

Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 8e >

Chapter 240: Emergency Complications of Malignancy

J. Stephan Stapczynski

INTRODUCTION

The incidence of cancer is increasing as the general population ages and individual longevity grows. More patients with active malignancy are likely to come to the ED for care because of this increase, coupled with more intensive and varied treatments being applied in the outpatient setting.¹ Many conditions that prompt these patients to come to the ED will not be due to cancer.^{2,3} Conversely, there are disorders often or uniquely related to malignancy that collectively are termed *oncologic emergencies*.^{4,5,6,7} These malignancy-related emergencies are broadly categorized as: (1) those due to local physical effects, (2) those secondary to biochemical derangement, (3) those that are the result of hematologic derangement, and (4) those related to therapy (**Table 240-1**).

TABLE 240-1

Emergency Complications of Malignancy

Related to local tumor effects	Malignant airway obstruction Bone metastases and pathologic fractures Malignant spinal cord compression Malignant pericardial effusion with tamponade Superior vena cava syndrome
Related to biochemical derangement	Hypercalcemia Hyponatremia due to inappropriate antidiuretic hormone secretion Adrenal insufficiency Tumor lysis syndrome
Related to hematologic derangement	Febrile neutropenia and infection Hyperviscosity syndrome Thromboembolism
Related to therapy	Chemotherapy-induced nausea and vomiting Chemotherapeutic drug extravasation

EMERGENCIES RELATED TO LOCAL TUMOR EFFECTS

MALIGNANT AIRWAY OBSTRUCTION

Malignancy-related airway compromise is usually an insidious process that results from a mass originating in the oropharynx, neck, or superior mediastinum progressively obstructing air flow.^{6,8} Acute compromise may occur with supervening infection, hemorrhage, or loss of protective mechanisms, such as muscle tone. Iatrogenic factors, such as radiation therapy, may create additional difficulties by producing local

inflammation with tissue breakdown. It is helpful to classify airway impairment due to malignant tumor obstruction in two manners, as to location—from the lips and nares to the vocal cords (**upper airway**) versus those from the vocal cords to the carina (**central airway**)—and, as to nature of the obstruction—**endoluminal**, **extraluminal**, or **mixed**. Almost regardless of the cause, airway obstruction usually presents with symptoms of shortness of breath and signs of tachypnea and stridor. The physical examination may show evidence of a mass in the pharynx, neck, or supraclavicular area.

Patients with airway obstruction due to a malignant tumor are evaluated with a combination of plain radiographs, CT, and endoscopic visualization.^{6,8} Direct laryngoscopy is discouraged because injudicious manipulation of the upper airway may convert a partial obstruction into a complete one by provoking bleeding or edema.⁹

Emergency management includes the administration of supplemental humidified oxygen and maintenance of the best airway possible through patient positioning. Heliox—typically a 50:50 mixture of helium and oxygen—may provide symptomatic improvement in upper airway obstruction due to cancer when combined with other therapy.¹⁰

Mechanical intervention for critical airway obstruction from a tumor is rarely required in the ED. For patients with critical upper airway obstruction, emergency transtracheal jet ventilation or cricothyroidotomy could be lifesaving if the obstruction is above the vocal cords (see [chapter 30](#), "Surgical Airways"). However, the presence of an overlying tumor or swelling may render such procedures technically difficult. Alternatively, passage of the endotracheal tube beyond the area of obstruction is a consideration when the patient is progressing to complete airway occlusion.^{6,9} This is best done using awake fiberoptic intubation with a 5-0 or 6-0 endotracheal tube, wire reinforced, if possible. Placement of such a tube can provide symptomatic relief and time until procedures with more sustained benefit can be performed.

The two procedures that provide sustained relief of airway obstruction are neodymium-yttrium-aluminum-garnet laser photoradiation for vaporization of obstructing tissue and placement of a self-expanding stent at the stenotic site; these two modalities are often combined.^{11,12} Alternatively, variations of radiotherapy—endobronchial brachytherapy, photodynamic therapy, and external-beam radiation therapy—can be directed to the obstructing tumor, but the time for symptomatic response is longer than the mechanical approaches of laser photoradiation and stenting.

BONE METASTASES AND PATHOLOGIC FRACTURES

Anatomic disruption of bone weakened by preexisting conditions is termed a *pathologic fracture*. Pathologic fractures due to malignancy most commonly affect the axial skeleton (calvarium included) and the proximal aspect of the limbs. Most pathologic fractures are due to metastases

from solid tumors (e.g., breast, lung, prostate) that localize in areas of bones with high blood flow, identified as containing red marrow.¹³ Most patients with pathologic fractures have a known malignancy. Patients with bone metastases usually present with localized pain and a benign outward appearance of the involved area.

Malignancy alters the normal radiographic appearance of bone, including loss of trabeculae with indistinct margins (osteolytic, or "moth eaten"), poorly demarcated areas of increased density (osteoblastic), and/or a periosteal reaction. Plain radiographs may identify only about half of metastatic bone lesions.¹⁴ Advanced imaging is often required; CT with IV contrast, particularly when using reconstruction software, can visualize three-dimensional bone integrity and soft tissue extension, whereas MRI best delineates soft tissue and bone marrow involvement. A total-body radionuclide bone scan can be used as a screening tool to identify areas of increased bone activity that could represent additional metastatic spread.¹⁴ However, areas of radionuclide localization on the bone scan are not specific for cancer, and additional imaging studies of these areas are necessary for confirmation.

Treatment priorities are pain relief and restoration or salvage of function. For acute pain or fracture, parenteral analgesics are recommended for rapid treatment. Patients with bone metastases often require long-acting oral opioids and other adjunctive medications for pain relief (see [chapter 38](#), "Chronic Pain"). Approximately 80% of painful bone metastases can be helped with palliative radiotherapy, although it may take several weeks after completion of a typical 5-day course of treatment to experience maximal benefit. The majority of pathologic fractures require open surgical repair.

MALIGNANT SPINAL CORD COMPRESSION

Up to 20% of cancer patients will develop neoplastic involvement of the vertebral column, and 3% to 6% will develop spinal cord compression.^{4,5,6,15} Most cases of malignant spinal cord compression are due to metastases to vertebral bodies from solid organ tumors, with the thoracic vertebrae being the most common location for such metastases. Spinal cord compression occurs when these metastases enlarge, erode through the vertebral cortex into the spinal canal, and compress on the spinal cord. Less common causes of malignant spinal cord compression include local spread from paraspinal tumors through the intervertebral foramen or tumors (primary or metastatic) directly involving the spinal cord or meninges.

