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Symptom Control in

Patients with Cancer THE FIRST STEP: IMPORTANCE OF PROPER SYMPTOM ASSESSMENT AND RESOLUTION Several randomized trials have now shown that for metastatic cancer patients, prompt symptom assessment and resolution lead to substan tially increased survival. Basch and colleagues at Memorial Sloan Ket tering Cancer Center randomized 766 metastatic solid tumor patients to usual care or once-a-week monitoring of 12 common symptoms (the patient-reported outcomes [PRO] group); these patients checked in once a week by computer or smartphone. Nurses monitored the symptom for “spikes” such as in pain and contacted the patient or brought them in for evaluation. Quality of life was significantly better in the PRO group. Surprisingly, median overall survival (OS) was 31.2 months in the PRO group and 26 months in the usual care group ($p = .03$). There was an absolute difference in OS of 6 per 100 patients at 5 years in the PRO group compared to the control group. In a similar trial of 121 stage III and IV lung cancer patients randomized to usual care or once-weekly PRO reporting, the median OS was 22.5 months versus 13.5 months. The absolute OS difference at 2 years was 10–12 of every 100 patients. In a cluster randomized trial of 52 oncology practices and 1191 patients, PROs completed each week led to statistically significant improvements in quality of life outcomes at 3 months; the primary outcome, OS, has not been reported. This extra attention to symptom assessment and manage ment may be part of the reason that patients randomized to concurrent palliative care in addition to their cancer care live longer. PART 4 Oncology and Hematology A general principle from the above trials is that the health care pro vider should use some form of PRO-related scale to assess symptoms. Homsi et al. evaluated 200 patients referred to the Cleveland Clinic using a 48-item symptom checklist versus what the patients volun teered. The median number of volunteered symptoms was one; the median number using a checklist was 10. Fifty-two percent of these symptoms were rated moderate or severe, 48% mild, and 53% distress ing. Fatigue and pain were the most common symptoms reported in both groups. Not everyone has access to an electronic computer-based PRO system or the ability to integrate this into the electronic medical record (EMR). Readily available and free scales such as the Edmonton Symptom Assessment System–Revised can be done on

paper or elec tronic tablets and pasted into the EMR. The most recent scale includes questions on spirituality and financial distress and is available in many languages (Fig. 74-1). Even with a nurse assisting the patient, the aver age completion time was only 117 s, so time should not be a barrier. Using pain as the most common example of cancer symptoms, many clinicians have been conditioned to use pain as the fifth vital sign and almost immediately ask for a number from 0–10. First, try to establish the generators of the symptom and classify it into a treatable subtype (Table 74-1). It may be helpful to categorize how much each symptom actually bothers the patient; for instance, anorexia may bother the family but not the patient. Next, clinicians can attempt to manage the cancer symptom. We have listed the most common cancer symptoms in Table 74-1 and will review each in turn, including some uncommon ones, and provide current therapeutic modalities. INDIVIDUAL SYMPTOMS ■ ■FATIGUE Frequency Fatigue is the most commonly reported symptom by patients, with often an 80% or higher prevalence. Etiology Fatigue can be due to the cancer, electrolyte abnormalities especially hypercalcemia, anemia, hypothyroidism, chemotherapy, and

