

EPECTM-O

Education In **P**alliative And **E**nd-Of-Life **C**are For **O**ncology

Self-Study Module 3a:

Symptoms; General Introduction

Module 3a: General Introduction

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Abstract

Many symptoms and syndromes are commonly encountered in patients with cancer. This module first presents general approaches to symptom management, followed by management of the specific symptoms and syndromes, including: anorexia/cachexia, anxiety, constipation, depression, diarrhea, fatigue, insomnia, menopausal symptoms and sexual health, mucositis, nausea and vomiting, and skin problems.

Any symptom can be debilitating and prevent the patient and family from achieving goals that are important to them. As with other aspects of medicine, tailored management is based on the underlying etiology and pathophysiology. When several symptoms occur together, they can be interrelated and management can be complex.

Introduction

Most patients suffer from pain and a number of other common symptoms. This module discusses many of the symptoms that are frequently seen in cancer care, including those listed in Table 1 below.

Table 1: Common Symptoms and Syndromes in EPEC™-O

Anorexia/cachexia	Dyspnea
Anxiety	Fatigue
Ascites	Insomnia
Bowel obstruction	Malignant pleural effusions
Constipation	Menopausal symptoms
Delirium	Mucositis
Depression	Nausea/vomiting
Diarrhea	Skin problems

Several of the other EPEC™-O modules present related topics: EPEC™-O Module 1: Comprehensive Assessment discusses approaches to a comprehensive patient assessment. Pain is addressed in EPEC™-O Module 2: Cancer Pain Management. Symptom management issues in the last hours of life, including terminal delirium and rattle, are discussed in EPEC™-O Module 6: Last Hours of Living.

Some symptoms, such as fatigue, are more prevalent than pain. Others, such as dyspnea, can be more distressing to patients and families than pain. If unrelieved, they preclude any possibility of completing cancer treatment, or relieving psychological, social, and spiritual issues that are causing suffering, or improving quality of the patient's and family's lives.

Symptoms are more than clues that can lead to diagnoses. It would be a mistake for oncologists to assume that all symptoms improve with anticancer treatment. While it is expected that oncologists will direct their therapeutic efforts at the cancer, they also need to understand the possible causes and pathophysiology associated with each symptom, and tailor therapeutic interventions to have the greatest potential for benefit and the least risk of causing harm or burden to the patient and family.

Symptoms frequently interfere with the patient's and family's capacity to do the things they enjoy. They can impair the oncologist's ability to administer anticancer therapy, particularly when the symptoms are the result of the anticancer treatment itself. If left unmanaged, they may lead to changes that shorten survival.

Conversely, if symptoms are well-managed and the patient eats well, sleeps well, maintains function, and has minimal stress, he or she will be more likely to sustain full anticancer therapy and live a longer and more fulfilling life.

Objectives

After studying this module, for each symptom and syndrome, oncologists and other members of the cancer care team will be able to:

- Discuss general assessment and management guidelines.
- Describe the possible causes and underlying pathophysiology.
- Conduct a careful assessment.
- Initiate an appropriate management strategy, including rapid titration and breakthrough dosing.
- Describe principles of multi-symptom management.
- Understand the principle of double effect.

General Management Guidelines

The general approach to managing a symptom is similar to the standard approach used to manage cancer:

- Prevention and early detection will not only alleviate suffering faster and more effectively, they may also prevent future complications that will be more challenging to manage.
- Therapies are chosen to have the greatest potential for benefit and the least risk of causing harm and burden to the patient and family, according to the following ethical principles:
 - Beneficence: the provision of benefits and the balancing of harms and benefits for the purpose of doing the most good.
 - Nonmaleficence: the avoidance of doing harm.
- Treat the cause and the experience:
 - Use pharmacologic, surgical, radiation, and chemotherapeutic agents as appropriate.
 - Consider clinical trials, including Phase I trials as appropriate, keeping in mind that full palliative care during a trial is necessary and rarely restricted.
- For multiple symptoms, rationalize the therapeutic approach to minimize the number of interactions and the potential for interference among interventions.

Understand the underlying cause and pathophysiology

Symptoms are often interrelated with concurrent medical problems in addition to the cancer, the adverse effects of cancer therapy, and side effects of other medical therapy. Management can be challenging. It is not sufficient to have a simplistic approach to symptom management, because causes and appropriate therapies can vary widely. Before embarking on the management of a symptom, the team should have a conceptual framework of the possible causes and associated pathophysiology to guide assessment and management. Frameworks are presented in each of the symptom management modules that follow.

Besides the physical manifestations of a symptom, always look for the influence of psychological, social, spiritual, end-of-life, and loss issues. Dame Cicely Saunders was the first to understand these interrelationships with her description of total pain in the 1960s. (Ref. 1) Spiritual pain may be expressed as physical pain. Dyspnea causes anxiety. Uncontrolled symptoms interrupt psychosocial relationships. A comprehensive assessment (see EPEC™-O Module 1: Comprehensive Assessment) will be helpful in discerning the underlying causes of individual symptoms.