Approximately 90% of patients with malignant spinal cord compression will have back pain ([Table 240-2](#)). Such pain is often described as unrelenting, progressive, worse when supine, and located in the thoracic vertebral area. Approximately 80% of patients with malignant spinal cord compression have a prior diagnosis of cancer, so individuals with known cancer and back pain should undergo radiographic imaging. Other symptoms of malignant spinal cord compression may include muscular weakness, radicular pain, and bladder or bowel dysfunction. Weakness is

most apparent in the proximal extremity musculature and may progress to complete paralysis. Sensory changes initially may be confined to a band of hyperesthesia around the trunk at the involved spinal level and that eventually becomes anesthetic distal to the level. Urinary retention (with overflow incontinence), fecal incontinence, and impotence are late manifestations.

TABLE 240-2

Malignant Spinal Cord Compression

Suspect	Patient with known cancer: especially lung, breast, prostate Thoracic location: 70% Progressive pain and worse when supine Motor weakness: proximal legs Sensory changes: initially radicular, later distal anesthesia Bladder or bowel dysfunction: late findings
Imaging	Plain radiographs: may detect vertebral body metastases but less sensitive and specific for malignant spinal cord compression MRI: modality of choice, image entire vertebral column CT myelography: used when MRI not available or accessible
Corticosteroids	Dexamethasone, 10 milligrams IV followed by 4 milligrams PO or IV every 6 h Consider starting in ED if imaging is delayed
Radiotherapy	Standard approach, beneficial in approximately 70% No specific radiotherapy regimen proven superior Prognosis highly dependent on pretreatment neurologic function
Surgery	Consider in highly selected cases, such as Patient in good general condition and able to undergo extensive surgery Appropriate prognostic life expectancy Rapidly progressive symptoms Clinical worsening during radiotherapy Unstable vertebral column

MRI is the imaging modality of choice to define the site and degree of cord compression and to identify the presence of additional vertebral lesions. The entire spinal column is usually imaged due to the potential for multiple level involvement, although because cervical metastases are

unusual, it may be reasonable to not image the cervical spine if there are no symptoms referable to that region. CT with or without myelography is used when MRI is contraindicated or inaccessible. Plain radiography may identify an abnormality in approximately 80% of patients with painful vertebral metastases. However, plain radiographs are less useful in patients with suspected malignant spinal cord compression, because radiographic findings do not always correlate with the level of spinal cord compression, and causes of malignant spinal cord compression other than vertebral body metastases will not produce visible changes in vertebral body radiographic appearance.

Use opioid analgesics for initial pain control. Consider administration of corticosteroids in the ED, especially if there will be a delay in MRI or CT myelography.^{4,5,6,15} Typically [dexamethasone](#), 10 milligrams IV bolus, followed by 4 milligrams PO or IV every 6 hours, is used. Further treatment, with continued corticosteroids, radiation therapy, surgery, or a combination of modalities, will depend on the life expectancy of the patient, extent of disease, and degree of motor impairment. Radiation therapy has been the typical treatment for patients with malignant spinal cord compression, and a beneficial response is seen in approximately 70% of those treated.¹⁶ The overall prognosis for those treated with radiotherapy is highly dependent on pretreatment functional ability; approximately 90% of those who can walk at the time of diagnosis remain ambulatory after radiation treatment, about half of those who have motor function but cannot walk will recover ambulatory ability with radiotherapy, but few patients with complete paraplegia at the time of diagnosis will recover lower extremity motor function. Therefore, **malignant spinal cord compression is considered a radiotherapy emergency**. Select patients with malignant spinal cord compression may benefit from surgical tumor resection, including those with neurologic impairment ([Table 240-2](#)).¹⁵ Because of the complex decision making from among the therapeutic options, specialists in oncology, radiotherapy, and spinal surgery should be consulted early.

MALIGNANT PERICARDIAL EFFUSION WITH TAMPONADE

Pericardial involvement, often with effusion, occurs in up to 35% of patients with all types of cancer, although the effusions are often small and remain undiagnosed.^{4,5,6} Symptomatic pericardial effusions occur less frequently and usually result from lung or breast cancer. Other etiologies for pericardial effusions in patients with malignant disease include other tumor types (such as melanoma, leukemia, or lymphoma) and a complication of treatment (radiotherapy or chemotherapy).

Symptoms and physical examination findings are a function of pericardial fluid accumulation rate and volume (see [chapter 55](#), "Cardiomyopathies and Pericardial Disease"). Large effusions can develop gradually and are surprisingly well tolerated. Symptoms of a pericardial effusion include dyspnea, orthopnea, chest pain, dysphagia, hoarseness, and hiccups. Physical findings include distant cardiac sounds, jugular venous distention, and a pulsus paradoxus.

A sudden increase in fluid between the nondistensible pericardium and compressible heart creates a cardiac tamponade: the low-pressure right heart is unable to accept vena caval return or pump forward to the pulmonary arteries, and the left ventricle cannot fill or produce a sustainable ejection fraction. Signs and symptoms include accentuation of those noted with pericardial effusion with additional manifestations of circulatory shock. There is usually tachycardia, hypotension, and a narrowed pulse pressure.

The ECG may demonstrate reduced voltage in the QRS complex throughout all leads, a reflection of the insulating characteristics of the effusion. Electrical alternans is a classic, although infrequent, finding with a large pericardial effusion. The cardiac silhouette on chest radiography may appear large, reflecting the gradually accumulated effusion in the stretched pericardial sac. **Echocardiography is the diagnostic tool of choice, being noninvasive, portable, and highly accurate in trained hands.** Echocardiography can not only detect the presence of a significant pericardial effusion but also assess cardiac function and identify physiologic changes associated with cardiac tamponade.

Asymptomatic pericardial effusions do not require specific treatment. Patients with symptomatic effusions should undergo pericardiocentesis, ideally with echocardiographic guidance. See [chapter 34](#), "Pericardiocentesis." Most often, this procedure can await the arrival of the specialist and transport of the patient to the appropriate procedural area. If patients with cardiac tamponade require emergent pericardiocentesis in the ED, use a portable US device to guide needle direction during the procedure.

