activity. The ACC/AHA stage is stage D because the patient has an LVAD, which is a specialized intervention.

Stages of heart failure

Because symptoms can improve with heart failure treatment and patients can move between NYHA classes, the ACC/AHA developed a staging system that does not allow patients to move to earlier stages. Only patients in ACC/AHA stages C and D with symptoms of heart failure can be classified by the NYHA staging system. Both systems should be used by clinicians when determining prognosis and/or hospice eligibility.

NYHA functional class

- Class I: No symptoms with ordinary activity
- Class II: Symptoms with ordinary activity
- Class III: Symptoms with minimal activity
- Class IV: Symptoms at rest

ACC/AHA staging system for heart failure

- Stage A: At risk for heart failure but without structural heart disease or symptoms of heart failure
- Stage B: Structural heart disease but asymptomatic without signs or symptoms of heart failure
- Stage C: Structural heart disease with prior or current symptoms of heart failure
- Stage D: Refractory heart failure requiring specialized interventions (e.g., IV inotropes, ventricular assist device, transplant, and end-of-life care)

Further Reading

Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: Executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128:1810.

Question 32.4

Mr. C is a 74-year-old male with hypertension, type II diabetes, osteoarthritis of the knees, and heart failure with reduced ejection fraction of 25% who presents to the palliative clinic for knee pain that limits his function. He asks why several of his medications were discontinued due the new diagnosis of heart failure.

Which of the following medications should be avoided in patients with heart failure?

- A. Nonsteroidal anti-inflammatory drug (NSAIDs)
- B. Nondihydropyridine calcium channel blocker
- C. Thiazolidinedione
- D. All of the above

Answer 32.4

The correct answer is (D)

NSAIDs should be avoided due to sodium retention, peripheral vasoconstriction, and blunted response to diuretics and ACE inhibitors. Nondihydropyridine calcium channel blockers should be avoided because of the negative inotropic effects. Their use is contraindicated in severe left ventricular dysfunction. Thiazolidinediones should be avoided due to sodium and fluid retention.

Drugs that are potentially inappropriate in patients with heart failure

Common potentially inappropriate medications are NSAIDs and oral hypoglycemics. NSAIDs are associated with increased risk of heart failure exacerbation, increased renal dysfunction, and impairment of responses to ACE inhibitors and diuretics. Oral hypoglycemics such as thiazolidinediones cause fluid retention, and metformin increases the risk of deadly lactic acidosis. Palliative clinicians should be mindful that other common palliative pharmacological agents could increase the risk of adverse effects, including glucocorticoids, tricyclic antidepressants, sodium-containing preparations such as Fleet PhosPho-soda, and sodium load QT-prolonging drugs such as haloperidol and erythromycin.

Further Reading

- Colucci WS. Drugs that should be avoided or used with caution in patients with heart failure. UpToDate website. <https://www.uptodate.com/contents/drugs-that-should-be-avoided-or-used-with-caution-in-patients-with-heart-failure>. Accessed December 31, 2016.
- Yancy CW, Jessup M, Bozkurt B, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128(16):e240–e327.

Question 32.5

Mr. E is a 76-year-old male with hypertension, atrial fibrillation, and ACC/AHA stage D heart failure who is currently maintained on IV milrinone at home. He presents to the clinic with depressed mood most of the day for more than several weeks. He also has associated preoccupation with death, insomnia, inability to concentrate, and anorexia.

In addition to referring the patient for cognitive-behavioral therapy, which of the following drug classes of antidepressants would have the least potential adverse drug effects?

- A. Tricyclic antidepressants (TCAs)
- B. Selective serotonin/norepinephrine reuptake inhibitors (SNRIs)
- C. Psychostimulants
- D. Selective serotonin reuptake inhibitor (SSRIs)

Answer 32.5

The correct answer is (D)

TCAs have negative inotropic effects and are proarrhythmic (e.g., changes in QT interval). SNRIs can cause hypertension and tachycardia. Psychostimulants can increase the risk of ventricular arrhythmias.

Pharmacological management of depression in patients with heart failure

There are limited data regarding the interventions for depression in patients with heart failure; nevertheless, SSRIs have a better side effect profile compared to other agents. SSRIs do not adversely affect ejection fraction, do not cause hypertension and cardiac arrhythmia, and have fewer drug–drug interactions. Sertraline has been suggested by some authors as the drug of choice, but the SADHART-CHF (Sertraline Against Depression and Heart Disease in Chronic Heart Failure) trial concluded that sertraline was safe but not superior to placebo. A smaller controlled trial of paroxetine observed reduction in depression and improvements in the psychological aspects of quality of life. Hyponatremia should be monitored, particularly in older patients.

Further Reading

- Gottlieb SS, Kop WJ, Thomas SA, et al. A double-blind placebo-controlled pilot study of controlled-release paroxetine on depression and quality of life in chronic heart failure. *Am Heart J*. 2007;153:868.
- O'Connor CM, Jiang W, Kuchibhatla M, et al. Safety and efficacy of sertraline for depression in patients with heart failure: Results of the SADHART-CHF (Sertraline Against Depression and Heart Disease in Chronic Heart Failure) trial. *J Am Coll Cardiol*. 2010;56:692.

33

**Palliative Care
in End-Stage
Chronic Obstructive
Pulmonary Disease**

LINH MY THI NGUYEN

Question 33.1

Mr. F is a 68-year-old male with end-stage chronic obstructive pulmonary disease (COPD) who has been hospitalized repeatedly for infectious complications and respiratory failure. He has poor performance status and stays mainly in a bed or chair.

In addition to having severe chronic lung disease as evidenced by disabling shortness of breath at rest and progression of disease (repeated emergency department visits and hospitalizations for pulmonary infection and respiratory failure), which of the following would best support this patient's eligibility for hospice?

- A. Resting heart rate of 120 beats per minute
- B. Cachexia
- C. Cor pulmonale
- D. Oxygen saturation of 88%

Answer 33.1

The correct answer is (D)

Hypoxemia or hypercapnia should be present for patients to be considered in the terminal stage of pulmonary disease (i.e., 6 months or less). Resting tachycardia, cachexia, and cor pulmonale lend supporting documentation but are not required for hospice eligibility.

Hospice referral for patients with pulmonary disease

Patients must have severe disease as evidenced by disabling despite optimal medical therapy that results in impaired function and increasing utilization of the health care system (e.g., emergency department visits, hospitalizations, and physician home visits). In addition, patients must have hypoxemia at rest on room air ($pO_2 \leq 55$ mm Hg or oxygen saturation $\leq 88\%$; may be obtained from recent health records) or hypercapnia ($pCO_2 \geq 50$ mm Hg; may be obtained from recent health records within the past 3 months). Forced expiratory volume in 1 second (FEV1) $<30\%$ after bronchodilator or serial decrease of FEV1 >40 ml/year are both objective evidence of severe pulmonary disease but are not necessary.

Supporting documentation includes cor pulmonale (right heart failure due to pulmonary disease not due to left heart disease or valvular disease), unintentional weight loss $>10\%$ of body weight during the past 6 months, and resting tachycardia >100 /minute.

Further Reading

Local coverage determination (LCD) for hospice determining terminal status (L33393). Centers for Medicare & Medicaid Services website. http://www.highpeakshospice.org/files/public/pdf/Local_Coverage_Determination_for_Hospice_-_Determining_Terminal_Status_L33393.pdf. Accessed December 29, 2016.

Stuart B. The NHO medical guidelines for non-cancer disease and local medical review policy: Hospice access for patients with diseases other than cancer. *Hosp J*. 1999;14(3-4):139-154.

Question 33.2

Ms. G is a 77-year-old female with end-stage COPD. She has been admitted to the hospital with increasing frequency for dyspnea and respiratory failure. In the emergency department, she is alert and clear she does not want to be intubated but needs non-invasive positive pressure ventilation (NIPPV) at times for moderate to severe dyspnea. The patient's medical team and family are worried that the patient may become dependent on NIPPV indefinitely for the palliative of dyspnea.

When should NIPPV be discontinued in this patient?

- A. When the patient has severely impaired consciousness
- B. When the patient is vomiting
- C. When NIPPV is no longer meeting the patient's goals of care
- D. All of the above

Answer 33.2

The correct answer is (D)

In the nonpalliative patient population, the non-invasive positive pressure ventilation (NIPPV) is an absolute contraindication: cardiac or respiratory arrest; inability to cooperate, protect the airway, or clear secretions; severely impaired consciousness; nonrespiratory organ that is acutely life threatening (e.g., upper gastrointestinal bleed); facial surgery/trauma/deformity; high aspiration risk; prolonged duration of mechanical ventilation anticipated; and recent esophageal anastomosis. In addition, active nausea and vomiting is another contraindication.

The use of NIPPV

Several conditions are considered responsive to NIPPV, including exacerbations of COPD with hypercapnic acidosis ($p\text{CO}_2 > 45$ mm Hg, $\text{pH} < 7.3$, or respiratory rate > 25 beats/minute), cardiogenic pulmonary edema, and acute hypoxemic respiratory failure.

One possible exception to the contraindication of severely impaired consciousness is hypercapnic encephalopathy, which may respond to NIPPV. The likelihood of response is inversely related to the severity of the hypercapnia. Clinical improvement occur within 1 or 2 hours of NIPPV therapy.

Further Reading

Hyzy RC. Noninvasive ventilation in acute respiratory failure in adults. UpToDate website. <https://www.uptodate.com/contents/noninvasive-ventilation-in-acute-respiratory-failure-in-adults>. Accessed January 1, 2017.

International Consensus Conferences in Intensive Care Medicine: Noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med*. 2001;163:283–291.

Question 33.3

Mr. H is a 68-year-old male with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage IV (very severe) COPD. His symptoms are controlled on inhaled corticosteroids, tiotropium (long-acting antimuscarinic), and oxygen by nasal cannula at night for prevention of cor pulmonale. He comes to the palliative clinic for symptom management and advance care planning. His wants to stay alive so that he can spend as much time with his grandchildren as possible.

Which of the following chronic treatments has been proven to decrease mortality in patients with COPD?

- A. Bronchoscopic lung reduction with endobronchial valves or coils
- B. Long-term oxygen therapy
- C. Inhaled corticosteroids
- D. Inhaled long-acting bronchodilators

Answer 33.3

The correct answer is (B)

Long-term oxygen therapy is the only therapy proven to decrease mortality in patients with advanced COPD and hypoxemia. Inhaled corticosteroids and bronchodilators palliate symptoms of dyspnea, but there is no evidence that they reduce mortality. Bronchoscopic lung reduction surgery is an experimental therapy that is associated with improved lung function but with significant complications of pneumothorax and pneumonia.

Chronic treatment of patients with advanced COPD

Patients with GOLD stage III (severe) and stage IV (very severe) should be treated optimally with inhaled corticosteroids, long-antimuscarinic or long-acting beta-agonist, and experimental therapies as indicated. The PDE-4 inhibitor, roflumilast, can also be considered. In addition, long-term oxygen therapy is indicated for patients with resting hypoxemia ($pO_2 \leq 55$ mm Hg or oxygen saturation $\leq 88\%$). Pulmonary rehabilitation is recommended for patients with GOLD stages II–IV because of the improvement in symptoms, exercise capacity, and quality of life. Patients who continue to have symptoms may be considered for surgical therapies such as lung volume reduction surgery and possibly transplantation.

Further Reading

Ferguson GT, Make B. Management of stable chronic obstructive pulmonary disease. UpToDate website. <https://www.uptodate.com/contents/management-of-stable-chronic-obstructive-pulmonary-disease>. Accessed January 1, 2017.

Sin DD, McAlister FA, Man SF, Anthonisen NR. Contemporary management of chronic obstructive pulmonary disease: Scientific review. *JAMA*. 2003;290(17):2301.