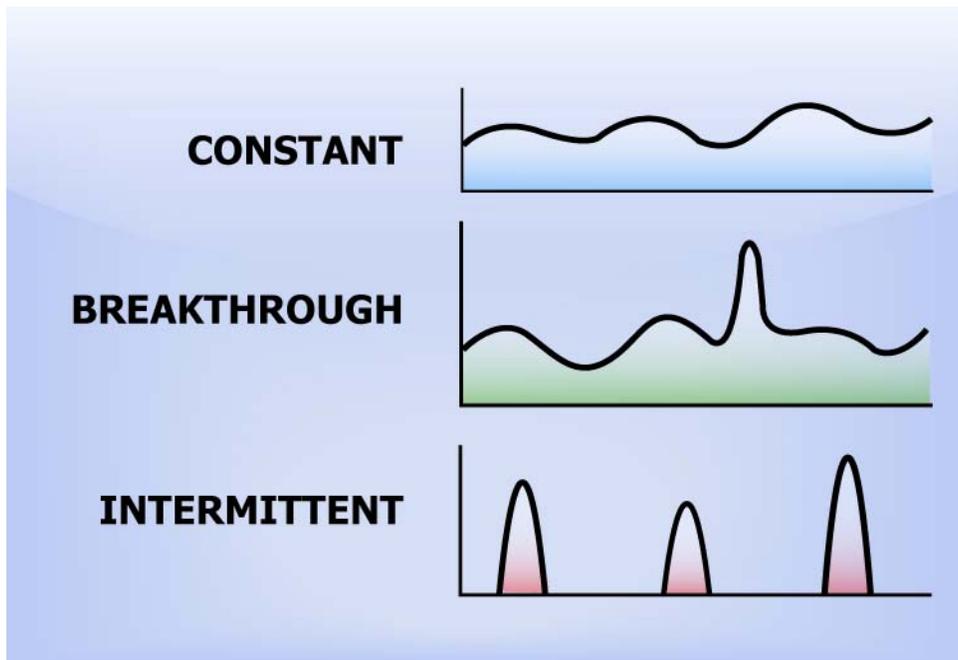
Assess carefully

For each symptom, conduct a thorough assessment including a history, functional inquiry, physical examination, and laboratory and/or radiologic investigations appropriate for the patient's situation. Use this information to gain the best possible understanding of the cause and underlying pathophysiology for each symptom; this understanding will guide symptom management.

Some symptoms routinely (and predictably) occur together (e.g., nausea, constipation, and anxiety commonly accompany pain therapy). Assess for these symptoms routinely during your functional inquiry. Include strategies to prevent/manage them in your treatment plan (e.g., prescribe anti-emetics with chemotherapy and a bowel regimen to preempt opioid-induced constipation; counsel the patient and family as soon as they present with a serious new illness to preempt adjustment disorders).

For each symptom, collect basic data about the onset, location, description of the experience, temporal profile (change over time; Figure 1), severity, effect of medications, and presence of any adverse effects (Table 1). Based on patient preferences, use any one of the assessment scales in Figure 2 to assess severity.

Figure 1: Common Temporal Profiles



facilitate clear communication between team members and guide management choices. Comparison of assessments from one day to the next will establish the effectiveness of therapeutic interventions.

Manage quickly

The ideal plan of care includes therapies to:

- Treat the cause of the symptom.
- Manage the experience.

Many journal articles and textbooks have been written on the management of the underlying causes; this module focuses primarily on managing the experience caused by the symptom.

When symptoms are severe or the patient is weak, oncologists will not be able to wait for the results of investigations to initiate therapy. Initial therapeutic efforts based on history, examination, and inference about the underlying pathophysiology may produce symptom relief and provide additional information as to the cause and pathophysiology.

When modification of the disease process is no longer feasible, symptom relief to manage the experience may become the total focus of care.

Always consider both pharmacologic and non-pharmacologic therapeutic interventions to manage symptoms, including counseling and complementary therapies.

To ensure consistent care planning and delivery, members of the interdisciplinary cancer care team must work together to ensure consistent care planning and delivery. As changes in the patient's condition can occur rapidly, be prepared to respond quickly.

Choose medications appropriate for the underlying cause and pathophysiology, and the severity of the symptom. Plan dosing strategies based on the temporal profile of the symptom, the pharmacokinetics of the medication, and the patient's lifestyle. Most of the medications used in palliative care follow simple first-order kinetics. Fortunately, most of the clinical responses to these medications correlate closely with their plasma concentration.