Malignant pericardial effusions are treated depending on the tumor type and overall patient condition. Reduction in fluid production can be done by treating the tumor with appropriate systemic chemotherapy or radiotherapy. Intrapericardial chemotherapy may be useful in tumors sensitive to these agents. A pericardial window or partial pericardial resection can be done to prevent accumulation of fluid within the pericardial space. A percutaneous indwelling intrapericardial catheter can also prevent accumulation of fluid, but with the risks associated with percutaneous devices. Malignant pericardial effusion typically indicates the presence of advanced disease, and most patients die within 1 year after diagnosis.

SUPERIOR VENA CAVA SYNDROME

The term *superior vena cava (SVC) syndrome* describes the clinical effects of elevated venous pressure in the upper body that result from obstruction of venous blood flow through the SVC.^{4,5,6,17,18} This syndrome is most commonly caused by external compression of the SVC by an extrinsic malignant mass. The most common tumors associated with malignant SVC syndrome are lung cancer in 70% and lymphoma in approximately 20%. Benign conditions and intravascular thrombosis (precipitated by indwelling vascular catheters or pacemaker leads) currently account for about one third of all SVC syndrome cases. SVC syndrome rarely constitutes an emergency; the vast majority of patients do not materially deteriorate during the initial 1 to 2 weeks after diagnosis. The exception is when neurologic abnormalities are present due to increased intracranial pressure.

Symptom development correlates roughly with the severity of obstruction and the rate of narrowing. If compression occurs over weeks, collateral vessels dilate to compensate for impaired flow through the SVC. Most patients will describe symptoms developing a few weeks before seeking medical attention. Clinical manifestations correlate with a jugular venous pressure of 20 to 40 mm Hg (2.7 to 5.4 kPa), as compared with a normal range of 2 to 8 mm Hg (0.3 to 1.0 kPa). The most common symptoms are facial swelling, dyspnea, cough, and arm swelling.¹⁸ Less common symptoms include hoarse voice, syncope, headache, and dizziness. In rare but extreme cases, venous obstruction can lead to increased intracranial pressure that produces visual changes, dizziness, confusion, seizures, and obtundation. Physical examination findings may show swelling of the face and arm, sometimes with a violaceous hue or plethora, and distended neck and chest wall veins.

The plain chest radiograph will usually show a mediastinal mass in cases of malignant SVC syndrome. CT of the chest with intravascular contrast is the recommended imaging modality to assess the patency of the SVC.^{17,18} MRI is useful for patients who cannot receive IV contrast. Contrast venography is rarely needed, except in uncertain cases or as part of an intravascular interventional procedure. In patients with a known diagnosis of lung cancer, biopsy for pathologic confirmation of a malignancy is usually not required. For patients without a known intrathoracic cancer, tissue confirmation of a malignant cause is highly desirable before initiation of radiotherapy and required before initiation of chemotherapy.^{17,18}

Initial management is with head elevation to decrease venous pressure in the upper body and supplemental oxygen to reduce the work of breathing. Corticosteroids and loop diuretics are commonly used, but there is no evidence that they contribute to clinical improvement, with the exception that corticosteroids would be expected to be helpful when the cause of the obstruction is lymphoma.

Radiation therapy is effective in reducing symptoms in approximately 75% of patients with SVC syndrome, reflecting the approximate incidence of radiosensitive tumors producing this disorder.¹⁸ Many patients will experience a reduction in symptoms within 3 days after the start of radiation treatment. The mechanism by which radiotherapy reduces symptoms in SVC syndrome is unclear, because the majority of patients receiving such treatment do not achieve complete relief of the obstruction. It is likely that continued development of collaterals contributes to the reported benefit seen during radiotherapy.

Intravascular stents, with or without angioplasty, can be used to reduce obstruction to SVC flow.^{17,18} These stents appear to produce a more rapid improvement in symptoms and signs compared with radiotherapy or chemotherapy, suggesting a preferential benefit in patients with severe manifestations who require urgent treatment.¹⁸ Stent placement should also be considered for malignant causes that do not respond well to radiotherapy or chemotherapy (like mesothelioma), for benign causes (like fibrosing mediastinitis), or for intravascular thrombosis associated with an indwelling catheter.^{17,18}

Chemotherapy is effective in producing symptomatic relief from SVC syndrome in approximately 80% of patients with lymphoma, 80% of patients with small-cell lung cancer, and 40% of patients with non-small-cell lung cancer. For these chemotherapy-sensitive cancers, there is no evidence of benefit from additive radiotherapy, again indicating that dilation of venous collaterals may play a role in clinical improvement.

Patients with SVC syndrome due to intravascular thrombosis can be treated with catheter-directed fibrinolytics.¹⁸ Removal of an inciting intravascular object, such as a central venous catheter, should be considered. Postfibrinolytic anticoagulation is generally recommended to prevent recurrence, although there is no firm supporting evidence.¹⁸ For cancer patients with an indwelling central venous catheter, there is no proven role for prophylactic anticoagulation to reduce the risk of venous thromboembolism.¹⁹

Recurrence of SVC syndrome is seen in approximately 20% of lung cancer patients treated with radiotherapy and/or chemotherapy and 10% treated with intravascular stents.¹⁸ For patients with malignant SVC syndrome, survival is dependent in the causative cancer; with lung cancer, median survival is approximately 6 to 12 months.

EMERGENCIES RELATED TO BIOCHEMICAL DERANGEMENT

HYPERCALCEMIA

Hypercalcemia is seen in 5% to 30% of patients with advanced cancer at some time during their disease course.²⁰ Breast cancer, lung cancer, and multiple myeloma are the malignancies most commonly associated with hypercalcemia. The three key mechanisms whereby malignancy produces hypercalcemia are: (1) by production of a parathyroid hormone-related protein that is structurally similar to [parathyroid hormone](#), (2) by extensive local bone destruction associated with osteoclast-activating factors, and (3) by production of vitamin D analogues. The most common mechanism with solid tumor-associated hypercalcemia is the production of the parathyroid hormone-related protein that binds to [parathyroid hormone](#) receptors, thereby mobilizing calcium from bones and increasing renal reabsorption of calcium.²⁰ Hypercalcemia from enhanced osteoclastic activity is associated with bone metastases from lung and breast cancer, and multiple myeloma. Production of vitamin D analogues is generally seen in lymphomas, usually Hodgkin's disease.