Question 33.4

Ms. I is a 73-year-old female who is mostly bedbound due to her advance COPD. She is currently being treated with optimal pharmacotherapy, including inhaled corticosteroids and long-acting bronchodilators. She comes to the palliative clinic for management of her dyspnea.

In addition to considering opioids, which of the following nonpharmacological interventions alleviates dyspnea in patients with COPD?

- A. Handheld fan
- B. Neuromuscular electrical stimulation in the calves and quadriceps
- C. Acupuncture
- D. Relaxation

Answer 33.4

The correct answer is (B)

Patients with severe COPD (including mostly bedbound patients) had associated improvements in dyspnea, muscle strength, and improvement in performance of daily tasks. A 2010 randomized controlled trial could not prove the effectiveness of handheld fans. The Canadian Thoracic Society (CTS) guidelines and Cochrane review concluded that there was insufficient evidence for acupuncture, acupressure, distractive auditory stimuli, relaxation, and psychotherapy despite other sources recommending these in certain situations.

Nonpharmacologic management of dyspnea in patients with advanced COPD

In addition to neuromuscular electrical stimulation in the calves and quadriceps, the Cochrane review and the CTS guidelines concluded that improvements in dyspnea may be obtained with the use of rolling walkers (walking aids), pursed lip or diaphragmatic breathing (breath training), chest wall vibration, and pulmonary rehabilitation including home care and self-management education.

Non-invasive positive pressure ventilation can alleviate dyspnea in the palliative setting. In the nonpalliative setting, other interventions offered include lung reduction surgery, lung transplantation, and newer bronchoscopic lung volume reduction with endobronchial valves or coils, which may be an alternative in patients under consideration for lung transplantation.

Further Reading

- Bausewein C, Booth S, Gysels M, Higginson I. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant disease. *Cochrane Database Syst Rev.* 2008;2008(2):CD005623.
- Marciniuk D, Goodridge D, Hernandez P, et al. Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: A Canadian Thoracic Society clinical practice guideline. *Can Respir J.* 2011;18(2):69–78.

Question 33.5

Mr. J is a 56-year-old male with advanced COPD and chronically elevated CO_2 . He is admitted to the hospital for acute exacerbation of COPD. His oxygen saturation is 86% or 87% on room air.

Which of the following is the preferred method of oxygen delivery and least likely to cause hypercapnia?

- A. Venturi mask
- B. Nasal cannula
- C. Simple face mask
- D. Non-rebreathing mask

Answer 33.5

The correct answer is (A)

Venturi masks are preferred because they deliver a precise fraction of inspired oxygen (FiO_2). Nasal cannula and simple face mask are not preferred because variations in minute ventilation and inconsistent entrainment of room air affect the FiO_2 delivered. The non-rebreathing mask delivers the highest FiO_2 of the options listed and is unlikely to be necessary in this context.

Oxygen therapy in the management of exacerbations of COPD

The target pulse oxygen saturation should be 88%–92% or pO_2 60–70 mm Hg. Excess supplemental oxygen can decrease the hypoxemic respiratory drive and cause hypercapnia. Two trials observed that titrating to this target was associated with lower mortality compared with high-flow (nontitrated) oxygen. Excessive or inappropriate oxygen can result in cellular injury and clinical consequences such as absorptive atelectasis, accentuation of preexisting hypercapnia, airway injury, parenchymal lung injury, and extrapulmonary toxicity.

- Venturi masks can deliver precise FiO_2 of 24%, 28%, 31%, 35%, 40%, or 60%.
- Nasal cannula flow rates can be as high as 6 liters per minute (LPM): 1 LPM = 24%, 2 LPM = 27%, 3 LPM = 30%, 4 LPM = 33%, 5 LPM = 36%, and 6 LPM = 39%.
- Simple face masks deliver FiO_2 up to 55%.
- Non-rebreathing masks deliver FiO_2 up to 90%.

Further Reading

Stoller JK. Management of exacerbations of chronic obstructive pulmonary disease. UpToDate website. <https://www.uptodate.com/contents/management-of-exacerbations-of-chronic-obstructive-pulmonary-disease>. Accessed January 1, 2017.

34

**Palliative Care
in End-Stage
Liver Disease**

LINH MY THI NGUYEN

Question 34.1

Mr. P is a 51-year-old male with cirrhosis due to alcohol. He is admitted to the intensive care unit for worsening encephalopathy and infectious complications and has now developed hepatorenal syndrome. He has severe abdominal discomfort due to ascites and requires frequent large-volume paracentesis for relief. The medical team requests a palliative consultation to assist with the management of opioids.

Which of the following is the best option for pain control?

- A. Morphine
- B. Tramadol
- C. Fentanyl
- D. Meperidine

Answer 34.1

The correct answer is (C)

Fentanyl is a good choice for patients with renal failure in the setting of cirrhosis. This patient is considered to have decompensated cirrhosis (i.e., major complications); therefore, tramadol should be avoided. Morphine should be avoided in patients with renal failure and/or cirrhosis. Meperidine and codeine should be avoided in patients with advanced chronic liver disease (CLD) or cirrhosis.

Opioid analgesic use in patients with advanced chronic liver disease or cirrhosis

Fentanyl is a good choice for patients with CLD or cirrhosis and renal failure. Alternatively, hydromorphone is another option in this case and could be used with caution. Morphine should be avoided due to renal failure.

In patients with advanced CLD or cirrhosis without renal failure, fentanyl and hydromorphone may be better tolerated than hydrocodone or oxycodone due to the variability of onset and analgesia in these patients. Meperidine and codeine should be avoided. Tramadol at a reduced dose may be considered in advanced CLD or well-compensated cirrhosis. However, tramadol should be avoided in patients with decompensated cirrhosis or those at risk for seizures.

Patients are considered to have decompensated cirrhosis if they have any of the following major complications: variceal hemorrhage, ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, hepatocellular carcinoma, hepatorenal syndrome, or hepatopulmonary syndrome. Other complications not included in decompensated cirrhosis are portal vein thrombosis and cardiomyopathy.

Further Reading

Goldberg E, Chopra S. Cirrhosis in adults: Overview of complications, general management, and prognosis. UpToDate website. <https://www.uptodate.com/contents/cirrhosis-in-adults-overview-of-complications-general-management-and-prognosis>. Accessed January 3, 2017.

Question 34.2

Ms. Q is a 73-year-old female with hepatocellular carcinoma and hepatitis C cirrhosis who is on home hospice. She developed jaundice, scleral icterus, and ascites and now complains of severe generalized itching. She continues to have severe itching despite treatment with cholestyramine and rifampin.

Which of the following is most likely to alleviate this patient's pruritus?

- A. Naloxone
- B. Topical corticosteroids
- C. Duloxetine
- D. Gabapentin

Answer 34.2

The correct answer is (A)

This patient with end-stage liver disease has cholestatic pruritus caused by endogenous opioid buildup that can be relieved with an opioid antagonist. Topical steroids are not directly antipruritic and may alleviate pruritus related to inflammatory skin dermatoses. In the treatment of cholestatic pruritus, there is evidence for the selective serotonin reuptake inhibitors (SSRIs) sertraline and paroxetine but not duloxetine, which is a serotonin norepinephrine reuptake inhibitor. Gabapentin and pregabalin may be useful in the treatment of neuropathic pruritus but not cholestatic pruritus.

Cholestatic pruritus

Cholestatic pruritus can be seen in patients with primary biliary cholangitis, primary sclerosing cholangitis, malignant biliary tract obstruction, chronic viral hepatitis, nonmalignant biliary tract obstruction, and cirrhosis. A presumptive diagnosis can be made in a patient with cholestasis and the complaint of itching. The treatment of choice is to correct the underlying disease when possible.

For patients with primary biliary cholangitis and moderate to severe pruritus, the treatment is a bile acid sequestrant along with ursodeoxycholic acid.

For patients without primary biliary cholangitis and moderate to severe pruritus, the treatment is a bile acid sequestrant such as cholestyramine or colestipol. For patients who do not respond, it is recommended to switch to rifampin. If symptoms persist, the opioid antagonist naltrexone can be given to reverse the endogenous opioid buildup. Naltrexone should not be given to patients who are on opioid medications. Last-line therapies include sertraline and phenobarbital.

Further Reading

Poupon R, Copra S. Pruritus associated with cholestasis. UpToDate website. https://www.uptodate.com/contents/pruritus-associated-with-cholestasis?search=Pruritus+associated+with+cholestasis&source=search_result&selectedTitle=1~150. Accessed January 3, 2017.

Question 34.3

Ms. R is a 57-year-old female with cirrhosis autoimmune hepatitis and early stage compensated cirrhosis. She does not consume alcohol or any medications that induce hepatic enzymes. She complains of mild pain due to tension headache and wants to avoid strong opioids.

Which of the following analgesics would most likely be tolerated by this patient?

- A. Acetaminophen
- B. Nonsteroidal anti-inflammatory drugs (NSAIDs)
- C. Aspirin
- D. Celecoxib

Answer 34.3

The correct answer is (A)

Acetaminophen is generally well tolerated. Both NSAIDs and aspirin should be avoided. NSAIDs can impair renal function and decrease glomerular filtration rate. NSAIDs are metabolized by cytochrome P450 and highly bound to albumin; this can increase drug bioavailability and potential toxicity. NSAIDs should also be avoided in cirrhotic patients on diuretic treatment because NSAIDs interfere with diuretic action. NSAIDs can also precipitate hepatorenal syndrome. In the general population, NSAIDs (e.g., diclofenac) have been associated with hepatotoxicity. There are inadequate data regarding the safety of selective COX-2 inhibitors for celecoxib for patients with advanced CLD or cirrhosis.

Non-opioid analgesic use in patients with advanced chronic liver disease or cirrhosis

Acetaminophen is well tolerated in patients who do not consume alcohol, with a limit of acetaminophen of 2 g/day. For short-term or one-time use, a maximum daily dose of up to 3 g/day may be considered for CLD or early stage or compensated cirrhosis. However, acetaminophen should be avoided in patients with advanced CLD or cirrhosis who are actively consuming alcohol, malnourished, not eating, receiving multiple medications that undergo hepatic biotransformations, or receiving any coadministered medication that is a potent inducer of hepatic enzymes.

Further Reading

Goldberg E, Chopra S. Cirrhosis in adults: Overview of complications, general management, and prognosis. UpToDate website. https://www.uptodate.com/contents/cirrhosis-in-adults-overview-of-complications-general-management-and-prognosis?search=Cirrhosis+in+adults%3A+Overview+of+complications%2C+general+management%2C+and+prognosis&source=search_result&selectedTitle=1~150. Accessed January 3, 2017.

Mitsialis V, Ufere NN, Friedman LS. Cirrhosis. In: Sabatine MS, ed. *Pocket Medicine*. 6th ed. Philadelphia, PA: Wolters Kluwer; 2017, Chapter 3, page 23.

Question 34.4

Mr. S is a 55-year-old male with advanced CLD and decompensated cirrhosis with recurrent hepatic encephalopathy due to alcoholism. He is admitted to the intensive care unit for sepsis. On exam, he has marked confusion and is incoherent. He is given both rifaximin and lactulose by mouth. The patient is not a candidate for liver transplantation. The next of kin agree to a transition to home hospice; however, they are concerned about the management of the hepatic encephalopathy on hospice.

Which of the following is the most cost-effective and convenient agent for lowering this patient's blood ammonia concentration?

- A. Lactulose
- B. Rifaximin
- C. Neomycin
- D. Lactulose enema

Answer 34.4

The correct answer is (A)

The disaccharides such as lactulose are the best choice based on cost. If cost is not a concern, rifaximin is a reasonable alternative. Neomycin is second-line therapy. Lactulose enema is not necessary because the patient is able to take medications by mouth.