immunotherapy such as pembrolizumab, nivolumab, and ipilimumab. Besides general fatigue due to checkpoint inhibitors, 5–22% (average 6%) of patients will develop hypothyroidism and another 1–2% de novo hypophysitis. Assessment Check for hypothyroidism, anemia, hypercalcemia and other electrolyte abnormalities, and renal failure, also screen for depression and/or demoralization. It is important to remember that while most cases of hypothyroidism manifest in 6–8 weeks, it can appear months after the patient has stopped the immunotherapy. Treatment The simplest treatments consist of correcting anemia, hypothyroidism, and/or electrolyte abnormalities (hypercalcemia). There are few other modalities that work quickly or reliably. Paradoxi cally, structured exercise (e.g., 45 min of walking daily) has been shown to be preventative and therapeutic. Rather than prescribe a new exer cise regimen, ask the patient what they have done before and urge them to resume it. One can consider a trial of methylphenidate 5 mg at 7 and 11 a.m. for 48 h, with continuation if some benefit, or modafinil or congeners. Bupropion helps; in a systematic review, six of seven studies reported significant reductions in fatigue with minimal side effects. In a recent randomized trial, 40 patients were randomized to bupropion sustained release or placebo. The bupropion group had significant improvements in fatigue and quality of life but no improvements in depression. Steroids (e.g., dexamethasone 8 mg in the morning) can benefit some patients, usually toward the end of life. Long-term use has not been studied, and patients should be observed for hyperglycemia. ■ ■PAIN Frequency At least 80% of cancer patients will experience pain during their lifetime. While secondary to fatigue in prevalence, it is the most feared symptom. Etiology Try to characterize the type of pain (Table 74-2). Assessment Ask for a 0–10 rating for best, worst, and average pain and what an acceptable pain score would be. List what the person has tried before, including acupuncture, massage, other alternative/ complementary treatments, and medications. Ascertain if the patient is on anticoagulants given the widespread use of novel oral anticoagu lants (NOACs). Treatment • NOCICEPTIVE PAIN For nociceptive pain, start with acetaminophen, then nonsteroidal anti-inflammatory agents, and then opioids, which should always be used with constipationpreventing measures. Recent studies have shown that the addition of acetaminophen to high doses of opioids has no additional effect. Ste roids did slightly improve pain compared to placebo in cancer patients and improved fatigue, nausea, and well-being; a Cochrane systematic review found a reduction in pain of 0.84 on a 0-10 point scale at 1 week. VISCERAL PAIN Visceral pain is among the hardest to treat of all pains. Nonsteroidal anti-inflammatory agents or neuropathic pain medica tions such as gabapentin or

pregabalin, combined with opioids, may be required. Octreotide in combination with opioids reduces visceral hyperalgesia and may be helpful if nothing else works for malignant bowel obstruction. NEUROPATHIC PAIN Several different classes of drugs are useful, but the number needed to treat ranges from 3 to 7 or even 10 for all of them. This necessitates 3- to 4-week trials of alternate drugs alone or in combination. Contrary to common teaching, randomized trials show that opioids do help neuropathic pain with as much benefit as gabapentin or nortriptyline; the combination is even more effective. A variety of neuropathic pain drugs are used: gabapentin, pregabalin, duloxetine, nortriptyline, amitriptyline, carbamazepine, lamotrigine, and many others. One systematic review reported that a reduction in cancer pain intensity of >1 point was unlikely with any of these drugs. Pain relief occurred in 4–8 days, if it occurred, so trials do not need to be >2–3 weeks. Chemotherapy-induced peripheral neuropathy (CIPN) is a promi nent clinical problem that is applicable to the vast majority of patients

Edmonton Symptom Assessment Scale (ESAS–FS) Please circle the number that best describes your symptoms: No Pain

No Fatigue Worst Fatigue

No Nausea Worst Nausea

No Depression Worst Depression

No Anxiety Worst Anxiety

No Drowsiness Worst Drowsiness

No Shortness of Breath Worst Shortness of Breath

Best Appetite Worst Appetite

Best Feeling of Well-being Worst Feeling of Well-being

Best Sleep Worst Sleep

No Financial Distress (Distress/suffering experienced secondary to financial issues)

No Spiritual Pain (Pain deep in your soul/being that is not physical)

FIGURE 74-1 Edmonton Symptom Assessment System–Revised. TABLE 74-1 Common Cancer Symptoms and Their Association SYMPTOM PREVALENCE COMMONLY FOUND CAUSES/EXAMPLES Fatigue 70–80% Chemotherapy Immunotherapy Pain, all 40–70% overall Nociceptive Pancreatic cancer pain Visceral Intestinal obstruction Neuropathic Chemotherapy-induced neuropathy Incident (movement) Bone metastases Oral and gastrointestinal toxicity Dependent on agents used; estimates from 30 to 40% Standard chemotherapy such as doxorubicin Molecularly targeted agents such as palbociclib, infigratinib, everolimus, lenvatinib Radiation therapy Nausea due to chemotherapy Dependent on emetogenic potential of drugs administered; 10–90% Nausea not due to chemotherapy Limited information on incidence but common Due to small-bowel obstruction,

opioids Anorexia/cachexia 20–80% due to cancer Most common in lung and pancreas cancers Dyspnea 10–80% during a lifetime, more common near end of life Most common in lung cancer patients or those with effusions, multiple pulmonary metastases Hot flashes Two-thirds of breast cancer and three-quarters of prostate cancer patients with androgen deprivation Nasal vestibulitis Up to 75% of patients Those receiving taxanes, bevacizumab, etc.