Classic symptoms of hypercalcemia include lethargy, confusion, anorexia, and nausea (see [chapter 17](#), "Fluids and Electrolytes"). Because most patients with hypercalcemia due to malignancy have advanced cancer, symptoms of general debility due to tumor may be difficult to distinguish from those caused by hypercalcemia. Hypercalcemia reduces intestinal motility, so constipation is common, although that symptom can be produced by concomitant opioid therapy for pain. Hypercalcemia produces an osmotic diuresis, so some of the nonspecific symptoms can be due

to relative hypovolemia. **Clinical symptoms of hypercalcemia are most correlated with the rate of rise in the serum calcium level, as opposed to the actual calcium level. Therefore, slow increases in serum calcium may be relatively asymptomatic until reaching high levels.**

Hypercalcemia does not always require treatment, especially if the patient is asymptomatic and well hydrated and the total serum calcium is less than 14 milligrams/dL (3.5 mmol/L). The initial treatment of symptomatic hypercalcemia is with IV isotonic saline at a rate adjusted to the ability of the patient's cardiovascular system to tolerate a volume load.⁷ A typical dose would be normal saline, 1 to 2 L bolus, to restore intravascular volume, followed by an infusion at a rate of 200 to 250 mL/h.⁷ Such treatment will result in clinical improvement and a modest decrease in the plasma calcium over 24 to 48 hours but rarely normalizes the level. Furosemide is useful in patients with heart failure or renal insufficiency to prevent volume overload from normal saline infusion but has little additive effect to the use of IV saline alone in the treatment of hypercalcemia in patients with normal cardiac and renal function. **Therefore, furosemide is not routinely recommended in the treatment of hypercalcemia due to malignancy.**

Because the initial priority is restoration of intravascular volume with IV saline, pharmacologic treatment of hypercalcemia is usually not initiated in the ED.⁷ **Bisphosphonates** are the recommended agents to treat malignancy-associated hypercalcemia.^{7,20} Bisphosphonates are potent inhibitors of bone resorption and produce a sustained decrease in calcium 12 to 48 hours after administration, with the effect lasting for approximately 2 to 4 weeks. Bisphosphonates, such as pamidronate, [etidronate](#), or zoledronic acid, are given by slow IV infusion to prevent precipitation of bisphosphonate-calcium complexes in the kidney and subsequent renal failure.

Other agents have a limited role in the treatment of malignancy-induced hypercalcemia. [Calcitonin](#), 4 units/kg SC or IV every 12 hours, lowers plasma calcium within 2 to 4 hours, but it may cause a hypersensitivity response, and tachyphylaxis develops within 3 days, so the beneficial effect is short lived. Glucocorticoids, such as prednisone 60 milligrams PO per day, may be helpful with steroid-sensitive tumors, such as lymphomas and multiple myeloma.⁷ Gallium nitrate, mithramycin, and plicamycin are used infrequently due to their toxicity. Hemodialysis can be used to treat hypercalcemia and is indicated for those with profound mental status changes or renal failure or for those unable to tolerate a saline load.

HYPONATREMIA DUE TO INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION

Inappropriate secretion of antidiuretic hormone is most commonly associated with bronchogenic cancer but may be seen in other malignancies and can also occur from chemotherapy, opioids, carbamazepine, and selective serotonin reuptake inhibitors.²¹ Regardless of the etiology, the syndrome of inappropriate antidiuretic hormone consists of hyponatremia, decreased serum osmolality, and less than maximally dilute urine, all

in the presence of euvoemia, absence of diuretic therapy, and normal renal, adrenal, and thyroid function (see [chapter 17](#)). **Syndrome of inappropriate antidiuretic hormone secretion should be suspected if a patient with cancer presents with normovolemic hyponatremia.**

Signs and symptoms of hyponatremia are primarily neurologic and correlate with severity and with rapidity of development. Anorexia, nausea, and malaise are the earliest findings, followed by headache, confusion, obtundation, seizures, and coma. Seizures are usually generalized tonic-clonic in nature; focal seizures are uncommon from hyponatremia, and their occurrence suggests focal CNS lesions. Life-threatening symptoms are almost invariably associated with sodium concentrations <110 mEq/L (<110 mmol/L).

Water restriction is the mainstay of treatment in euvolemic asymptomatic patients. Patients with sodium levels >125 mEq/L (>125 mmol/L) are generally asymptomatic and can be managed with water restriction of 500 mL/d and close follow-up. More severe hyponatremia—serum sodium between 110 and 125 mEq/L with mild to moderate symptoms—may require furosemide 0.5 to 1.0 milligram/kg PO with concomitant IV normal saline to maintain euvoemia and affect a net free water clearance. **For severe hyponatremia—serum sodium <110 mEq/L, usually with coma or repetitive or sustained seizures—use 3% hypertonic saline (510 mEq/L). Infuse carefully, usually at a rate of 25 to 100 mL/h, to avoid volume overload or too rapid correction in sodium level,** with subsequent osmotic demyelination syndrome (central pontine myelinolysis). The rate of correction of hyponatremia is controversial, but serum sodium increasing at a rate of 0.5 to 1.0 mEq/L per hour, with not more than a total increase of 12 to 15 mEq/L in the first 24 hours, is recommended (see [chapter 17](#)).

ADRENAL INSUFFICIENCY

Adrenal insufficiency associated with malignancy may be secondary to adrenal tissue replacement by metastases but is more commonly due to abrupt physiologic stress in the face of chronic glucocorticoid therapy with pharmacologic adrenal suppression (see [chapter 230](#), "Adrenal Insufficiency"). The subsequent vasomotor collapse may be sudden and severe.²² Clues for acute adrenal insufficiency include mild hypoglycemia, hyponatremia, and hypotension refractory to volume loading and vasoconstrictor therapy.

Along with rapid IV rehydration, the stressed and steroid-dependent patient should be given [hydrocortisone](#), 100 to 150 milligrams IV, followed by an infusion of an additional 100 to 200 milligrams IV over 6 hours.²² If possible, obtain a serum cortisol level before steroid treatment. While results will generally not be available to the ED, values can help future management.