Treatment of hepatic encephalopathy or portosystemic encephalopathy

Based on cost, lactulose is the initial treatment and should be titrated to achieve two to four soft stools per day. Patients who cannot take lactulose orally can be given enemas. For patients who have not improved within 48 hours or who cannot take lactulose, rifaximin is suggested. Antibiotics such as rifaximin should be added to, rather than substituted for, lactulose. One study suggested that combination rifaximin plus lactulose may be more effective than lactulose alone.

For patients unable to take rifaximin, neomycin is an option because it has not been shown to be efficacious in randomized trials and is associated with ototoxicity and nephrotoxicity. For patients with recurrent encephalopathy, lactulose should be administered daily rather than waiting for overt hepatic encephalopathy.

Further Reading

Ferenci DW, Runyon BA. Hepatic encephalopathy in adults: Treatment.

UpToDate website. <https://www.uptodate.com/contents/hepatic-encephalopathy-in-adults-treatment>. Accessed January 2, 2017.

Sharma BC, Sharma P, Lunia MK, et al. A randomized, double-blind, controlled trial comparing rifaximin plus lactulose with lactulose alone in treatment of overt hepatic encephalopathy. *Am J Gastroenterol*. 2013;108:1458–1463.

Question 34.5

Ms. T is a 56-year-old female with cirrhosis due to alcoholic liver disease who is hospitalized for gastrointestinal bleeding. The exam was significant for ascites, and laboratory tests revealed acute kidney injury. After discontinuation of diuretics and volume expansion, she was diagnosed with type 1 hepatorenal syndrome (HRS).

Which of the following statements is true regarding prognosis in patients with cirrhosis?

- A. The Model for End-Stage Liver Disease (MELD) predicts prognosis on the order of months and is more precise than the modified Child–Turcotte–Pugh scoring system.
- B. Hepatocellular carcinoma (HCC) is the most common standard MELD exception.
- C. Hepatorenal syndrome (HRS) portends a poor prognosis, and type 1 HRS is worse than type 2 HRS.
- D. All of the above.

Answer 34.5

The correct answer is (D)

The MELD score is a validated cirrhosis severity scoring system that uses laboratory values to predict 3-month survival, and it is used for organ allocation for patients awaiting liver transplantation. The MELD score may be helpful in standard MELD exceptions, including the most common condition, HCC, which may result in impaired survival but may not be accounted for in the MELD scoring system.

Type 1 HRS is associated with a median survival of 2 weeks, whereas type 2 HRS is associated with a median survival of 6 months. Type 1 HRS usually occurs in severe liver failure and often following a precipitating event (i.e., gastrointestinal bleed, overdiuresis, infection, serial large-volume paracentesis, and drugs such as aminoglycosides and NSAIDs). HRS is a condition that supports hospice eligibility.

Patients are eligible for hospice if they have (a) prothrombin time prolonged >5 seconds or international normalized ratio >1.5 and serum albumin <2.5 g/dl and (b) end-stage liver disease (i.e., refractory ascites or patient noncompliant; spontaneous bacterial peritonitis, HRS, refractory hepatic encephalopathy; or patient noncompliant; and recurrent variceal bleeding despite intensive therapy).

Further Reading

Bambha K, Kamath PS. Model for end-stage liver disease (MELD).

UpToDate website. <https://www.uptodate.com/contents/model-for-end-stage-liver-disease-meld>. Accessed January 2, 2017.

Runyon BA. Hepatorenal syndrome. UpToDate website. https://www.uptodate.com/contents/hepatorenal-syndrome?search=Hepatorenal+syndrome&source=search_result&selectedTitle=1~150. Accessed January 2, 2017.

35

**Palliative Care
in End-Stage
Renal Disease**

LINH MY THI NGUYEN

Question 35.1

Ms. L is a 68-year-old female with end-stage renal disease (ESRD) who has been on dialysis for 11 years. She recently had a massive stroke and continues to be anuric. Her wishes were to stop dialysis if she was no longer cognitively intact. The team and family have agreed on a date to withdraw dialysis along with other measures not directed at comfort. The family asks how long the dying phase might last.

Based on available evidence, when is this patient expected to die?

- A. 1–2 days
- B. 7–9 days
- C. 14–21 days
- D. 30 days

Answer 35.1

The correct answer is (B)

The mean survival from the last dialysis treatment to death is approximately 7–9 days. Option A is too short of a time frame, and options C and D are unlikely because the patient has no evidence of residual renal function, which would point to a longer prognosis.

Discontinuation of dialysis

Patients with ESRD on maintenance dialysis will most likely die 7–9 days after discontinuation of dialysis (range, 2–100 days). Patients with residual renal function should be expected to survive longer. According to data from the United States Renal Data System, for patients who died between January 2001 and December 2002, 22% of dialysis patients stopped dialysis prior to death, and of those patients, only 42% used hospice. Not surprisingly, the cost of care at the end of life was significantly lower for the group who withdrew and used hospice versus the group who died in the hospital.

Discussion of discontinuation of dialysis usually occurs when the dialysis is no longer serving to substantially prolong life (e.g., advanced cancer or multiorgan failure) or the burdens outweigh the life-prolonging benefits (e.g., progressive frailty and becoming bedbound and also severe cognitive impairment such as in the patient in this case). In this case, dialysis could prolong life, but it is not achieving an acceptable quality of life to the patient or her surrogate decision-maker.

Further Reading

Holley JL. Palliative care: End-stage renal disease. UpToDate website.

<https://www.uptodate.com/contents/palliative-care-end-stage-renal-disease>. Accessed January 2, 2017.

O'Connor NR, Dougherty M, Harris PS, Cassarett DJ. Survival after dialysis discontinuation and hospice enrollment for ESRD. *Clin J Am Soc Nephrol*. 2013;8(12):2117–2122.

Question 35.2

Mr. K is a 65-year-old male with ESRD and on hemodialysis. He initially presented with painful violaceous, plaque-like subcutaneous nodular skin lesions on the legs. The lesions later progressed to ischemic and necrotic ulcers with eschars. A biopsy revealed calciphylaxis (calcific uremic arteriopathy). The patient wants to know his prognosis and plan.

Which of the following is the best response?

- A. "Because your condition occurs in less than 1% of ESRD patients, I cannot tell you your chances of survival. That is best left to your nephrologist."
- B. "There are many treatments available based upon randomized control trials."
- C. "Because of your illness, dialysis should be continued indefinitely."
- D. "The 1-year mortality risk is 60%, and therefore, I'd like to talk to you about planning for the future."

Answer 35.2

The correct answer is (D)

Option A is incorrect because calciphylaxis occurs in 4% of ESRD patients. Option B is incorrect because no randomized control trials have been performed for calciphylaxis. Option C is incorrect because the 1-year mortality risk is high, and therefore the diagnosis of calciphylaxis is a potential decision point of whether to withhold/withdraw hemodialysis.

Uremic calciphylaxis

The multifactorial approach involves IV sodium thiosulfate; local wound care; pain management; avoiding tissue trauma including subcutaneous injections; treating abnormalities of calcium, phosphorus, and hyperparathyroidism; optimizing the dialysis prescription; and avoiding medications that may contribute (vitamin D, calcium supplements, warfarin, and iron). Other options for treatment-resistant patients are oxygen therapy (hyperbaric or high flow), bisphosphonates, and other novel and experimental therapies. One promising report of the multi-intervention approach observed that six of seven patients completely recovered. Nonetheless, the 1-year mortality risk for ESRD patients is estimated to be 60%, which should prompt clinicians to discuss advance directives, prognosis, and goals of care.

Further Reading

Nigwekar SU, Kroshinsky D, Nazarian RM, et al. Calciphylaxis: Risk factors, diagnosis, and treatment. *Am J Kidney Dis*. 2015;66(1):133–146.

Nigwekar SU, Thadhani RI. Calciphylaxis (calcific uremic arteriopathy). UpToDate website. <https://www.uptodate.com/contents/calciphylaxis-calcific-uremic-arteriopathy>. Accessed January 2, 2017.

Question 35.3

Mr. M is a 64-year-old male with ESRD who has been on dialysis for the past several years. He has developed multiorgan failure, which has not responded to treatment. Based on the patient's living will, it was decided to withdraw dialysis and discharge the patient with home hospice. Several days after the last dialysis treatment, the patient now has significant muscle jerks.

Which of the following is the most feasible pharmacological treatment option for his distress?

- A. Levetiracetam
- B. Diazepam
- C. Valproic acid
- D. Phenytoin

Answer 35.3

The correct answer is (B)

Uremic-associated or drug-induced myoclonus, muscle twitching, and seizures should be treated with benzodiazepines such as clonazepam. Levetiracetam, valproic acid, and phenytoin are indicated in status epilepticus lasting more than 10 minutes in the nonpalliative setting.

Myoclonus and seizure related to uremia

For patients with uremic encephalopathy and mild myoclonus (e.g., a few jerks of hands or feet per minute), benzodiazepines can be used if the symptoms are distressing or waking the patient from sleep.

Because fewer than 10% of patients who stop dialysis develop seizure, the routine or prophylactic use of antiepileptic drugs is not recommended. However, if a patient develops uremic seizure or myoclonus, benzodiazepines are the primary symptomatic treatment at end of life. For non-intravenous routes, rectal diazepam reaches peak serum more quickly compared to other rectal benzodiazepines. Sublingual lorazepam and intranasal midazolam are available but not well studied. For parenteral therapy, IV lorazepam (typical adult dose 2–4 mg IV pushes) has a longer half-life. Subcutaneous benzodiazepines include clonazepam and midazolam (typical adult dose 10 mg subcutaneously), which has a shorter onset of action. Midazolam is also available intramuscularly.

Patients with refractory seizure at end of life can be treated with midazolam or a barbiturate titrated to deep sedation.

Further Reading

Holley JL. Palliative care: End-stage renal disease. UpToDate website.

<https://www.uptodate.com/contents/palliative-care-end-stage-renal-disease>. Accessed January 2, 2017.

Schell JO, Arnold RM. Conservative care of end-stage renal disease.

UpToDate website. <https://www.uptodate.com/contents/conservative-care-of-end-stage-renal-disease>. Accessed January 2, 2017.

Question 35.4

Ms. N is an 87-year-old female with ESRD who has chosen to forgo dialysis. She opts for conservative care of her disease. She complains of persistent nausea. A review of her laboratory values reveals chronically elevated blood urea nitrogen levels.

Which of the following is most likely to alleviate this patient's nausea?

- A. Haloperidol
- B. Scopolamine
- C. Dexamethasone
- D. Promethazine

Answer 35.4

The correct answer is (A)

The patient's nausea is likely related to uremia and may respond to pharmacotherapy with a dopamine antagonist because the nausea is mediated by the chemoreceptor trigger zone. Scopolamine is an anticholinergic indicated for motion- or movement-related nausea and vomiting mediated by the vestibular apparatus. Dexamethasone and prednisone could be considered in patients with hepatic capsular distention, anorexia, and increased intracranial pressure (nausea and vomiting mediated by the cerebral cortex). Promethazine is an antihistamine and, therefore, relatively contraindicated (as is the entire class of antihistamines, including diphenhydramine and hydroxyzine), but it may be helpful with nausea mediated by the vestibular apparatus or the gastrointestinal tract.

Metabolic-related nausea

Uremia-related nausea often responds well to dopamine antagonists such as haloperidol (can be given subcutaneously), chlorpromazine, prochlorperazine, and olanzapine. Uremic toxins affect the chemoreceptor trigger zone in the floor of the fourth ventricle, then the vomiting center is stimulated, and subsequently emesis can occur. Among the other classes of antiemetics, one small study observed that ondansetron was more effective than metoclopramide for uremia-induced nausea.

Dopamine antagonists are also indicated in the treatment of nausea and vomiting related to hypercalcemia and drugs.