Continuous dosing

For a symptom that is constantly present around-the-clock, provide the medication routinely once every half-life ($t_{1/2}$). When the medication follows first-order kinetics, steady state will be reached within five half-lives. Try not to adjust the routine dose before steady state has been reached. Premature adjustments increase the risk of unwanted adverse effects. See the **Medication Tables** Section in **EPEC™-O** for specific $t_{1/2}$, t_{Cmax} (time to maximum concentration), and dosing data.

Breakthrough/intermittent dosing

For acute breakthrough or intermittent exacerbations of a symptom, extra or breakthrough doses of medication can be offered once every “time to maximum concentration.” Choose a medication whose absorption-excretion profile comes as close as possible to the temporal profile of the acute exacerbation of the symptom. As an example, the use of morphine ($t_{1/2} = 4$ hours) to manage movement-related breakthrough pain that lasts 5-10 minutes will inevitably lead to unwanted drowsiness and other adverse effects.

Rationalize management of multiple symptoms

Since most cancer patients have many symptoms, management of multiple symptoms is the daily challenge of palliative care. Occasionally, a patient may need to decide which symptom's management is the highest priority, but the goal is to be able to manage all symptoms.

Optimal use of noninvasive, non-pharmacologic approaches (e.g., use of enteral medication routes before parenteral, use of sleep hygiene before pharmacologic therapy) can assist.

A well-rationalized medication list that avoids the hazards of polypharmacy is essential. Especially in patients with late-stage disease, declining renal or hepatic function, reduced fat stores, and general frailty, medication side-effects can be devastating in their own right. Be aware of medications that can accumulate.

Choose one agent to treat more than one symptom whenever possible (e.g., use of steroids to reduce fatigue and the pain of bony metastases). Be aware when treatment of one symptom later conflicts with an emerging issue (e.g., non-steroidal anti-inflammatory agents may need to be discontinued if diuresis for ascites has become a problem, or a patient on a serotonin antagonist who starts to need opioids may need an alternative as part of expectant or proactive management of constipation).

Specific instances of multi symptom management can be found throughout the symptom management modules (EPEC™-O Module 3: Symptoms).

Coordinate care

Educate the patient, family, and caregivers

Education and involvement of the patient, family, and all caregivers as partners is key to successful symptom management. After their initial education and training in specific care giving skills, they will likely need considerable reinforcement and support to optimize the plan of care.

Encourage the patient and family to keep a diary when symptoms are out of control or adverse effects occur. Each time the patient takes a dose of medication, record the date and time, present severity of the symptom, medication and dose used, and any adverse effects at that time.

Table 3: Symptom Diary

Date, Time	Severity	Medication Used	Adverse Effects

Include the interdisciplinary team

Symptoms are experienced in multiple domains. The busy oncologist can rarely discharge all the duties of comprehensive care without the assistance of an interdisciplinary team. The oncologist will need to ensure that the nursing, social work, pharmacy, and pastoral members of the team are all coordinating in the implementation of a single care plan to attend to the cancer patient's many needs. Regular team meetings and attention to communication and coordination are essential in quality comprehensive cancer care.

Obtain palliative care consultations

When symptoms do not resolve quickly or management becomes complex, consult with a palliative medicine expert to help optimize therapies and minimize the risk of adverse events and drug interactions.

Reassess periodically

As etiologies and pathophysiology may change, frequent reassessment and review of the goals of care, treatment priorities, and plan of care are critical, particularly when symptoms recur or worsen.

Intended vs. Unintended Consequences

Many physicians believe that medications used to manage symptoms have an unacceptably high risk of adverse events and may shorten a patient's life, particularly when the patient is frail or close to the end-of-life. These clinicians fail to fully understand and discuss with the patient the potential benefits and risks of these therapies within the framework of the patient's goals of care. The fear of an adverse unintended consequence often leads clinicians to withhold appropriate symptom management or to dose inadequately, leading to unnecessary suffering of the patient.

The intent in offering a treatment determines whether it is ethical medical practice:

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

All medical treatments have both intended effects and the risk of unintended, potentially adverse, secondary consequences. Some examples are listed in Table 4:

Table 4: Intended vs. Unintended Consequences

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

Principle of double effect

The principle of double effect refers to the ethical dilemma that occurs when a person takes an action with an expected good outcome that has an unavoidable, known bad effect as well. The primary intended effect can sometimes justify the action. The principle of double effect applies when a physician uses a treatment for an intended effect such as relief of a symptom, knowing that there may also be a dire, undesired, secondary effect such as death.