TUMOR LYSIS SYNDROME

Tumor lysis syndrome is a metabolic crisis resulting from massive cytolysis and release of intracellular contents into the systemic circulation.^{7,23} Of particular concern are the individual ions ([potassium](#), [phosphate](#), calcium), nucleic acids (which metabolize to uric acid), and intracellular

proteins. Tumor lysis syndrome most commonly occurs with treatment of hematologic malignancies because of rapid cell turnover and growth rates, bulky tumor mass, and high sensitivity to antineoplastic agents. Tumor lysis syndrome is uncommon with solid tumors or without prior therapy ("spontaneous tumor lysis syndrome").

The manifestations of tumor lysis syndrome can be categorized by clinical effects (acute kidney injury, seizure, cardiac dysrhythmia or arrest) and laboratory abnormalities (hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia). Renal failure is the strongest predictor of morbidity in tumor lysis syndrome and usually results from uric acid precipitation within the renal tubules. Phosphorus released from tumor cells may combine with calcium and precipitate in renal tubules and parenchyma as well. Hypovolemia may contribute to the renal impairment seen with tumor lysis syndrome. The release of intracellular potassium can produce acute hyperkalemia and provoke or contribute to cardiac dysrhythmias or cardiac arrest. Because malignant cells can contain fourfold the amount of phosphorus as normal cells, the abrupt release of extensive phosphate into the circulation may produce a drop in serum calcium. The resultant hypocalcemia may induce tetany and seizures and contribute to dysrhythmias.

Recognize the potential for tumor lysis syndrome with treatment of hematologic malignancies. Prophylactic allopurinol and maintaining good hydration can reduce the risk of tumor lysis syndrome developing. Patients with established tumor lysis syndrome may experience sudden electrolyte changes and life-threatening complications, so admission to an intensive care unit with cardiac rhythm monitoring is indicated. Aggressive IV fluid administration to increase urinary excretion of the released intracellular solutes is the cornerstone for treatment of tumor lysis syndrome. Increased urine flow will counteract the precipitation of urate and calcium phosphate crystals in the renal tubules.

Hyperkalemia is the most immediate life-threatening element with tumor lysis syndrome because of induced cardiac dysrhythmias and cardiac arrest.^{7,23} Treatment is identical to other causes of hyperkalemia: β -adrenergic agonists, sodium bicarbonate, and dextrose-insulin therapy (see [chapter 17](#)). Avoid calcium administration unless there is cardiovascular instability (ventricular dysrhythmias or wide QRS complexes) or neuromuscular irritability (seizures) because supplemental calcium may cause metastatic precipitation of calcium phosphate. Hyperphosphatemia is managed with phosphate binders (limited effect) or by the administration of dextrose and [insulin](#). Hemodialysis can correct all biochemical abnormalities of tumor lysis syndrome, although a large phosphate burden may require repeat frequent and prolonged dialysis sessions or continuous renal replacement therapy.^{7,23}

EMERGENCIES RELATED TO HEMATOLOGIC DERANGEMENT

FEBRILE NEUTROPENIA AND INFECTION

Infections are a common source of morbidity and mortality in patients with malignancies.²⁴ A common feature associated with the increased risk of infection in these patients is the presence of impaired immunity, especially neutropenia.^{24,25} The absolute neutrophil count normal range is 1500 to 8000/mm³ (1.5 to $8.0 \times 10^9/L$). For clinical decision making, neutropenia is defined as an absolute neutrophil count $<1000/mm^3$ ($<1.0 \times 10^9/L$), severe neutropenia is defined as an absolute neutrophil count $<500/mm^3$ ($<0.5 \times 10^9/L$), and profound neutropenia is defined as an absolute neutrophil count $<100/mm^3$ ($<0.1 \times 10^9/L$).^{25,26} Fever, the most consistent finding in bacterial infection, is defined for the purposes of clinical decision making as a temperature of 38.3°C (100.9°F) on one occasion or 38.0°C (100.4°F) persisting >1 hour.^{25,26}

Neutropenia in cancer patients is most commonly caused by chemotherapy, with the lowest neutrophil count typically seen 5 to 10 days after the last chemotherapeutic dose and recovery usually seen within 5 days afterward.^{25,26,27} The risk of developing an infection primarily depends on the severity and duration of neutropenia. Comorbid conditions and other circumstances, like indwelling devices, also contribute to the risk.^{4,5,7,25,26}

Fever is the most common finding seen with bacterial infections in the neutropenic patient. Common symptoms and signs that usually localize the infectious source are often absent or muted in the neutropenic patient because the lack of neutrophils impairs the inflammatory response and diminishes the occurrence of expected findings.²⁵ Thus, a pulmonary infection may have minimal cough, have no productive phlegm, and lack radiographic infiltrates. A kidney infection may not produce pyuria.

Perform a careful physical examination, with attention to three areas typically overlooked in routine examination: the oral cavity, the perianal area, and entry sites of intravascular catheters. **Digital rectal examination is relatively contraindicated in neutropenic patients—withhold until after initial antibiotic administration. Evaluate the entry sites of IV and tunneled catheters for evidence of infection.** Clotted catheters represent a high risk of infection due to bacterial colonization, and central venous catheters may cause endocarditis.

Localizing signs and symptoms of a specific infection are often lacking, and an evaluation for an occult infection is indicated.^{25,26,27,28} Obtain two blood culture samples, one from a peripheral vein and the other from a central catheter, if present. A urinalysis, urine culture, and chest radiograph should be performed. Sputum, stool, and wound drainage Gram stain and culture should be obtained if productive cough, diarrhea, or wound drainage, respectively, are present. Assess serum electrolyte levels, renal function, and hepatic function.

Risk Factors

If an infectious source is found, therapy and disposition are guided by the presumed pathogens and the expected clinical course. If, after assessment, no localized infection can be found, the two major clinical decisions are: (1) Does this patient require hospitalization, and (2) should

empiric antibiotics be started? To assist in addressing both these questions, consult with the patient's oncologist.