Further Reading

Douglas C, Murtagh FE, Chambers EJ, Howse M, Ellershaw J. Symptom management for the adult patient dying with advanced chronic kidney disease: A review of the literature and development of evidence-based guidelines by a United Kingdom Expert Consensus Group. *Palliat Med.* 2009;23(2):103–110.

Holley JL. Palliative care: End-stage renal disease. UpToDate website. <https://www.uptodate.com/contents/palliative-care-end-stage-renal-disease>. Accessed January 2, 2017.

Question 35.5

Mr. O is a 58-year-old male with ESRD who has been on hemodialysis for several years. He was recently diagnosed with stage IV head and neck cancer. Due to severe cancer pain associated with treatment and radiation, the patient was given extended- and immediate-release morphine around the clock. The patient presented to the emergency department with excessive sedation. Palliative care was consulted to manage the patient's pain.

Which of the following is the safest choice of opioid for this patient?

- A. Codeine
- B. Morphine
- C. Hydromorphone
- D. Tapentadol
- E. Methadone

Answer 35.5

The correct answer is (E)

Methadone and fentanyl are considered to be the safest in renal insufficiency. Options A and B are incorrect because codeine and morphine are not recommended in patients with a glomerular filtration rate (GFR) <30 ml/min. Hydromorphone can be used with caution, but active metabolites can accumulate between dialysis sessions. Tapentadol is a newer mu-opioid antagonist that also inhibits the reuptake of norepinephrine (modifying the ascending pain pathway). Its use is not recommended in renal impairment.

Opioid use in renal failure

Fentanyl and methadone are considered the safest in renal failure. Oxycodone and hydromorphone can be used with caution, although there are conflicting reports of the safety of hydromorphone in patients with renal failure. However, hydromorphone can be considered for patients with renal insufficiency (not failure). Meperidine and tramadol are not recommended in renal failure. Both codeine and morphine are not recommended for use in patients with GFR <30 ml/min or stage IV chronic kidney disease (CKD). Some authors suggest that morphine is not desirable in patients with milder renal disease with GFR <60 ml/min or stage IV CKD. In general, renal dosing is rarely necessary if the GFR is >50 ml/min.

Further Reading

Cancer Pain (PDQ)—Health Professional Version: Pharmacologic therapies for pain control. National Cancer Institute website. https://www.cancer.gov/about-cancer/treatment/side-effects/pain/pain-hp-pdq#section/_58. Updated September 15, 2016. Accessed January 2, 2017.

Portenoy RK, Mehta Z, Ahmed E. Cancer pain management with opioids: Optimizing analgesia. UpToDate website. <https://www.uptodate.com/contents/cancer-pain-management-with-opioids-optimizing-analgesia>. Accessed January 2, 2017.

36

**Palliative Care
in End-Stage
Neurological Disease**

TOBIAS WALBERT
AND JOEL PHILLIPS

Question 36.1

A 62-year-old male comes to the clinic with his wife and daughter. Six months ago, he noticed his voice “catching” as he talked. This was followed by weakness in his arms. Today, speech is slow, with mild dysarthria. He has not noticed any difficulty in swallowing. Weight has been stable. Breathing is normal; he denies any dyspnea with exertion or daytime somnolence. He was diagnosed with amyotrophic lateral sclerosis (ALS) by an electromyogram last month and is coming to his follow-up appointment. On his last visit, he received news of the diagnosis and prognosis.

Which of the following issues should be discussed during today’s visit?

- A. Assistive speech and communication devices
- B. Artificial ventilation (mechanical or noninvasive)
- C. Artificial feeding through a percutaneous endoscopic gastrostomy (PEG) tube
- D. All of the above
- E. Both A and C

Answer 36.1

The correct answer is (D)

The patient likely has bulbar-onset ALS, which typically has a fast progression. Anticipatory guidance is essential in ALS because patients are faced with making challenging decisions that require much thought and discussion. These topics should be broached on a subsequent visit after diagnosis has been delivered and the patient has had time to process the news. Speech is becoming difficult; therefore, it would be best for the patient to begin training with augmentative devices in order to be proficient with these tools before he is completely dependent on them for communication. Although breathing is not currently problematic, it will become difficult as the disease progresses. This is also true with artificial feeding, particularly because a PEG tube should ideally be placed before forced vital capacity decreases below 50%. Other issues that should be discussed early in the disease are advanced directives and code status, mobility, and other assistive devices to maintain function in activities of daily living.

Further Reading

Creutzfeldt C, Robinson M, Holloway R. Neurologists as primary palliative care providers: Communication and practice approaches. *Neurol Clin Pract.* 2016;6(1):40–48.

Question 36.2

A 71-year-old female with ALS for 2 years complains of shortness of breath and sleepiness during the day. On previous visits, she has expressed that she would not want a tracheostomy or mechanical ventilation. Nocturnal pulse oximetry reveals several desaturations throughout the night, and it is apparent she would benefit from non-invasive ventilation (NIV).

Which of the following is the most appropriate to discuss with the patient?

- A. NIV should be discontinued as soon as it causes discomfort by either the face mask or the high-pressure airflow.
- B. NIV should be used to reduce the number of desaturations on nocturnal oximetry.
- C. NIV is for symptomatic control and can be stopped at any time she does not perceive benefit; triggers for discontinuing treatment should be made clear between the patient, family, and physician.
- D. NIV is for symptomatic control and can be stopped at any time she does not perceive benefit; triggers for discontinuing treatment can be discussed once the disease progresses.
- E. NIV has long-term benefits and therefore must be continued regardless of the patient's perceived benefit.

Answer 36.2

The correct answer is (C)

NIV comes in many different forms, including bilevel positive airway pressure and continuous positive airway pressure. Newer technology is allowing for more advanced and dynamic settings on assistive machines, including portable devices. NIV is often started with nocturnal treatments to improve fatigue and daytime sleepiness. Over time, many ALS patients may begin to use the devices during the day for symptomatic control. As respiratory function decreases, patients may become dependent on devices for continuous ventilation. It should be stopped if the patient does not perceive benefit. Before initiation of NIV, discussion should take place regarding the patient's preferences and goals, including triggers for discontinuation. This will reduce emotional distress among the patient and family when making this decision in the future, and it will reduce the likelihood of continuing the treatment beyond the time point a patient wishes. Patient discomfort is often encountered early in the treatment and is not necessarily an indication to discontinue treatment. Patients should be encouraged to continue because it may take several weeks to adjust to the technology. Respiratory therapists can also help in titrating airflow to comfort and adjusting nasal and oral interfaces. NIV should never be used for the sole purpose of improving the results on nocturnal oximetry.

Further Reading

- Quill C, Quill T. Palliative use of noninvasive ventilation: Navigating murky waters. *J Palliat Med.* 2014;17(6):657–661.
- Yeow M, Szmilowicz E. Practical aspects of using noninvasive positive pressure ventilation at the end of life. *J Palliat Med.* 2010;13(9):1150–1151.

Question 36.3

A 55-year-old female has been treated for multiple sclerosis (MS) for many years. Recently, she reports urinary problems. It started a year ago when she noticed she needed to use the bathroom more frequently. Over time, she began to experience episodes of urgency throughout the day. Twice in the past 6 weeks she was unable to get to a toilet on time.

What is the next step in treatment?

- A. Behavioral interventions such as pelvic floor muscle training and timed voiding
- B. Begin treatment with tolterodine
- C. Begin treatment with oxybutynin
- D. Behavioral interventions such as intermittent self-catheterization
- E. Botulinum injections

Answer 36.3

The correct answer is (A)

This patient is experiencing urge incontinence from detrusor overactivity. If cognition is not impaired, treatment should begin with behavioral interventions. Pelvic floor muscle training (Kegel exercises) helps prevent leaking or dribbling, and timed voiding ensures the bladder remains empty in the setting of urinary urgency. Intermittent self-catheterization is another behavioral intervention, but this is indicated for urinary retention when post-void residuals are >100–150 ml. Both tolterodine and oxybutynin are antimuscarinic antispasmodics that are preferred medications, but only after behavioral interventions have been tried or cognitive impairment precludes behavioral intervention. Botulinum toxin is used in refractory cases of detrusor overactivity.

Further Reading

Pintér A, Cseh D, Sárközi A, Illigens BM, Siepmann T. Autonomic dysregulation in multiple sclerosis. *Int J Mol Sci*. 2015;16(8):16920–16952.

Question 36.4

The daughter of a 78-year-old female brought her mother to the clinic. The patient was diagnosed with Parkinson's disease 10 years ago. Her daughter reports that the patient has been getting increasingly agitated. At home, she sees little children who are not in the room, and during the consult, she continues to point to spiders on the wall that are clearly not present. Her medication regimen includes amantadine, and carbidopa/levodopa was added 2 weeks ago.

What is the most appropriate treatment for the patient?

- A. Add quetiapine 25 mg at bedtime
- B. Increase carbidopa/levodopa
- C. Stop amantadine
- D. Start tolcapone

Answer 36.4

The correct answer is (C)

The patient is suffering from hallucinations, likely drug induced. It is best to remove offending agents in the order of least potency: anticholinergic medications, amantadine, catechol-*O*-methyltransferase inhibitors, and dopamine agonists. Therefore, amantadine should be discontinued. Tolcapone should not be added nor should carbidopa/levodopa be increased because they would further exacerbate her symptoms. Quetiapine and clozapine are both effective. More recently, pimavanserin was approved for psychosis in Parkinson's disease; however, de-escalation of medications should be tried first. Clozapine is rarely used because of the risk of agranulocytosis.

Further Reading

Miyasaki JM, Shannon K, Voon V, et al. Practice parameter: Evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2006;66(7):996–1002.

Question 36.5

A 68-year-old male suffered a thalamic stroke 1 year ago. He has recovered much of his function. However, he complains of persistent severe pain in his right arm, with a tingling sensation. He is wearing a T-shirt, despite it being winter, because he cannot tolerate sleeves touching his arm.

Which of the following medications is likely to help?

- A. Morphine
- B. Lamotrigine
- C. Pregabalin
- D. Amitriptyline
- E. B, C, and D
- F. All of the above

Answer 36.5

The correct answer is (E)

This patient is suffering from central pain syndrome. Central pain is often associated with a stroke in the thalamus or corticospinal tract. Hyperalgesia, dysesthesias, and allodynia are frequently present along with sensations of burning pain with a superficial quality. Of the medications listed, lamotrigine, amitriptyline, and pregabalin have been proven to be effective at relieving the pain in randomized studies. Titration to comfort, starting with small doses, is suggested. Central pain is refractory to opioids. In recent years, buprenorphine has also been shown to be effective at reducing symptoms of hyperalgesia and central pain. In the United States, it is available in weekly transdermal patches of 5, 10, and 20 $\mu\text{g/hr}$.

Further Reading

- Khanna I, Pillarisetti S. Buprenorphine—An attractive opioid with underutilized potential in treatment of chronic pain. *J Pain Res.* 2015;8:859–870.
- Klit H1, Finnerup NB, Jensen TS. Central post-stroke pain: Clinical characteristics, pathophysiology, and management. *Lancet Neurol.* 2009;8(9):857–868.

37

**Human
Immunodeficiency
Virus and
Palliative Care**

JOHN WERU

Question 37.1

Patient BS was diagnosed with HIV in 2000. He is on first-line antiretroviral drugs (ARVs) with a CD4⁺ count of 500 cells/ μ l, and his last viral load was 1,000/ml. He is complaining of burning, shooting pain in the lower limbs that was of insidious onset and started at the toes but has spread proximally.

What type of pain is this patient experiencing?

- A. Nociceptive pain
- B. Neuropathic pain
- C. Chronic pain
- D. Hyperalgesic syndrome

Answer 37.1

The correct answer is (B)

Patients suffering from HIV neuropathies present with a myriad of descriptive terms for their pain. It is reported as tingling, numbness, burning, or aching shock-like or knife-like. The pain typically starts on the periphery and radiates proximally.