Worst Pain CHAPTER 74 Symptom Control in Patients with Cancer Worst Financial Distress Worst Spiritual Pain Particularly common with cisplatin and doxorubicin Very common but often not reported by either men or women

TABLE 74-2 Types of Commonly Encountered Cancer Pain TYPE OF PAIN CAUSE CHARACTERISTICS EXAMPLES Nociceptive Pressure on nerves Deep, dull, aching, constant and worsening with time Visceral Distention of a hollow viscus Cramping, bloating pain, intermittent Intestinal obstruction, renal colic Neuropathic Direct damage to the nerves from cancer, treatment, or both Local pain, sharp shooting, burning, stabbing, often with allodynia (painful sensation with normal touch) or hyperalgesia Chemotherapy-induced neuropathic pain; direct damage to the longest nerves with damaged receptors and even loss of nerve fiber density Numbness, tingling, pain, which may be mixed together; longest nerves affected most, giving a stocking-glove neuropathy Incident or movement pain Pathologic fractures, bone damage from cancer, residual damage left after cancer Minimal pain at rest, but excruciating pain with movement “bone on bone” receiving chemotherapy. Some chemotherapeutic agents are much more prone to cause neuropathy than are others. Among the biggest offenders are taxanes, platinums, epothilones, eribulin, vinca alka loids, bortezomib, and lenalidomide. At the time that this chapter was written, there were no clearly established means for preventing CIPN from any agent, other than decreasing the dose or stopping the offend ing drug. The most promising approach at the time this chapter was penned involved attempts to decrease the concentration of paclitaxel in the peripheral extremities using cryotherapy, compression therapy, or both. Multiple preliminary trials have suggested that these approaches are helpful. In 2024, a randomized clinical trial is ongoing to com pare compression therapy versus cryo-compression therapy versus a control arm (minimal compression that is not thought to be enough to decrease paclitaxel delivery to the distal extremities). At present, American Society of Clinical Oncology (ASCO) guidelines suggest that in patients who develop substantial CIPN in the midst of a treatment course, the attending clinicians should consider stopping the offending chemotherapy drug(s) or attenuating their dose. PART 4 Oncology and Hematology In terms of treating established CIPN in patients who have com pleted all planned neurotoxic chemotherapy, there is evidence from more than one clinical trial that supports that duloxetine can attenuate established neuropathy symptoms to a small degree (0.6–1.0 on a 0–10 scale). Currently, there are no other proven treatments for treating established CIPN. INCIDENT (MOVEMENT) PAIN DUE TO BONE METASTASES There is minimal evidence for any one modality to treat this type of pain. In one convenience trial, six of six patients with bone metastasis–

incident pain had complete or near-complete responses to low doses of gabapentin (100–200 mg three times a day) added to opioids, but this has not been repeated (trial in the works). There is one case report of complete pain remission for weeks until death after four treatments with Scrambler Therapy, a form of cutaneous nerve stimulation, and one report of “burst” ketamine with morphine. ■ ■GASTROINTESTINAL AND ORAL MUCOSITIS RELATED TO TREATMENT Frequency Oral mucositis varies by drug but is reported in 30–40% of people receiving molecularly targeted agents

such as regorafenib, sorafenib, or erdafitinib, or the breast cancer drug palbociclib. The worst offending chemotherapy drug for oral mucositis, fluorouracil, is not used frequently anymore. The most common cause of oral mucosi tis among commonly used chemotherapy drugs is doxorubicin. Gastrointestinal (GI) mucositis can involve the entire GI tract, and estimates range from 50–80% of cancer patients experiencing some level of chemotherapy-induced diarrhea. Etiology The most common cause is interference by the tyrosine kinase inhibitors with endothelial growth factor receptors (GFRs) or vascular GFRs. Drugs used for both chemotherapy and immune sup pression, such as everolimus, cause both inflammation and the usual disruption of endothelial cells. At its worst, the entire GI tract can be