Although hospitalization enhances the ability to reassess the patient and intervene early if a severe infection or clinical deterioration develops, hospitalization exposes the immunocompromised patient to hospital flora that is often drug resistant. Patients who appear well, have no abdominal pain, have no physical signs of infection, have a normal chest radiograph, and are expected to resolve their neutropenia within 7 days have a low risk of severe infection and can be considered for outpatient care.^{25,26} Scoring systems, such as the Multinational Association for Supportive Care in Cancer Risk Index^{29,30} or the Clinical Index of Stable Febrile Neutropenia³¹ can be used to determine if the febrile neutropenic patient is at low risk for serious complications and eligible for outpatient care. High-risk febrile neutropenic patients for whom hospitalization is recommended are defined by one or more of the following features: profound neutropenia expected to last >7 days, comorbid medical conditions, acute liver or renal injury, or non-low-risk scores by the Multinational Association for Supportive Care in Cancer Risk Index or Clinical Index of Stable Febrile Neutropenia tool.^{25,26,29,30,31}

Treatment

Empiric broad-spectrum antibiotics are used in febrile neutropenic patients when the benefits of early treatment are greater than the adverse side effects associated with such drugs.^{25,26,27,28} **Clinical evidence consistently supports the benefits of empiric antibiotics when the absolute neutrophil count is $\leq 500/\text{mm}^3$ ($<0.5 \times 10^9/\text{L}$).** There is little convincing evidence for empiric antibiotics when the absolute neutrophil count is $>1000/\text{mm}^3$. For neutrophil counts between 500 and $1000/\text{mm}^3$ (0.5 and $1.0 \times 10^9/\text{L}$), other risk factors for bacterial infection are used to make a decision regarding empiric antibiotics.^{25,26,27}

Gram-positive bacteria currently account for 60% of microbiologically confirmed infections in febrile neutropenic patients, although gram-negative bacteria are undergoing resurgence in some institutions.²⁵ Bacteremia is most frequently due to aerobic gram-positive cocci (*Staphylococcus aureus*, coagulase-negative staphylococci, *Viridans* streptococci, or *Enterococcus faecalis/faecium*) or aerobic gram-negative bacilli (*Escherichia coli*, *Klebsiella* species, or *Pseudomonas aeruginosa*).

Administer the initial empiric antimicrobial therapy to cover the range of potential bacterial pathogens (**Table 240-3**).^{25,26,27,28,32,33} No specific antibiotic regimen has proven consistently superior in clinical trials, and monotherapy with an appropriate broad-spectrum agent is as effective as dual-agent treatment in most circumstances. Add vancomycin in the following situations: hemodynamic instability, radiographic pneumonia, catheter-related infection, skin or soft tissue infection, known colonization with resistant gram-positive organism, or severe mucositis when fluoroquinolone prophylaxis was recently used.²⁶

TABLE 240-3

Empiric Antibiotic Therapy in Febrile Neutropenia

Circumstance	Drug and Adult Dose	Comments
Outpatient	Ciprofloxacin 500 milligrams PO every 8 h or 1000 milligrams twice daily <i>or</i> Levofloxacin 750 milligrams PO daily <i>plus</i> Amoxicillin/clavulanate 500/125 milligrams PO every 8 h or 1000/62.5 milligrams PO twice daily <i>or</i> Moxifloxacin 400 milligrams PO daily	For low-risk patients with daily assessments by a medical provider for the initial 3 d
Monotherapy	Cefepime 2 grams IV every 8 h <i>or</i> Ceftazidime 2 grams IV every 8 h <i>or</i> Imipenem/cilastatin 1 gram IV every 8 h <i>or</i> Meropenem 1 gram IV every 8 h <i>or</i> Piperacillin/tazobactam 4.5 grams IV every 6 h	Monotherapy with these broad-spectrum agents is as good as dual-drug therapy in most circumstances
Dual therapy	One of the monotherapy agents <i>plus</i> Vancomycin 1 gram IV every 12 hours <i>or</i> Metronidazole 1 gram IV, followed by 500 milligrams IV every 6 h	Increased risk of adverse effects If hemodynamic instability, catheter-related infection, cellulitis, pneumonia, or known colonization with resistant organism If abdominal symptoms are present

The median duration of fever after initiation of empiric antibiotics is 2 days in low-risk patients and 5 to 7 days in high-risk patients. Therefore continue initial empiric antibiotic therapy for 2 to 4 days before assessing clinical response and making therapeutic adjustments. Adjustments may be made earlier if clinical deterioration occurs or culture results become available. Continue empiric antibiotics until either a documented infection has clinically resolved and/or the absolute neutrophil count is $>500/\text{mm}^3$ ($>0.5 \times 10^9/\text{L}$).^{25,26}

HYPERVISCOSITY SYNDROME

Hyperviscosity syndrome is a pathologic condition in which blood is "thicker" than normal and its flow is impaired.^{34,35} Blood viscosity depends on its plasma and cellular contents. Abnormal plasma contents that most commonly produce hyperviscosity are Waldenström's macroglobulinemia and immunoglobulin A–producing myeloma.³⁴ Hyperproduction of any cell line can lead to hyperviscosity. Polycythemia (with a hematocrit $>60\%$) and leukemia (with a WBC count $>100,000/\text{mm}^3$ ($>100 \times 10^9/\text{L}$) or a leukocrit $>10\%$) are often associated with clinically significant hyperviscosity.³⁵ Dehydration exacerbates hyperviscosity.

Initial symptoms are vague and may include fatigue, abdominal pain, headache, blurry vision, or, most commonly, altered mental status.^{32,33,34,35,36} Cutaneous or mucosal bleeding is common. Intravascular thrombosis may occur, with the creation of focal or unusual findings. Patients with hyperleukocytosis often report dyspnea and fever. Funduscopy findings include retinal venous engorgement appearing as linked sausages, along with exudates, hemorrhages, and papilledema.

Laboratory findings suggesting hyperviscosity include rouleaux formation (red cells stacked like coins) on a peripheral blood smear and being unable to perform chemical testing due to serum stasis in the laboratory analyzers. Laboratory testing of blood viscosity is usually done on plasma or serum, and specific analytic methodology varies.³⁶ A common approach is to report the viscosity of the sample as a ratio to that of water; normal plasma viscosity is 1.7 to 2.1 and normal serum viscosity is 1.4 to 1.8, compared with water. Symptomatic patients usually have a serum viscosity >4 .³⁶ **Laboratory measurement of plasma or serum viscosity will not identify hyperviscosity from polycythemia or leukemia.**

Initial therapy is intravascular volume repletion, early involvement of a hematologist, and emergency plasmapheresis or leukapheresis.^{34,35,36} If coma is present and the diagnosis established, a temporizing measure can be a 2-unit (1000-mL) phlebotomy with concomitant volume replacement using 2 to 3 L of normal saline.³⁵ Transfusion of red blood cells should be done with caution because such treatment may increase blood viscosity. Long-term management is appropriate chemotherapy.