HIV/AIDS patients are prone to neuropathic pain due to multiple factors, including HIV-related peripheral neuropathy, ARV toxic neuropathy, and, in some cases, malnutrition leading to lack of essential elements for the functioning of nerves. High viral loads and low CD4 counts increase the likelihood of HIV-related neuropathy (HRN).

HIV-related neuropathy is due to chronic immune activation with increased production of pro-inflammatory cytokines in the peripheral nervous system. When associated with ARVs, the neuropathy is thought to be related to mitochondrial toxicities of these drugs, leading to destruction of the usual functioning of the peripheral nervous system. The most common class of ARVs associated with HRN is the dideoxynucleoside reverse transcriptase inhibitors (dNRTIs).

The goal of treatment is usually to manage pain and stop the progression of the symptoms and patient distress. Patient education is key to their understanding of the causative factors and treatment modalities. Pharmacologic treatment is multimodal, involving several types of medications. Treatment can commence with an anticonvulsant such as gabapentin or pregabalin and titrating to effect. An antidepressant such as a selective serotonin reuptake inhibitor (e.g., duloxetine) can be added. For refractory symptomatology, adding a long-acting opioid has been shown to have a pain-relieving effect.

Further Reading

- Demmer C. AIDS and palliative care in South Africa. *Am J Hosp Palliat Care*. 2007;24(1):7–12.
- Vogl D, Rosenfeld B, Breitbart W, et al. Symptom prevalence, characteristics, and distress in AIDS outpatients. *J Pain Symptom Manage*. 1999;18(4):253–262.

Question 37.2

Mr. TM is a 65-year-old widower who has been on ARVs for the past 25 years. He has failed first-line and second-line treatment with declining CD4 count (from 1,200 to 100). He has been diagnosed with cryptococcal meningitis, tracheal candidiasis, and intestinal cryptosporidiosis. The patient is semicomatose, jaundiced, and dehydrated, with multiple skin and mouth lesions.

This patient is in which World Health Organization (WHO) clinical stage of HIV?

- A. End stage
- B. Category C
- C. Stage 3
- D. Stage 4

Answer 37.2

The correct answer is (D)

HIV disease staging is important to clinicians and patients because it guides clinical management. Two major classification systems are currently in use: the Centers for Disease Control and Prevention (CDC) classification system and the WHO Clinical Staging and Disease Classification System. The WHO classification is from 1 to 4, with those with failed treatment combined with systemic infection or complications classified as stage 4.

Due to the reduced immunity, patients in stage 4 are prone to multiple opportunistic infections and reactivation of dormant maladies. These afflict all systems in the body. It is evident that the depletion of CD4 and monocyte/macrophage cell lineage is the main cause of immune degradation in this patient. At this point, symptom management focused on the patient's quality of life is a significant consideration. Timely, quality patient and family communication with individualized social support is also a key consideration.

Further Reading

Demmer C. AIDS and palliative care in South Africa. *Am J Hosp Palliat Care*. 2007;24(1):7–12.

Guide for HIV/AIDS clinical care—HIV classification: CDC and WHO staging systems. AIDS Education & Training Center Program website. <https://www.aidsetc.org/guide/hiv-classification-cdc-and-who-staging-systems>. Published April 2014.

Ira B. End-of-life care in HIV disease. *J Gen Intern Med*. 1997;12(12):784–786.

Question 37.3

Mrs. X is a 44-year-old HIV-positive female who has spurious diarrhea not controlled on home remedies for the past 4 months.

Which of the following statements is false regarding diarrhea in HIV?

- A. It is usually self-limiting.
- B. Use of ARVs in naive patients is the best approach.
- C. Chronic diarrhea is an AIDS-defining condition.
- D. Viral effects on the intestinal cells are the major factor in causation.

Answer 37.3

The correct answer is (A)

HIV infection is a significant risk factor for developing chronic diarrhea. In the developing world, almost 100% of people who are HIV positive report diarrhea at some time during their disease trajectory. Patients are usually diagnosed with diarrhea when three or more bowel movements occur per day, and this is referred to as chronic diarrhea when it lasts 3 or more months. Chronic diarrhea in HIV patients is also an AIDS-defining condition, according to WHO criteria.

HIV virus destroys the enterocytes leading to partial villous atrophy with subsequent malabsorption and thus diarrhea, which is usually associated with malnutrition. Common pathogens, such as viruses and helminthes, also causes diarrhea. The quality of life in such patients is severely restricted due to the diarrhea, and its management is a significant determinant of general well-being.

In ARV naive patients, commencing on the same improves the management outcome. Treating the causative organism is recommended when this can be identified. Supportive care with hydration, proper nutritional support, and avoidance of exacerbating factors have been shown to be of benefit.

Further Reading

Demmer C. AIDS and palliative care in South Africa. *Am J Hosp Palliat Care*. 2007;24(1):7–12.

Nokwanda E, Joanne R. Nurses experiences in palliative care of terminally-ill HIV patients in a level 1 district hospital. *J Democratic Nursing Org South Africa*. 2014;37(1):Art. 1238.

Schietinger H. Supportive and palliative care for people living with HIV/AIDS. *Common Health*. 2005;Spring:36–41.

Selwyn PA, Arnold R. From fate to tragedy: The changing meanings of life, death, and AIDS. *Ann Intern Med*. 1998;129(11):899–902.

Question 37.4

Mr. Y, a 57-year-old HIV-positive male on ARVs, has noted a significant unintentional weight loss from 65 kg to 54 kg during the past 2 months. He also reports poor appetite, occasional loose bowel movements, and low-grade fever.

Which of the following best describes this patient's condition?

- A. Malnutrition
- B. Severe weight loss
- C. Moderate weight loss
- D. Wasting syndrome

Answer 37.4

The correct answer is (D)

HIV wasting syndrome (HWS) is defined as unintentional loss of >10% of weight in a patient with advanced HIV disease. This could be a combination of loss of both muscle and fat mass and is usually difficult to regain. Presentation is associated with anorexia, low-grade fever, loose bowel movements, and fatigue.

The causative factors are thought to be HIV, inflammatory processes in HIV disease, and opportunistic infections that afflict HIV-positive patients. Myostatin, a growth factor beta protein, is important in muscle growth and maintenance. In wasting syndrome, there is increased expression of myostatin as myostatin immunoreactive protein, which is thought to contribute to and attenuate muscle wasting.

Timely effective treatment of HIV with antiretroviral medications is key to treatment of wasting syndrome. Because ARVs are being commenced earlier in the disease trajectory, fewer cases of HWS are being recorded. A diet rich in calories and protein is recommended so as to stop or minimize loss of muscle mass.

Progressive strength-building exercises such as weight lifting are also recommended. Patient and family education regarding the cause and prognosis in HWS is a significant factor in overall quality of life.

Further Reading

- Lee EJ, Jan AT, Baig MH, et al. Fibromodulin: A master regulator of myostatin controlling progression of satellite cells through a myogenic program. *FASEB J*. 2016;30(8):2708–2719.
- Nokwanda E, Joanne R. Nurses experiences in palliative care of terminally-ill HIV patients in a level 1 district hospital. *J Democratic Nursing Org South Africa*. 2014;37(1):Art. 1238.

Question 37.5

Mr. B, a widower for the past 5 years, is seen at the comprehensive care clinic for HIV-positive patients. He reports that he misses his wife dearly and feels depressed, anxious, and sometimes confused about how to proceed with life. His son reports that he has not been taking his ARVs for the past week because he flushed them down the toilet. Mr. B has told his son not to allow visitors to see him, and he spends most of his days locked in his bedroom.

Approximately what percentage of people with HIV suffer mental health problems?

- A. 90%
- B. 50%
- C. 25%
- D. 10%

Answer 37.5

The correct answer is (C)

It is reported that 20%–30% of HIV-positive patients suffer from mental health issues, and special attention is required for them to have a good quality of life. Some of the conditions these patients exhibit are depression, anxiety, post-traumatic stress disorder, suicidal thoughts, and insomnia.

Stressful situations—such as the death of a loved one, loss of a job, and exposure to violence or abuse—can have a negative effect on a person's mental health. HIV infection and related opportunistic infections are major sources of stress that negatively affect a person's mental health and also have effects on the entire nervous system, including the central nervous system. ARVs and other supportive drugs have side effects that affect the nervous system and can have negative effects on mental health.

Management of HIV-related mental health problems is interdisciplinary involving the patient and family, counselor, primary physician, and psychiatrist. This is geared toward the patient's emotional, psychological, and social well-being. The use of pharmacological agents such as antidepressants, anxiolytics, and sleeping pills is also an approach that supplements psychosocial support. Treating the HIV and opportunistic infections in a timely manner is a significant contributor to well-being.

Further Reading

Freeman M, Patel V, Collins PY, Bertolote J. Integrating mental health in global initiatives for HIV/AIDS. *Br J Psychiatry*. 2005;187:1–3.

Selwyn PA, Arnold R. From fate to tragedy: The changing meanings of life, death, and AIDS. *Ann Intern Med*. 1998;129(11):899–902.

38

**Burnout
in Palliative Care**

REGINA M. MACKEY
AND SURESH REDDY

Question 38.1

Dr. M is a 40-year-old male palliative care fellow who is about to finish a 2-month rotation in a busy inpatient consultation. You are his attending, and you noticed that for the past week, he has been detached and disengaged when talking to patients and their families. He acknowledged feeling drained and tired most of the time, and he has also experienced difficulty sleeping. When you spoke to him, he confessed self-doubt and a personal sense of failure.

Which of the following is the most significant intervention at this time?

- A. Tell him that it will improve because he will be doing a less busy rotation next month
- B. Recommend for him to see his primary doctor and discuss medication for depression
- C. Recommend for him to use bright light therapy
- D. Recommend an educational program in mindful communication

Answer 38.1

The correct answer is (D)

The fellow has symptoms suggesting burnout. Burnout encompasses three dimensions: a feeling of emotional exhaustion, low sense of personal accomplishment, and cynicism or depersonalization (detachment from the job). The standard for measuring burnout is the Maslach Burnout Inventory (MBI). There is limited high-quality evidence to approach and treat burnout, but one study suggests that participation in a mindful communication program is associated with the improvement of well-being, including burnout.

Regarding option A, ignoring the problem will not help the trainee physician or solve the problem; therefore, it is an incorrect answer.

Regarding option B, he does not meet criteria for depression, although he has some symptoms suggesting it. Further exploration would be required.

With regard to option C, there is no evidence that bright light therapy will help burnout symptoms. However, there is some evidence of the benefit of bright light therapy for depression symptoms.

Further Reading

Kearney MK, Weininger RB, Vachon ML, Harrison RL, Mount BM.

Self-care of physicians care for patients at end of life: "Being connected . . . a key to my survival." *JAMA*. 2009;301(11):1155–1164.

Krasner MS, Epstein RM, Beckman H, et al. Association of an educational program in mindful communication with burnout, empathy, and attitudes among primary care physicians. *JAMA*. 2009;302(12):1284–1293.

Question 38.2

Dr. M, a palliative care physician, Dr. H, an emergency medicine physician, and Dr. K, an oncologist, meet for lunch at the hospital in which they have all worked since completing their fellowship. They talk about the changes that have occurred since they became faculty members, including work hours, patient load, and the stress at work. Dr. M has more time to talk to patients and fewer hours, but he sometimes feels devastated by the loss of a patient or by very complicated social situations. Dr. H works long hours and has to make quick decisions in emergency situations, which sometimes makes him feel drained of energy at the end of his day. The oncologist, Dr. K, is satisfied with his working hours and time to research and teach. However, he confesses that some conversations with patients, when no more treatment is indicated, are very hard on him.

Which of the following specialties has the highest risk of burnout?