Pancreatic cancer pain, deep boring, and epigastric Increasingly common and dose limiting; 40–70% of people getting modern treatments. Duloxetine only proven medication, which is only moderately effective. Very difficult to control denuded, and the intestine cannot reabsorb the 25 L of intestinal fluid made daily, producing high-output diarrhea. Most mucositis happens 7–10 days after treatment. Assessment If the time course is right and the patient has received a drug known to cause mucositis, suspicion should be high. Other considerations for oral mucositis include thrush, aphthous stomatitis, herpes, or other infections. Exam may show denuded raw areas that are very painful. GI mucositis is usually manifest by diarrhea, often accompanied by cramps and pain. The diarrhea can be copious, resulting in liters per day. If the time course is not right (very soon or weeks after cancer therapy initiation), other causes such as infections or too many laxa tives should be sought. Treatment For patients receiving bolus fluorouracil, sucking on ice chips during infusion (oral cryotherapy) reduces the incidence and severity by ~50%. There is conflicting evidence on the use of oral dexa methasone or other steroid rinses to prevent oral mucositis from drugs such as everolimus and palbociclib. Most studies show improvement after treatment with glucocorticoid rinses, regardless of the steroid. Viscous lidocaine 2% is commonly recommended for pain. For ulcer ations, topical high-potency steroids are indicated, and a short course of high-dose steroids may be necessary. For GI mucositis manifested as diarrhea, loperamide is the first choice, up to 24 mg a day. Octreotide up to 300 mg a day is reserved for refractory cases. Glucocorticoids are also commonly employed. ■ ■NAUSEA AND VOMITING RELATED TO CHEMOTHERAPY Frequency and Etiology It is well established that chemotherapy can cause substantial nausea and/or vomiting, noting that this problem is strongly associated with individual chemotherapy agents. Some agents, such as cisplatin and doxorubicin, cause substantial nausea and vomiting, whereas other agents, such as fluorouracil, do not cause any substantial nausea and vomiting. Assessment Clinical determination of whether a patient developed nausea or vomiting from chemotherapy is obtained by talking to the patient and/or their family and asking questions regarding these symp toms. This is often done when the patient comes back for another cycle of therapy. Clinical trials use established PRO data that could also be used in clinical practice. In clinical trials, data are usually obtained before chemotherapy and then daily for a few days after each chemo therapy dose. Treatment With highly emetogenic chemotherapy regimens, anti emetic drugs are started with initiation of chemotherapy and com monly given for a few days thereafter. Dexamethasone was established as a helpful agent in the 1970s. In the 1990s, 5-HT3 receptor antagonists became established agents. In the 2000s, NK1 receptor antagonists were established as helpful agents for decreasing nausea and vomiting

in the days following highly emetogenic chemotherapy. These agents did not decrease nausea and vomiting in the first 24 h, as did the 5-HT3 receptor antagonists; thus, NK1 receptor antagonists