THROMBOEMBOLISM

Thromboembolism occurs with all tumor types and is the second leading proximate cause of death in cancer patients.^{37,38,39} Symptomatic deep venous thrombosis occurs in approximately 15% of all patients with cancer and up to 50% of those with advanced malignancies.^{37,38,39} Multiple factors contribute to an increased risk for thromboembolism. The tumor may release procoagulant factors or inflammatory cytokines that directly activate the coagulation system. Large tumors may cause venous obstruction and promote thrombosis. Impaired production of proteins C and S and [antithrombin](#) can produce a hypercoagulable state. Surgery with attendant postoperative immobilization or long-term central venous catheterization can incite thrombosis. Chemotherapy or hormonal therapy for breast cancer increases the risk for thromboembolism. The angiogenesis inhibitors [thalidomide](#), [sunitinib](#), and [bevacizumab](#) are associated with significant thrombotic risks.^{37,38,39}

Low-molecular-weight heparin (LMWH) is recommended as the initial treatment for 5 to 10 days in cancer patients with venous thromboembolism, both deep venous thrombosis and pulmonary embolism.^{40,41} Continued treatment with low-molecular-weight heparin for at least 6 months is also recommended because of better efficacy in preventing recurrent thromboembolic events compared to vitamin K antagonists.^{41,42} There is little experience with the novel oral anticoagulants, so their use is not recommended.⁴¹

EMERGENCIES RELATED TO THERAPY

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

Nausea and vomiting can be debilitating to an already compromised patient. Because most IV chemotherapeutic agents are emetogenic, antiemetics are commonly administered on the day of therapy and for 2 to 4 days afterward.⁴³ Guidelines recommend specific antiemetic regimens based on the emetogenic potential of the chemotherapeutic agent.^{43,44} Recommended antiemetics include neurokinin-1 receptor antagonists, serotonin receptor antagonists, and corticosteroids ([Table 240-4](#)).⁴⁵ For refractory nausea and vomiting, benzodiazepines, [dopamine](#) receptor antagonists, or antipsychotic agents are added.⁴³

TABLE 240-4

Antiemetic Agents for Chemotherapy-Induced Vomiting

Class and Agent	Initial Adult Dose	Comments
Neurokinin-1 (NK1) Receptor Antagonists		
Aprepitant	125 milligrams PO	Expensive, use restricted to highly emetogenic chemotherapy agents, half-life 9–14 h
Fosaprepitant	150 milligrams IV	
Serotonin Receptor Antagonists		
Granisetron	1 milligram (10 micrograms/kg) IV	Common reactions: headache, abdominal pain Serious reactions: serotonin syndrome, QT interval prolongation Half-lives vary from 5 h for ondansetron, 9 h for granisetron, and 40 h for palonosetron
Ondansetron	8 milligrams (0.15 milligrams/kg) IV	
Palonosetron	0.25 milligram IV	
Tropisetron*	5 milligrams IV	
Ramosetron*	0.3 milligram IV	
Corticosteroids		
Dexamethasone	8–12 milligrams IV	Mechanism unknown
Benzodiazepines		
Lorazepam	1–2 milligrams IV	Sedation, half-life 14 h

Class and Agent	Initial Adult Dose	Comments
Midazolam	1 milligram IV or 5 milligrams IM	Sedation, half-life 2–3 h
Dopamine Receptor Antagonists		
Metoclopramide	10 milligrams IV or IM	Dose-related extrapyramidal side effects, half-life 5–6 h
Prochlorperazine	5–10 milligrams IV or IM	Extrapyramidal side effects, half-life 7 h
Antipsychotics		
Olanzapine	10 milligrams PO or IM	Not FDA approved for this indication, half-life 21–54 h

Abbreviation: FDA = U.S. Food and Drug Administration.

* Not available in the United States.

Chemotherapy-induced vomiting can be anticipatory, acute, or delayed.⁴⁵ Anticipatory vomiting is a conditioned reflex where vomiting occurs prior to administration of the chemotherapeutic agent. Acute vomiting occurs during the first 24 hours with maximal intensity at 5 to 6 hours after administration. Delayed vomiting has maximal intensity 48 to 72 hours after administration and can last up to 7 days.

EXTRAVASATION OF CHEMOTHERAPEUTIC AGENTS

Most chemotherapeutic agents cause local tissue reaction when extravasated, but the agents associated with significant tissue damage are the vesicants primarily in the anthracycline, taxane, platin salt, and vinca alkaloid classes.^{46,47,48} Clinical manifestations of chemotherapeutic drug extravasation include pain, erythema, and swelling, usually within hours of the infusion. Occasionally, clinical signs may be delayed if only a small amount of highly cytotoxic drug is extravasated. Serious injury produces blistering, induration, ulceration, and necrosis over a few days to weeks.

If extravasation happens to occur through an active peripheral line, the infusion is stopped and aspiration through the line is attempted and continued while the catheter is removed.⁴⁸ Aspirate palpable cutaneous blebs containing the extravasated chemotherapeutic agent. Elevate and

immobilize the affected limb. Cooling or warming is beneficial for some agents (**Table 240-5**). Consult with the oncologist for treatment recommendations. Early referral to a plastic surgeon is suggested for anthracycline and vinca alkaloids.

TABLE 240-5

Antidotes for Selected Extravasated Chemotherapeutic Drugs

Drug	Antidotes	Comments
Anthracyclines (daunorubicin , doxorubicin , epirubicin, and idarubicin)	Dry cooling	Initially 1 h, then 15 min several times per day Hold during dexrazoxane therapy
	Dexrazoxane	IV infusion within 6 h, repeat doses at 48 and 72 h
	Dimethyl sulfoxide	Apply over involved area, repeat 4–6 times per day for 7 or more days
Vinca alkaloids (vincristine and vinblastine)	Dry warming	Do not press or rub area
	Hyaluronidase	Inject in and around extravasated area
Mitomycin , cisplatin , mechlorethamine	Dry cooling	Initially 1 h, then 15 min several times per day
	Dimethyl sulfoxide	Apply over involved area, repeat 4–6 times per day for 7 or more days
Paclitaxel	Hyaluronidase	Inject in and around extravasated area