- A. Anesthesiology
- B. Oncology
- C. Hospice and palliative care
- D. Surgery

Answer 38.2

The correct answer is (C)

Burnout is more common among physicians than among other workers in the United States. Also, physicians are more likely to be dissatisfied with their work–life balance compared to the general population in the United States. Unfortunately, little is known about how to address the problem. Physicians in specialties at the front lines of care access seem to be at greater risk (i.e., emergency medicine, family medicine, and internal medicine).

The palliative care specialty has recently experienced increasing demand, which requires an increase in the available workforce. However, the available workforce has not kept pace with the demand. The gap has led to an increased risk of burnout, characterized by depersonalization and work-related exhaustion. Palliative care clinicians report a burnout rate of 62%, which is remarkably higher than the rate of 45% reported for oncologists.

Further Reading

- Kamal A, Bull J, Wolf S, et al. Prevalence and predictors of burnout among specialty palliative care clinicians in the United States: Results of a national survey. *J Clin Oncol*. 2014;32(31);Abstract 87.
- Shanafelt TD, Boone S, Tan L, et al. Burnout and satisfaction with work–life balance among US physicians relative to the general US population. *Arch Intern Med*. 2012;172(18):1377–1385.

Question 38.3

Dr. Z is a 32-year-old female physician who is just starting her fellowship in palliative care. She is very motivated and has plans for her career in the specialty. In discussion with other fellows, she states that because she is single, she will not have any problems working long hours and weekends. She lives alone and recently moved to the town. She talks to her parents back in New York once a week and texts with friends occasionally. She actively seeks guidance from mentors and is eager to take up many projects. She is very energetic, enthusiastic, and willing to work on weekends to complete her projects.

Which of the following is a risk factor for burnout?

- A. Being a fellow
- B. Working in an academic institution
- C. Being single
- D. Working with a multidisciplinary team

Answer 38.3

The correct answer is (C)

The following personal and demographic risk factors are associated with burnout: being female, particular personality traits (obsessive–compulsive disorder and lack of resilience), being single, not having children, previous psychiatric history (personal or family), lack of social support, and having non-work-related stress. Occupational risk factors include high job stress (overload, feeling poorly managed and resourced, lack of professional status, dealing with the suffering of patients, and dealing with angry families), low job satisfaction, having inadequate communication and management skills training, fewer years of job experience, less than four colleagues on the same team, and working in acute settings.

There is a substantial and growing body of evidence indicating that well-functioning interdisciplinary teamwork characterized by shared philosophy of care, respectful interdisciplinary relationships, mutual trust and support, and strong culture of communication can mitigate the risk of burnout.

Further Reading

- Drybye LN, Varkey P, Boone SL, et al. Physician satisfaction and burnout at different career stages. *Mayo Clin Proc.* 2013;88(12):1358–1367.
- Jamieson L, Teasdale E, Richardson A, Ramirez A. The stress of professional caregivers. In: Hanks G, Cherny NI, Christakis NA, et al., eds. *Oxford Textbook of Palliative Medicine*. 4th ed. New York, NY: Oxford University Press; 2010:1445–1452.

Question 38.4

Dr. S is a 42-year-old female physician who is part of the inpatient consult palliative care team in a tertiary hospital. She has been friends with Dr. K, a pathologist, for a long time. Their families socialize frequently, and their kids go to the same school. They cross coverage to each other regularly. However, for the past 2 months, Dr. S has been busy at work and unable to socialize as much as she had in the past. She has been missing lunch with Dr. K. They eventually meet after 6 weeks. During their conversation, Dr. S seems to be restless and looks at her phone frequently. She tearfully talks to Dr. K about her increased workload and inability to socialize. During a subsequent meeting, Dr. S looks unkempt, emotionally labile, and irritable. She looks tired and talks about her self-esteem several times during the conversation.

Which of the following options is *not* an indication of burnout in Dr. S.' situation?

- A. Emotional lability
- B. Resentment, anxiety, and irritability
- C. Marital problems
- D. Increased workload

Answer 38.4

The correct answer is (C)

During approximately the past decade, physician burnout has generated sustained attention among researchers and policymakers. It is characterized by a syndrome of emotional exhaustion, cynicism, and work inefficacy. Burnout has been associated with poorer well-being, suicidal ideation, decreased professionalism, and compromised patient care. Burnout can affect individuals or sometimes an entire team. Common presenting symptoms include overwhelming physical and emotional exhaustion, feeling of cynicism, detachment from the job, a sense of ineffectiveness, lack of accomplishment, avoidance of emotionally difficult clinical situations, irritability and hypervigilance, interpersonal conflicts (overidentification or overinvolvement), perfectionism, rigidity, poor judgment (professional and personal boundary violations), social withdrawal, numbness and detachment, difficulty concentrating, questioning the meaning of life, questioning prior religious beliefs, sleep problems, intrusive nightmares and thoughts, addictive behaviors, and frequent illness (headache, gastrointestinal disturbances, and immune system impairment).

Further Reading

- Melamed S, Srieom A, Toker S, et al. Burnout and risk of cardiovascular disease: Evidence, possible causal paths, and promising research directions. *Psychol Bull.* 2006;132:327–353.
- Spickard A Jr, Cabbe SC, Christensen JF. Mid-career burnout in generalist physicians. *JAMA.* 2002;288(12):1447–1450.

Question 38.5

Dr. S is a 42-year-old female physician who is part of the inpatient consult palliative care team in a tertiary hospital. She has been friends with Dr. K, a pathologist, for a long time. Their families socialize frequently, and their kids go to the same school. They cross coverage to each other regularly. However, for the past 2 months, Dr. S has been busy at work and unable to socialize as much as she had in the past. She has been missing lunch with Dr. K. They eventually meet after 6 weeks. During their conversation, Dr. S seems to be restless and looks at her phone frequently. She tearfully talks to Dr. K about her increased workload and inability to socialize. During a subsequent meeting, Dr. S looks unkempt, emotionally labile, and irritable. She looks tired and talks about her self-esteem several times during the conversation.

All of the following interventions could help Dr. S *except*:

- A. Meditation
- B. Taking time off
- C. Techniques to develop resilience
- D. Antianxiety medication
- E. None of the above

Answer 38.5

The correct answer is (E)

The term *mindfulness meditation* (option A) refers to a quality of awareness that includes the ability to pay attention in a particular way: on purpose, in the present moment, and nonjudgmentally. Mindfulness includes the capacity for lowering one's own reactivity to challenging experiences.

It also is important to find ways to accommodate a professional's need for time off (option B) without creating more stress for the rest of the team. These might include having access to float staff as backups, banking hours of work in advance of the need for time off, and sharing on-call or fallback coverage with other palliative care providers in the community.

Professional and personal resilience predicated the capacity for positive outcomes from caring even in the most challenging circumstances. Boosting resilience (option C) can be achieved by reinterpreting negative events, enhancing positive emotions, becoming physically fit, accepting challenges, maintaining a close social network, and imitating resilient role models.

Use of anxiety medication (option D) is not indicated unless anxiety disorder is diagnosed. It may mask the symptoms and worsen the problem.

Further Reading

Siegel D. *The Mindful Brain: Reflection and Attunement in the Cultivation of Well-Being*. New York, NY: Norton; 2007.

Question 38.6

Dr. J is a 35-year-old palliative care physician who just started working her first job after finishing her fellowship. She is very motivated because it is a new palliative care service and she is joining a part-time palliative care and hospitalist physician and two nurse practitioners. There is also an opportunity to grow and build a department in the future. For now, there is only the inpatient consult team, but it seems that the administration will allow an outpatient clinic to start soon. Dr. J is very enthusiastic about her job. In the beginning, there is a low patient load, but after 6 months the consult volume has increased based on her good work. At this time, there is a need for another partner to share the work. She also needs other team members, such as a social worker and a counselor. Her partner is not able to share the increasing workload because he is also doing his hospitalist work. Dr. J's duty hours soon start increasing, but she manages her workload for another year. Then her team members begin to notice that Dr. J is arriving late to work, snapping at patients' families, arguing with referring colleagues, and calling in sick frequently. The administrative manager delivers the news that they are not able to hire any additional physicians or nurse practitioners.

Which of the following is a possible cause of burnout?

- A. Unclear job expectation
- B. High need to be in control of everything
- C. Lack of required team members, such as social workers, case managers, and counselors
- D. High patient volume and minimal support staff
- E. All of the above

Answer 38.6

The correct answer is (E)

Workload has been identified as a major stressor for palliative care clinicians, especially in the setting of staff shortages and financial strains. Dealing with dying patients and families as well as inadequate support (social worker, counselor, chaplain, and case manager), excessive bureaucracy, lack of control, and lack of time for patients and families are all related to burnout. Other work-related causes of burnout are working in a high-pressure environment, performing monotonous and unchallenging activities, unclear job expectation, and lack of recognition. Life-related causes include no time to relax and socialize, too many responsibilities, lack of supportive relationships, and lack of sleep. Personality-related causes include perfectionism, pessimism, a high need to be in control of everything, and being a high-achieving person.

Further Reading

- Nathan IC, Natsheva W, Keraney M. Burnout, compassion fatigue, and moral distress in palliative care. In: Cherny N, Fallon M, Kaasa S, Portenoy R, Currow DC, eds. *Oxford Textbook of Palliative Medicine*. 5th ed. New York, NY: Oxford University Press; 2015:246–259.
- Jamieson L, Teasdale E, Richardson A, Ramirez A. The stress of professional caregivers. In: Hanks G, Cherny NI, Christakis NA, et al., eds. *Oxford Textbook of Palliative Medicine*. 4th ed. New York, NY: Oxford University Press; 2010:1445–1452.

Question 38.7

Dr. D is a young doctor who just started her fellowship in hospice and palliative care. She is thrilled that she matched with a great palliative program and eager to start. The working hours are sometimes long, and fellows take weekend calls as well. Dr. D starts very well, but soon she begins to call in sick due to migraine attacks. The first 3 months pass and Dr. D frequently has pain or a medical problem that causes her to arrive late for work, miss lectures, and switch calls with other fellows. She also visits the local emergency room on several occasions for chest discomfort and possible urinary infection. Initially, her colleagues are very supportive and try to help. Soon, however, her problems increasingly occur, disrupting the work schedule. One day, she had to leave due to strong gastrointestinal symptoms and missed her clinical case presentation. Her mentor, Dr. E, calls her to the office to talk. Dr. E is concerned and wants to help. He asks about her health and symptoms. Dr. D is very emotional about her symptoms but describes them very vaguely. When Dr. E asks if her symptoms are new, she says she had problems during medical school and her residency, but she was able to manage with the help of her colleagues. She even had several surgeries during her previous training.

Which of the following is *not* a classic key dimension of burnout?

- A. Emotional exhaustion
- B. Depersonalization
- C. Reduced accomplishment
- D. Somatization

Answer 38.7

The correct answer is (D)

Dr. D exhibits somatization disorder. A person with somatization is chronically preoccupied with numerous “somatic” or physical symptoms over many years, involving several different areas of the body. For example, a person can have back pain, headaches, chest discomfort, and stomach or urinary complaints—to the point that it causes major emotional distress and problems functioning. The symptoms cannot be explained fully by any other diagnosis. The person is not “faking,” but it is a psychiatric disorder. It is probably a brain dysfunction or emotional regulation rather than an abnormality in a specific area of the body.

The difference between stress and physician burnout is the ability to recover during one’s time off. Physician burnout begins to occur when the physician is not able to recharge his or her batteries between night calls or days in the office. The physician begins a downward spiral that has three distinct symptoms:

Physical and emotional exhaustion: The physician is emotionally drained, depleted, and worn out by work and not able to recover during his or her non-working hours.

Depersonalization: The development of a negative, callous, and cynical attitude toward patients and their concerns. The cardinal sign here is cynicism, sarcasm, and feeling put upon by one’s patients.

Reduced sense of personal accomplishment: The tendency to view one’s work negatively, without value or meaningful (“What’s the use?”), and to view oneself as incompetent, lacking achievement and productivity at work.