were added to the antiemetic cocktail as opposed to replacing 5-HT3 receptor antagonists. In the 2010s, olanzapine was demonstrated to decrease nausea and vomiting when added to the three drug classes discussed above. Olan zapine appears to be the most effective of all of the drugs mentioned in this section, potentially paving the way for decreasing use of other agents in the four-drug antiemetic cocktail described above. Decreas ing dexamethasone doses and/or durations might decrease long-term dexamethasone-associated toxicity. ■ ■NAUSEA AND VOMITING UNRELATED TO CHEMOTHERAPY Frequency No recent data are available, but it is estimated that this problem affects up to 40–70% of patients. Etiology Nausea and vomiting in patients with cancer, not associ ated with chemotherapy, can be associated with multiple other etiolo gies, such as radiation therapy, bowel obstruction, other medications, electrolyte abnormalities, post-anesthesia, and cerebral metastases. Assessment Clinical determination of whether a patient has nausea or vomiting is obtained from talking to the patient and/or their family and asking questions regarding these symptoms. In clinical trials, data are generally obtained daily, including the day prior to the planned intervention and then for a few days following a proposed intervention. Treatment A variety of drugs have been studied for treating nausea and vomiting in this situation, but none of them are very effective; these include diphenhydramine, metoclopramide, prochlorperazine, haloperi dol, methotrimeprazine, dexamethasone, ondansetron, and dronabinol. In 2020, a double-blind, placebo-controlled clinical trial demon strated that a relatively low dose of olanzapine (5 mg/d) was very effective for decreasing nausea and vomiting in patients with advanced cancer who had not received chemotherapy or radiation therapy for at least 2 weeks prior to study entry. In this trial involving a total of 30 patients, nausea scores decreased from 9/10 to 2/10 on the day after olanzapine was started, in comparison to the placebo group whose nausea scores were 9/10 on both the day before and the day after the first dose of the placebo ($p < .001$). Another trial, published in 2023, demonstrated that 2.5 mg/d of olanzapine markedly reduced nausea and vomiting in patients with advanced cancer who were not receiving highly emetogenic chemotherapy. ■ ■ANOREXIA AND CACHEXIA Frequency Up to 20% of all cancer deaths are strongly associated with cancer cachexia. Anorexia is even more common, affecting 5–25% of community-dwelling adults and twice that number of patients with cancer. Etiology Although most anorexia is caused by release of hormones by cancer, it can be aggravated by drug treatments, radiation, mechanical dif ficulties in eating, and food insecurity. Cachexia is multifactorial and char acterized by weight loss of skeletal muscle and adipose tissue, an imbalance in metabolic regulation, and reduced food intake. In general, cancer cachexia cannot be reversed by simply replacing calories and nutrients. Assessment Anorexia is determined simply by asking the patient and family about appetite. Cachexia has been variously defined as 5 or 10% loss of precancer weight. More precise definitions have included the presence of fatigue, anorexia, increased inflammatory markers such as C-reactive protein, body mass index <20, and even sarcopenia on a computed tomography scan. Treatment Treatment is often unsatisfactory for both patients and their families. A systematic review done for an ASCO guideline regarding this topic showed that dietary counseling was associated with increased weight gain in some but not all trials and can be rea sonably offered. The magnitude of this approach, however, is not large.

Enteral feeding tubes and intravenous nutrition are not recommended and should not be used routinely. For anorexia, olanzapine is recom mended as the first-line agent and the only agent with good evidence of benefit without potentially serious harm. In the largest randomized controlled trial, 124 solid tumor patients received olanzapine 2.5 mg at bedtime versus placebo. Sixty percent of the olanzapine patients increased their weight by at least 5% versus 9% of placebo patients (p

<.001). Mirtazapine, which is commonly prescribed, was ineffective in a large randomized trial and should not be used. Megestrol acetate and corticosteroids do increase appetite in afflicted patients and lead to some weight gain but have untoward side effects and do not appear to improve patient survival. A novel approach is to block the elevated lev els of growth differentiation factor 15 (GDF-15), a serum cytokine that is elevated in cachexia with ponsegromab. This monoclonal antibody was associated with improved appetite, weight, and physical activity in a randomized phase 2 trial, but it has not been approved by the FDA.