Concerns about symptom management

Concerns that the principle of double effect may be an issue sometimes arise when managing symptoms. Like other medical treatments, there is a risk that treatments to control symptoms could produce adverse consequences, including death, either when improperly used or, very rarely, when properly used. Also, in some cases of life-threatening illness, death may seem appealing to the patient, and what is ordinarily intuitive may become complex. For many interventions, such as chemotherapy, total parenteral nutrition for short-gut syndrome, surgery, and non-interventions such as stopping all laboratory tests or avoiding surgery, decisions are made knowing there is a risk of adverse events, including death. As long as the following conditions are met, the action need not be ethically suspect:

- The intent is to relieve suffering and not hasten death.
- Death is a possible, not inevitable, outcome of the intervention.
- There is fully informed consent.

Fortunately, these difficult circumstances need not occur. Adequate symptom management can be achieved without causing death. If the reason for offering a medication such as an opioid is to relieve suffering (e.g., from pain and breathlessness) and accepted dosing guidelines are followed, the risk of a potentially dangerous adverse secondary effect is minimal. The risk of respiratory depression is vastly overestimated. Patients will become drowsy and confused and lose consciousness long before their respiratory rate is compromised. In truth, the usual palliative treatments of pain and dyspnea have a much better safety profile than many of the standard medical treatments used routinely by physicians.

Symptoms can be well controlled with the interventions outlined in this module and those in EPEC™-O Module 2: Cancer Pain Management and EPEC™-O Module 6: Last Hours of Living. None of these recommendations, properly used, will cause death. In this respect, they are like all other medical interventions-concerns about unintended consequences are no greater than normal and concerns about double effect rarely apply.

In contrast, if symptom control involves treatments that are intended to cause death as the means to relieve suffering, then there is ethical concern. If the patient seeks

hastened death by physician-assisted suicide or euthanasia, the clinical and ethical issues are different. Some of these issues are addressed in EPEC™-O Module 14: Physician-Assisted Suicide.

Terminal sedation

Occasionally, refractory symptoms lead the patient, family, and professional team to conclude that the only option for securing comfort for the patient is sedation. If it is not possible to lighten the sedation without a return to unbearable suffering, this sedation can be terminal.

Terminal sedation has been somewhat controversial. Concerns have been raised, for instance, about the use of nutrition and hydration during sedation, and about whether the complexity of human intentions can allow for a clear enough moral boundary in the application of the principle of double effect. Emotions can run very high when terminal sedation is being considered. Technical expertise in the procedure is also necessary.

For all these reasons, although it is clearly identified as good practice in some well-defined circumstances, terminal sedation should not be conducted without the involvement of palliative care experts. Even in circumstances when access to a palliative care expert is difficult, every effort should be made to gain expert involvement, even if only by telephone.

Module 3a - Video 2

Summary

Symptom control requires the physician to combine scientific knowledge of pathophysiology, pharmacotherapeutics, and human behavior with communication skills and clinical judgment. Multiple symptoms are present for most cancer patients, making management particularly challenging. Careful attention to symptom control may lead to better tolerance of disease-modifying therapies, and may even help prolong life. It is challenging and rewarding to help patients feel better no matter what the status of the underlying cancer. Continued symptom control as patients approach the end of their lives will give them more opportunity to realize their personal goals and allow them to die comfortably.

Key Take-Home Points for General Management

1. Symptoms demand active management, along with cancer treatment, as part of comprehensive cancer care.
2. Initial therapeutic efforts based on a comprehensive assessment and inference about the pathophysiology may provide symptom relief and/or information about the etiology and pathophysiology of the symptom.
3. Where possible (and consistent with the goals of care) treat the underlying cause of each symptom, but do not delay efforts to manage the experience while you investigate and treat the underlying etiology.
4. Manage quickly; use continuous and breakthrough dosing.
5. Rationalize the treatment plan to take multiple symptoms and adverse effects of medications into account as well as the need for renal and hepatic dosing.
6. Rely on the interdisciplinary team for optimal patient experience.

Pearls

1. Accept the patient's self-report of his or her experience.
2. Assess how much the patient (as opposed to family) is bothered by symptoms. Frequently the patient is comfortable, but the family is distressed.
3. When patients have multiple symptoms, ask which one is most important to improve—it's often not the one you thought it would be.
4. When treating multiple symptoms, choose drugs that can manage more than one symptom (e.g., opioids manage pain and breathlessness, metoclopramide for nausea also helps with constipation).
5. Non-pharmacologic techniques may also provide significant relief.
6. A symptom is easier and far less costly to prevent than to treat.
7. Make a partnership with your patient and the family caregiver; draw them into the interdisciplinary team and foster their active participation in the care plan.
8. Additional information can be found in Module 3: Health Professional Resources and Module 3: Patient Resources.

Pitfall

1. Trying to fix a symptom that isn't bothering the patient.

References

Module 3a: General Introduction

- 1 Clark D. "Total pain," disciplinary power and the body in the work of Cicely Saunders, 1958-1967. Soc Sci Med. 1999;49(6):727-736. PMID: 10459885; full text.

The article provides a review of the evolution of Dame Cicely Saunders' concept of "total pain."