Further Reading

Monson RA, Smith R Jr. Somatization disorder in primary care. *N Engl J Med.* 1983;308:1464–1465.

Murray A, Montgomery JE, Chang H, et al. Doctor discontent: A comparison of physician satisfaction in different delivery system settings, 1986 and 1997. *J Gen Intern Med.* 2001;16:451–459.

Spickard A, Gabbe S, Christensen J. Mid-career burnout in generalist and specialist physicians. *JAMA.* 2002;288:1447–1450.

Question 38.8

Several years ago, a group of young and well-trained physicians started a palliative care service in an academic hospital. At that time, palliative care was not a well-known specialty, and various stigmata about end-of-life care were still haunting the specialty. It was extremely difficult work, but this group did an excellent job and built a very highly respected and busy department. This group was able to excel and be recognized by other specialties. As a result, the department grew, with new physicians joining the department when needed, the addition of multidisciplinary team members, the expansion of the clinic, and the building of a palliative care unit. Department members are very proud of the important role they play in their patients' health and lives, helping make decisions and controlling symptoms. They have their own checklist to avoid burnout, and the team members help each other whenever necessary. Periodically, they meet outside and socialize among themselves. They feel very fortunate to have such a collaborative group, strong leadership, and financially stable jobs.

According to articles on managed care and physician burnout, which of the following is the key factor in physicians' satisfaction or dissatisfaction with their jobs?

- A. A sense of control over their practice environment
- B. A sense that they are making a difference in patients' health
- C. Satisfaction with life outside work
- D. Personal financial concerns

Answer 38.8

The correct answer is (A)

The larger the gap or mismatch between the person and the environment, the greater the chance of burnout. The closer the match or fit, the greater likelihood of engagement with work. Mismatches arise when the process of establishing a psychological contract leaves critical issues unresolved or when the working relationship changes to something that the person finds unacceptable. Six areas of work–life balance come together in a framework that encompasses the major organizational antecedents of burnout: workload, control, reward, community, fairness, and values. Additional variance in burnout scores over and above job stressors derives from emotion–work variables that require the individual to display or suppress emotions on the job and involve the requirement to be emotionally empathic. A sense that they are making a difference in patients' health (option B) is a feeling that physicians report as part of the calling for the profession but is not part of the antecedents for the burnout. Satisfaction with life outside work (option C) and personal financial concerns (option D) are not part of the antecedents for the burnout.

Further Reading

Vachon MLS, Fillion, L. Staff stress and burnout in palliative care.

In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine and Supportive Care*. 2nd edition. Boca Raton, FL: CRC Press; 2016:1033–1046.

Maslach C, Jackson SE. *The Maslach Burnout Inventory Manual*. 2nd ed. Palo Alto, CA: Consulting Psychologists Press; 1986.

Question 38.9

A new physician just joined a palliative care group in one of the larger hospitals in town. It is a large group, and it was just recently invited to be part of the hospital. The new physician recently finished her fellowship and is eager to start working with new colleagues. Dr. A works long hours and is not afraid to take more patients. The group began reaching out to the other specialties, and soon the number of consults increased. Approximately 6 months later, all team members were working long hours and asked the administration to hire new members. They were not able to meet as frequently as in the past and missed the opportunity to socialize as a group. One day, Dr. L, a senior member of the palliative care team, met with Dr. A and noticed some changes. Dr. A was not talking as much and did not look as motivated as in the past. She avoided eye contact and soon left the meeting. A few weeks later, Dr. A called in sick for several days. She returned to work with some back pain and a headache. She still avoids socializing with other members, but when asked how she is doing, she replies, "I am fine." Dr. L. calls Dr. A. to talk and tries to explore how to help her young colleague.

Which of the following is the best tool to diagnose burnout?

- A. Maslach Inventory
- B. Beck Inventory
- C. McGill Inventory
- D. Minnesota Inventory

Answer 38.9

The correct answer is (A)

Christina Maslach, who developed the Maslach Burnout Inventory, the most commonly used instrument to measure burnout, together with her colleagues reviewed research in the field of burnout over the first 25 years of the concept's existence. They concluded that burnout is a psychological syndrome in response to chronic interpersonal stressors on the job. The three key dimensions are (a) overwhelming *emotional exhaustion*—the fundamental individual stress dimension of burnout; (b) *depersonalization* (feelings of cynicism and detachment from the job)—the interpersonal context dimension of burnout (referring to a negative, callous, or excessively detached response to various aspects of the job); and (c) a sense of ineffectiveness and lack of *personal accomplishment*—the self-evaluation dimension of burnout (referring to feelings of incompetence and a lack of achievement and productivity at work).

The Beck Inventory (option B) is one of the most widely used psychometric tests for measuring the severity of depression. The McGill Pain Inventory (option C) is a self-report questionnaire that allows individuals to give their doctor a good description of the quality and intensity of pain that they are experiencing. The Minnesota Multiphasic Personality Inventory (option D) is a standardized psychometric test of adult personality and psychopathology.

Other tools for measuring burnout include the Oldenburg Burnout Inventory and the Copenhagen Burnout Inventory, both of which are free to use.

Further Reading

Maslach C, Jackson SE. *The Maslach Burnout Inventory Manual*. 2nd ed.

Palo Alto, CA: Consulting Psychologists Press; 1986.

Maslach C, Schaufell WB, Leiter MP. Job burnout. *Annu Rev Psychol*.

2001;52:397–422.

Question 38.10

In a large medical center, the palliative care center is experiencing a significant increase in the volume of consults since it hired two new fellowship-trained physicians. The team was able to communicate very well with other specialties in a timely manner and solved many problems. It avoided several emergency room and intensive care unit visits with good clinic assessments, symptom control skills, and communication skills. Despite increased volume of patients, no new physicians or interdisciplinary team members were hired. The team members believe they have little control over organization decisions, patient allocation, and clinical decisions. The team feels tired, and motivation is low. The team wishes to meet often to talk about cases, but due to lack of time and an increase in consults, there are few opportunities for meetings. With very little organization support, the team faces a very demanding population of patients. The team leader asks for a chaplain devoted to palliative care to help with counseling in some emotional situations among team members as they deal with the grief, loss, and very stressful situations of the families they help.

All of the following are occupational risk factors *except*:

- A. Workload or intensity of work
- B. Place of work
- C. Autonomy (control and reward)
- D. Social climate (support communication and community)
- E. Emotional demand

Answer 38.10

The correct answer is (B)

Although the place of the work is important, the work environment is not an occupational risk factor. Review of the literature suggests occupational stress is a result of a mismatch between the person and the following six areas of occupational risk factors: workload or intensity of work, autonomy (control and reward), social climate (support, communication, and community), emotional demand, values and meaning, and safety. Research from palliative care shows that stress and burnout occur in each of these six areas for palliative care providers, and compassion fatigue as well as compassion satisfaction occur in the area of emotional demand.

Further Reading

College d'expertise sur le suivi des risques psychosociaux au travail.

Rapport faisant suite a la demande du Ministre du travail, de l'emploi et de la sante. Mesurer les facteurs psychosociaux de risqué au travail pour les maitriser, 2011.

Vachon MLS, Fillion, L. Staff stress and burnout in palliative care.

In: Bruera E, Higginson I, von Gunten CF, Morita T, eds. *Textbook of Palliative Medicine and Supportive Care*. 2nd edition. Boca Raton, FL: CRC Press; 2016:1033–1046.

Question 38.11

Dr. H is a fellow in the Department of Palliative Care at a very prestigious cancer center. He hopes to be hired by the department as soon as he finishes his fellowship, so he works hard and does not complain about his increasing workload. One of the co-fellows noticed that Dr. H is very tired and falls asleep during some of the lectures. The colleague offers some ideas to help Dr. H deal with increasing stress at work.

Which of the following strategies used for stress reduction at work has been proven to help physicians?

- A. Regular time off from hassled, hectic routine
- B. Mindfulness
- C. Develop sense of competence
- D. Daily routine of good sleep and exercise
- E. Boosting resilience
- F. All of the above

Answer 38.11

The correct answer is (F)

Self-care strategies involve self-care, optimism, support from others, willingness and ability to confront challenging issues, and connectedness. True compassion may increase resilience, keeping physicians from burning out and preventing fatigue.

Having some control over schedule and hours worked is the strongest work characteristic related to emotional resilience. This is similar to an earlier finding that a sense of competence, control, and pleasure in one's work was the highest ranked coping mechanism of caregivers to the critically ill, dying, and bereaved.

Further Reading

Siegel D. *The Mindful Brain: Reflection and Attunement in the Cultivation of Well-Being*. New York, NY: Norton; 2007.

Vashon MLS. *Occupational Stress in the Care of the Critically Ill, the Dying, and the Bereaved*. New York, NY: Hemisphere; 1987.

39

**Research
in Terminally Ill
Patients**

SRIRAM YENNURAJALINGAM

Question 39.1

A 38-year-old female with metastatic pancreatic cancer is referred for anorexia and fatigue. The patient reports involuntary weight loss of 20 pounds over the past 3 months from a baseline weight of 116 pounds. Her body mass index (BMI) is 23, and her appetite score is 6 (0 being best and 10 worst). She is unable to work because of fatigue and has increasing difficulty doing chores. Her previous health care team tried various strategies, including dietary changes, exercise, and medication, without any benefit. You have recently read about an experimental medication that may be helpful in improving the patient's weight loss and fatigue.

All of the following are important prior to prescribing the experimental medication to this patient *except*:

- A. You need to obtain an approval from the institutional or regional research ethics committee to administer the medication as per protocol.
- B. You need to evaluate whether the patient understands the risks and benefits of the medication.
- C. Decline to provide other supportive care measures to help the patient with her symptoms if she declines the experimental treatment.
- D. Prior to signing the consent, it is important to know whether the patient has the cognition to understand and comply with experimental medication protocol.

Answer 39.1

The correct answer is (C)

Patients receiving palliative care are considered a vulnerable population due to the presence of severe symptom distress and limited treatment options available. It is therefore important to address all ethical issues related to participation in a clinical trial. These include obtaining approval of the institutional ethics committee, evaluating the ability of the patient to understand the protocol requirements, and having the patient sign an informed consent document. An important aspect of taking care of these patients is to provide evidenced-based quality palliative care irrespective of their intent to participate in clinical trials.

Further Reading

Addington-Hall JM, Bruera E, Higginson IJ, Payne S, eds. *Research Methods in Palliative Care*. New York, NY: Oxford University Press; 2007.

Question 39.2

An 86-year-old female with metastatic squamous cell cancer of the lung is referred for weight loss and fatigue. She is unable to do her day-to-day activities because of fatigue and reports multiple falls. Her previous health care team tried various strategies, including exercise, without any benefit. Unfortunately, there are very limited pharmacological treatments for her fatigue.

The challenges of conducting research in palliative care patients include which of the following?

- A. Poor accrual
- B. Attrition
- C. Limited funding
- D. Ethical issues
- E. All of the above

Answer 39.2

The correct answer is (E)

Prior studies suggest that poor accrual, dropouts due to disease progression, and limited funding are important challenges to conducting quality research in palliative care. However, with innovative design and proper patient selection, most of these challenges can be minimized. It is important to address all the issues associated with proper conduct of a study by drafting a well-written protocol reviewed by peers and continuous monitoring of the study so as to obtain optimal results.

Further Reading

Bennett MI, Davies EA, Higginson IJ. Delivering research in end-of-life care: Problems, pitfalls and future priorities. *Palliat Med.* 2010;24(5):456–461.

Blum D, Inauen R, Binswanger J, Strasser F. Barriers to research in palliative care: A systematic literature review. *Prog Palliat Care.* 2015;23:75–84.