■ ■CONSTIPATION Frequency Constipation occurs in 20–90% of all cancer patients at some time in their trajectory and can be both painful and associated with anorexia and nausea. CHAPTER 74 Etiology Causes include commonly used drugs such as opioids, acetaminophen, ondansetron, chemotherapy (vandetanib, thalido mide, lenalidomide), and noncancer drugs such as diuretics and antidementia drugs. Inactivity, dehydration, a low-fiber diet, hypercal cemia, and hypothyroidism (including up to 20% of patients receiving checkpoint inhibitors) can all be contributing factors. Symptom Control in Patients with Cancer Assessment Clinicians should ask what the personal bowel habits have been and when the patient last had a bowel movement. If it was 3 or more days ago, constipation is highly likely. Using a specific scale or grading the consistency of the stool is not recommended. Treatment Good bowel hygiene starts with prevention and using drugs that the patient can tolerate. Every opioid prescription should be accompanied by a plan to prevent constipation. Senna is the first choice, starting at 1–2 tablets a day and working up to 8, along with sufficient hydration. Some patients may have cramps from the stimulant action requiring multiple doses a day or switching drugs. Polyethylene glycol is added next, if needed and/or if senna is not tolerated. Lactulose and sor bitol are less commonly used because they commonly are less palatable. Magnesium oxide (1 oz of a 300-mL bottle hourly until movements start) can be helpful. Patients on opioids who are refractory to these measures usually have success with opioid antagonists that reverse the opioid in the periphery but not the brain. Because of cost, these agents currently may require insurance preauthorization, so they are likely not used very often. ■ ■DYSPNEA Frequency Dyspnea (or breathlessness or air hunger) is, like pain, a subjective experience that can only be assessed by the patient. Dyspnea is common, with 10–70% of patients reporting it, especially toward the end of life. Dyspnea portends a poor prognosis in advanced cancer with an average survival of only days, weeks, or months, and should trigger serious illness conversations such as being fully truthful about prognosis and creation of an advance directive. ASCO guidelines rec ommend a systematic assessment for dyspnea at every inpatient and outpatient visit in patients with advanced cancer. Etiology As with most cancer symptoms, dyspnea is multifactorial. Lung dysfunction may be due to the cancer, radiation, chemotherapy, and/or immunotherapy. With immunotherapy, the average time to onset was 52 days in one trial, and the incidence in one large series was 9.5%. Assessment The first attempt should be to find something that is reversible (e.g., hypoxia, pneumonia, pulmonary embolism, pleural effusion, chronic obstructive pulmonary disease, asthma, or bronchial constriction due to cancer). Next should come a careful review of medication history, especially for checkpoint inhibitors, remembering

that pneumonitis may develop months after the immunotherapy has stopped. The impact of the dyspnea on the patient and the family should be assessed. Management of immunotherapy-related lung dis ease may best be done by experts, as the therapies can be challenging and have been rapidly changing.

Treatment Treatment of the cancer, if deemed to have a good chance of success, should be a mainstay. Other contributing factors such as anxiety or chronic obstructive pulmonary disease (COPD) should be maximally treated. High-dose steroids are commonly used in the setting of lymphangitic carcinomatosis, COPD, or asthma. Opi oids at low doses are generally safe and can be helpful in relieving air hunger, and low-dose benzodiazepines can help relieve anxiety. A fan blowing cold air across the face can give some comfort. Supplemental oxygen should be available for patients with hypox emia (i.e., SpO2 ≤90% on room air). High-flow nasal oxygen (HFNO) is often used as a bridge to a next therapy, if there is one; commitment to HFNO complicates referral to hospice or home due to the cost. Refer ral to palliative care should always be considered, along with truthful information about prognosis and a serious illness conversation includ ing advance directives. ■ ■HOT FLASHES PART 4 Oncology and Hematology Frequency Hot flashes are common; they occur in about twothirds of postmenopausal women treated for breast cancer, and almost half have night sweats. Of men treated with chemical or surgical orchiectomy for prostate cancer, three-quarters will have hot flashes. Common knowledge, in the not too distant past, was that hot flashes usually only lasted a couple of years. However, it is now understood that patients can have them for decades. Etiology Lack of estrogen or testosterone is the proximate cause of hot flashes, especially when the decrease is rapid. Assessment Asking about hot flashes, including frequency, sever ity, and interference with life, should be part of the appropriate care of prostate or breast cancer patients. Treatment • FEMALES In the 1990s, four separate individuals clinically noted that patients receiving newer antidepressants, at least new at that time, appeared to have reduced hot flashes; these antide pressants were venlafaxine, paroxetine, sertraline, and fluoxetine. Such observations resulted in randomized, placebo-controlled clinical trials that showed that these and other antidepressants substantially helped women with hot flashes. The authors of this chapter, when it is decided to utilize an antidepressant for treating hot flashes, recommend citalo pram, 20 mg/d, as it appears as effective as other antidepressants and is well tolerated. Gabapentin also has efficacy against hot flashes and reduces anxiety in breast cancer survivors. Oxybutynin, immediate or sustained release, also showed efficacy in randomized trials. This can be a relatively inexpensive treatment approach. Caution is recom mended in older women, as there are concerns regarding mental status changes in the setting of long-term use. In refractory patients, 20–40 mg of megestrol acetate a day can control hot flashes. For women who desire a one-time intramuscular injection, 400–500 mg of medroxyprogester one acetate can nicely decrease hot flashes for many months. Fezolinetant, an NK3 receptor antagonist, became clinically avail able in 2023 as a nonhormonal agent for treating hot flashes in women in general. Although it works as well as some of the other treatments noted above, cross-study comparisons of the efficacy of this drug to the other options mentioned above suggest that hot flash reductions are similar. In a series of studies that included >1300 patients, some with a history of breast cancer (which amounted to ~75% of the subjects) and some without a history of breast cancer (the other 25% of patients), hot flash outcomes were similar. Additionally, this article revealed that hot flash reductions were similar whether or not a patient was receiving tamoxifen.

MALES Pilot trials of venlafaxine and paroxetine supported that they were useful for alleviating hot flashes in men with prostate cancer. However, a randomized trial was not able to demonstrate significant benefit from venlafaxine for controlling hot flashes in men. A prospec tive, randomized, placebo-controlled trial demonstrated that 900 mg/d of gabapentin works well for treating hot flashes in men, similarly to how it works in women. Progesterone analogues also decrease hot flashes in men, similarly to how they do so in women. Case reports support that oxybutynin is

helpful in men with hot flashes; a recently completed randomized, double-blind, placebocontrolled clinical trial demonstrated that this drug nicely decreased hot flashes in this population, too. ■ ■NASAL VESTIBULITIS Frequency Nasal vestibulitis refers to an unpleasant inflamma tion of the vestibule of the nose. An observational interview study of patients who had received at least 6 weeks of chemotherapy noted that

> 70% of those receiving taxanes and >80% of those receiving bevaci zumab experienced untoward nasal symptoms, such as pain, bleeding, and/or scabbing. A prospective study of patients receiving a variety of different chemotherapy regimens illustrated that >75% of patients who received paclitaxel, nab-paclitaxel, or bevacizumab developed bother some nasal symptoms in the following weeks to months. Etiology Chemotherapy can damage the epithelial cells in the nose, leading to dryness, cracking, and secondary infection. Like mucositis, it generally heals in 7–10 days but is a potential source for infection. Assessment Asking about symptoms of dryness, bleeding, crust ing, or pain and an exam should confirm local tissue irritation. Treatment Nasal sprays of saline and of rose geranium in sesame oil have been used to treat this clinical problem, with data supporting that the latter is more beneficial. This will have to be compounded; the recipe is available from the authors or the Mayo Clinic. ■ ■FURTHER READING Basch E et al: Overall survival results of a trial assessing patientreported outcomes for symptom monitoring during routine cancer treatment. JAMA 318:197, 2017. Correa-Morales JE et al: Cancer and non-cancer fatigue treated with bupropion: A systematic review. J Pain Symptom Manage 65:e21, 2023. Finnerup NB et al: Neuropathic pain: From mechanisms to treatment. Physiol Rev 101:259, 2021. Groarke JD et al: Ponsegromab for the Treatment of Cancer Cachexia. N Engl J Med 391:2291, 2024. Homsi J et al: Symptom evaluation in palliative medicine: Patient report vs systematic assessment. Support Care Cancer 14:444, 2006. Hui D, Bruera E: The Edmonton Symptom Assessment System 25 years later: Past, present, and future developments. J Pain Symptom Man age 53:630, 2017. Loprinzi CL et al: Prevention and management of chemotherapyinduced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. J Clin Oncol 38:3325, 2020. Mannix KA: Palliation of nausea and vomiting, in Oxford Textbook of Palliative Medicine, 2nd ed. Doyle D et al (eds). Oxford, UK, Oxford University Press, 1998, p. 48. Molinares D et al: Chemotherapy-induced peripheral neuropathy: Diagnosis, agents, general clinical presentation, and treatments. Curr Oncol Rep 25:1227, 2023. Navari RM et al: Olanzapine for the treatment of advanced cancerrelated chronic nausea and/or vomiting: A randomized pilot trial. JAMA Oncol 6:895, 2020. Roeland EJ et al: Cancer Cachexia Expert Panel. Cancer cachexia: ASCO guideline rapid recommendation update. J Clin Oncol 41:4178, 2023. Smith TJ, Saiki CB: Cancer pain management. Mayo Clin Proc 90:1428, 2015.

Revision #1
Created 2026-01-06 16:31:43 UTC by Omar Ayman

Updated 2026-01-06 16:31:43 UTC by Omar Ayman