40

**Palliative Care in
the Intensive
Care Unit**

MARGARET L. ISAAC
AND J. RANDALL CURTIS

Question 40.1

Mr. M is a 62-year-old male with a history of well-controlled diabetes mellitus and hypertension who was admitted with an ST-elevation myocardial infarction (STEMI) and cardiac arrest. He underwent successful cardiac reperfusion immediately after admission, but he sustained anoxic brain injury. He was living independently prior to admission with his partner and working part-time. He was treated according to the hospital's therapeutic hypothermia protocol for 48 hours and then was gradually rewarmed. It is currently hospital/intensive care unit (ICU) day 3, and he remains unresponsive and intubated for hypoxia and acute respiratory distress syndrome.

Which of the following characteristics suggests Mr. M might be an appropriate patient for palliative care consultation?

- A. Age >60 years
- B. ICU stay >2 days
- C. The presence of chronic illness (diabetes and hypertension)
- D. Severe acute illness (anoxic brain injury and respiratory failure)
- E. Male gender

Answer 40.1

The correct answer is (D)

Various criteria have been studied as triggers for palliative care consultation, aiming to identify the ICU patients with the highest likelihood of unmet palliative care needs. The following patient characteristics can serve as reasonable indications for palliative care consultation in the medical ICU: Age ≥ 80 years; Poor baseline functional status; Severe chronic medical comorbidities; Specific acute illnesses/injuries (e.g., severe anoxic encephalopathy after cardiac arrest, advanced dementia, and subarachnoid hemorrhage requiring mechanical ventilation); Chronic critical illness (i.e., ICU stay >5 – 14 days); Utilization of specific procedures in the setting of life-limiting illness (e.g., tracheostomy and percutaneous endoscopic gastrostomy tube); Poor prognosis as determined by the attending physician. Male gender has not been proposed as a risk factor for unmet palliative care needs, although men are less likely to have engaged in prior advance care planning.

In addition, palliative care involvement may be appropriate for patients who have an existing advance directive setting limits on medical interventions, situations in which there is a conflict between the care team and the patient and/or surrogates regarding an appropriate plan of care, and for whom clinicians believe that available interventions are inappropriate or medically futile.

Further Reading

Nelson JE, Curtis JR, Mulkerin C, et al. Choosing and using screening criteria for palliative care consultation in the ICU: A report from the Improving Palliative Care in the ICU (IPAL-ICU) Advisory Board. *Crit Care Med.* 2013;41:2318–2327.

Question 40.2

Mr. T is a 57-year-old male with oxygen-dependent chronic obstructive pulmonary disease (COPD) and poor functional status at baseline admitted to the ICU with a large subarachnoid hemorrhage (Fisher grade 4, Hunt & Hess grade 5). He was intubated in the field for airway protection. Upon admission, he had no purposeful movements and did not respond to commands or withdraw to pain. He remains unresponsive after an intraventricular drain is placed. He has had ongoing seizure activity, and his course has been additionally complicated by metabolic acidosis and hemodynamic instability. He has no durable power of attorney for health care (DPOA-HC). His legal next-of-kin (LNOK) is his daughter. He is described by her as a fiercely independent and private man. She does not believe that he would want to go through a prolonged course of treatment and dependence.

What is the best next step?

- A. Ask additional questions to better understand the patient's values and goals
- B. Advise the daughter that "withdrawal of care" and comfort measures are the best next steps
- C. Elicit the daughter's understanding of her father's condition and prognosis
- D. Discuss withdrawal of life-sustaining interventions and provision of aggressive symptom management as one potential option
- E. A, C, and D

Answer 40.2

The correct answer is (E)

Although it seems likely that the patient's prognosis is poor and that anything short of independent living would not be consistent with the patient's goals, it is still important to elicit a deeper understanding of the patient's values and goals and to discuss any prior advance care planning. It would be critical to ensure that the patient's LNOK understood the prognosis and prognostic uncertainty. If withdrawal of life-sustaining treatment is being considered, it is considered a best practice to avoid phrases such as "withdrawal of care," focusing on withdrawal of *life-sustaining interventions* and shifting the focus of care to comfort as a means to communicate non-abandonment to patients and families.

Withdrawing life support in the ICU

Most patients who die in the ICU do so after the withholding or withdrawal of life support. Discussions regarding the withdrawal of life support usually involve surrogate decision-makers and include an exploration of the patient's goals and values.

Following a decision to withdraw life support, it is important for clinicians to explain to surrogate decision-makers exactly what will occur and to provide anticipatory guidance; several studies have found that knowing what to expect improved family satisfaction during this process. Protocols for compassionate extubation should be followed, and any interventions not directly promoting comfort should generally be discontinued. When possible, a quiet and private space for families should be provided, and patients should be transferred to another ward or facility only when absolutely necessary.

Further Reading

Curtis JR, White DB. Practical guidance for evidence-based family conferences in the ICU. *Chest*. 2008;134:835–843.

Question 40.3

Ms. C is a 72-year-old female with COPD admitted with respiratory failure. She is currently on hospital day 3 and was successfully extubated yesterday, although she still requires high-flow supplementary oxygen. She has been hospitalized three times in the past year for COPD exacerbations and also has a history of severe coronary heart disease. Her forced expiratory volume in 1 second (FEV1) when checked a year ago was less than 20% predicted. She asks you, “How much longer do I have? It feels like I’m dying.”

Which of the following statements is true?

- A. Non-cancer diagnoses such as COPD generally have a less variable course, making prognosis more accurate.
- B. Physicians are generally quite accurate in estimating prognosis.
- C. Most patients do not want to discuss prognosis.
- D. Understanding prognosis impacts the medical decisions patients make.
- E. Physicians should avoid providing patients with quantitative estimates of prognosis.

Answer 40.3

The correct answer is (D)

Patients with advanced cancer generally follow a more predictable course compared to that of patients with many chronic organ failure diseases, which makes prognostication for patients with chronic diseases such as COPD or congestive heart failure difficult. Physicians have not been shown to have high accuracy in prognostication. Quantitative estimates can be a useful way to relay information to patients and to help avoid euphemistic language, but they must be used with care for patients with low literacy and numeracy.

Discussing prognosis

Most patients want to discuss prognosis, but many physicians feel uncomfortable doing so. Physicians who are younger and those who have longer continuous relationships with individual patients tend to be less accurate and more prone to overestimating life expectancy. Evidence suggests that patients who have a more favorable estimate of their own prognosis than is realistic are more likely to choose disease-directed therapies that might be associated with additional pain and discomfort. This makes discussion of prognosis particularly important in establishing a context for care decisions in the ICU, and discussions about prognosis for critically ill patients should begin early and be revisited as the clinical course evolves. It is also important to understand that discordance in prognostic understanding between physicians and patients/family members may exist for several reasons and may not be due simply to misunderstanding. Exploring the reasons for this discordance may help physicians improve their communication about prognosis with patients and family members.

Further Reading

Ahalt C, Walter LC, Yourman L, et al. "Knowing is better": Preferences of diverse older adults for discussing prognosis. *J Gen Intern Med.* 2012;27:568–575.

Question 40.4

Ms. B is a 65-year-old female with a history of end-stage renal disease secondary to diabetic nephropathy, on chronic hemodialysis, admitted to the ICU 5 days ago with hypotension and respiratory failure. Her course has subsequently been complicated by multiorgan system failure. She is intubated and sedated, and nursing notes indicate she has appeared comfortable with midazolam and fentanyl boluses. Her partner, Emily, who is her DPOA-HC, and her son have been at the bedside around the clock. Ms. B is currently mechanically ventilated, on two pressors, and requires continuous renal replacement therapy. She has an advance directive stating that she would not want life-prolonging measures in the event of an illness from which she was not expected to recover and would not want to live in a state of prolonged dependence (e.g., skilled nursing facility). Her chart indicates that she identifies as agnostic.

Which of the following statements is *not* true?

- A. Documentation of pain assessment and management is an important quality indicator for end-of-life care in the ICU.
- B. It is most appropriate to wait until later in the ICU stay when prognosis is more clear before holding a clinician–family conference to address goals of care.
- C. Identifying a surrogate decision-maker early in the ICU course is an important part of care for Ms. B.
- D. Open visitation by families in the ICU is associated with increased patient and family satisfaction.
- E. Spiritual support should be offered to Ms. B's family.

Answer 40.4

The correct answer is (B)

A number of quality indicators have been used for evaluating end-of-life care in the ICU. These include structural provisions and others directly related to care of patients and families, specifically the following: Patient and family-centered decision-making (assessment of decisional capacity and documentation of health care directives and goals of care); communication with clinicians, patients, and families, including timely family conferences; continuity of care, particularly information transmission during transfers of care out of the ICU; emotional support for patients and families; symptom assessment and management; spiritual support; and support for clinicians.

Identifying a surrogate decision-maker within the first day of admission is also important, particularly in a situation such as this, in which the DPOA-HC designated by the patient and the LNOK may be different. Open visiting hours in the ICU are associated with patient happiness and relaxation, family satisfaction, and enhanced communication between patients, families, and staff. Provision of spiritual support is also associated with increased patient and family satisfaction and should at least be offered regardless of the patient's stated religious/spiritual affiliation, which may differ from that of his or her family members.

Further Reading

Mularski RA, Curtis JR, Billings JA, et al. Proposed quality measures for palliative care in the critically ill: A consensus from the Robert Wood Johnson Foundation Critical Care Workgroup. *Crit Care Med*. 2006;34:S404–S411.

Question 40.5

Mr. Y is a 58-year-old male with metastatic lung cancer with known bone metastases and a history of opioid use disorder admitted to the ICU for hypotension and hypoxic respiratory failure due to a community-acquired pneumonia. He is hemodynamically stable, but he has an elevated lactate and a mildly elevated creatinine. He is intubated but able to nod “yes/no” consistently and appropriately in response to questions.

Which of the following statements is true?

- A. Pain, dyspnea, and thirst are the most common symptoms for critically ill patients.
- B. Because Mr. Y is intubated, it is difficult to assess his level of understanding, and he should not be relied on to participate in symptom assessment.
- C. Opioids should be avoided in this patient given his history of opioid use disorder and concerns about addiction.
- D. Both A and B.

Answer 40.5

The correct answer is (A)

Pain, dyspnea, and thirst are the most common symptoms reported by patients in the ICU. Mr. Y is intubated but seems to be responding appropriately to questions. Although clinicians might not be able to assess his capacity to participate in complex decision-making (and might therefore need to involve a surrogate decision-maker), it is important to involve him in the assessment of his symptom burden. A history of prior chronic opioid use is important to take into account when determining opioid dosing in this setting given the impact this might have on the patient's tolerance. Non-opioid agents can be useful adjuncts in the treatment of cancer pain, particularly bone pain (e.g., nonsteroidal anti-inflammatory drugs, bisphosphonates, and steroids), but may be contraindicated in the critical care setting. However, avoidance of opioids would likely *not* be appropriate in this case given the likelihood of severe pain related to his advanced malignancy and critical illness.

Symptom assessment and management in the ICU

Pain, dyspnea, and thirst are common symptoms in the setting of critical illness, as are anxiety and sleep disturbances. Assessment and management of these symptoms are a cornerstone of high-quality palliative care. For patients unable to participate in symptom assessment due to mental status or barriers to communication (e.g., intubation), validated objective structured assessment tools such as the Behavioral Pain Scale and the Respiratory Distress Observation Scale can be utilized.

Further Reading

Campbell ML, Templin T, Walch J. A respiratory distress observation scale for patients unable to self-report dyspnea. *J Palliat Med.* 2010;13:285–290.

Puntillo K, Nelson JE, Weissman D, et al.; Advisory Board of the Improving Palliative Care in the ICU (IPAL-ICU) Project. Palliative care in the ICU: Relief of pain, dyspnea, and thirst—A report from the IPAL-ICU Advisory Board. *Intensive Care Med.* 2014;40:235–248.

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