Antidotes vary according to the specific agent (**Table 240-5**).⁴⁸ Dexrazoxane is used for anthracycline extravasation at dose of 1000 milligrams/m² IV infused over 1 to 2 hours within 6 hours of the extravasation event, with additional doses of 1000 milligrams/m² at 48 hours and 500 milligrams/m² at 72 hours.⁴⁹ [Dimethyl sulfoxide](#) and [hyaluronidase](#) are used to enhance absorption of the extravasated agent.⁴⁸ [Dimethyl](#)

sulfoxide is applied as a generous trickle of the 99% solution over the involved area without pressing or rubbing and then covered with dry pads.⁴⁸ **Hyaluronidase** is reconstituted with normal saline to a concentration of 150 units/mL and then injected in and around the extravasation area via multiple punctures.⁴⁸ Inject about 0.2 mL per puncture site with a typical total dose of 1 mL, but up to 10 mL may be required. There is limited data supporting the use of **sodium thiosulfate** for reversal of alkylating agent toxicity.⁴⁸ Intralesional injections of corticosteroids or bicarbonate are not effective.

REFERENCES

1. Ahn S, Lee YS, Lim KS, Lee JL: Emergency department cancer unit and management of oncologic emergencies: experience in Asian Medical Center. *Support Care Cancer* 20: 2205, 2012.
[\[PubMed: 22555446\]](#)

2. Sadik M, Ozlem K, Huseyin M, Ayberk BA, Ahmet S, Ozgur O: Attributes of cancer patients admitted to the emergency department in one year. *World J Emerg Med* 5: 85, 2014.
[\[PubMed: 25215154\]](#)

3. Delgado-Guay MO, Kim YJ, Shin SH et al.: Avoidable and unavoidable visits to the Emergency Department among patients with advanced cancer receiving outpatient palliative care. *J Pain Symptom Manage* 49: 497, 2015.
[\[PubMed: 25131891\]](#)

4. Lewis MA, Hendrickson AW, Moynihan TJ: Oncologic emergencies: pathophysiology, presentation, diagnosis, and treatment. *CA Cancer J Clin* 61: 287, 2011. [Epub ahead of print]
[\[PubMed: 21858793\]](#)

5. McCurdy MT, Shanholtz CB: Oncologic emergencies. *Crit Care Med* 40: 2212, 2012.
[\[PubMed: 22584756\]](#)

6. Khan UA, Shanholtz CB, McCurdy MT: Oncologic mechanical emergencies. *Emerg Med Clin North Am* 32: 495, 2014.
[\[PubMed: 25060246\]](#)

7. Wagner J, Arora S: Oncologic metabolic emergencies. *Emerg Med Clin North Am* 32: 509, 2014.

[\[PubMed: 25060247\]](#)

8. Gaissert HA, Burns J: The compromised airway: tumors, strictures, and tracheomalacia. *Surg Clin North Am* 90: 1065, 2010.

[\[PubMed: 20955884\]](#)

9. Theodore PR: Emergent management of malignancy-related acute airway obstruction. *Emerg Med Clin North Am* 27: 231, 2009.

[\[PubMed: 19447308\]](#)

10. Hashemian SM, Fallahian F: The use of heliox in critical care. *Int J Crit Illn Inj Sci* 4: 138, 2014.

[\[PubMed: 25024941\]](#)

11. Ost DE, Ernst A, Grosu HB et al.: Therapeutic bronchoscopy for malignant central airway obstruction: success rates and impact on dyspnea and quality of life. *Chest* October 30, 2014. [Epub ahead of print]

[\[PubMed: 25358019\]](#)

12. Mahmood K, Wahidi MM: Ablative therapies for central airway obstruction. *Semin Respir Crit Care Med* 35: 681, 2014.

[\[PubMed: 25463159\]](#)

13. Coleman RE: Clinical features of metastatic bone disease and risk of skeletal morbidity. *Clin Cancer Res* 12: 6243s, 2006.

[\[PubMed: 17062708\]](#)

14. Wilkinson AN, Viola R, Brundage MD: Managing skeletal related events resulting from bone metastases. *BMJ* 337: a2041, 2008.

[\[PubMed: 18981017\]](#)

15. Penas-Prado M, Loghin ME: Spinal cord compression in cancer patients: review of diagnosis and treatment. *Curr Oncol Rep* 10: 78, 2008.

[\[PubMed: 18366964\]](#)

16. Lutz ST, Jones J, Chow E: Role of radiation therapy in palliative care of the patient with cancer. *J Clin Oncol* 32: 2913, 2014.

[\[PubMed: 25113773\]](#)

17. Wilson LD, Detterbeck FC, Yahalom J: Clinical practice. Superior vena cava syndrome with malignant causes. *N Engl J Med* 356: 1862, 2007.
[Erratum in: *N Engl J Med* 358: 1083, 2008.]
[\[PubMed: 17476012\]](#)

18. Lepper PM, Ott SR, Hoppe H et al.: Superior vena cava syndrome in thoracic malignancies. *Respir Care* 56: 653, 2011.
[\[PubMed: 21276318\]](#)

19. Akl EA, Vasireddi SR, Gunukula S et al.: Anticoagulation for patients with cancer and central venous catheters. *Cochrane Database Syst Rev* 2: CD006468, 2011.
[\[PubMed: 21328283\]](#)

20. Lumachi F, Brunello A, Roma A, Basso U: Cancer-induced hypercalcemia. *Anticancer Res* 29: 1551, 2009.
[\[PubMed: 19443365\]](#)

21. Rosner MH, Dalkin AC: Electrolyte disorders associated with cancer. *Adv Chronic Kidney Dis* 21: 7, 2014.
[\[PubMed: 24359982\]](#)

22. Charmandari E, Nicolaides NC, Chrousos GP: Adrenal insufficiency. *Lancet* 383: 2152, 2014.
[\[PubMed: 24503135\]](#)

23. Wilson FP, Berns JS: Tumor lysis syndrome: new challenges and recent advances. *Adv Chronic Kidney Dis* 21: 18, 2014.
[\[PubMed: 24359983\]](#)

24. Sutton SH: Infections associated with solid malignancies. *Cancer Treat Res* 161: 371, 2014.
[\[PubMed: 24706232\]](#)

25. White L, Ybarra M: Neutropenic fever. *Emerg Med Clin North Am* 32: 549, 2014.
[\[PubMed: 25060249\]](#)

26. Freifeld AG, Bow EJ, Sepkowitz KA et al.: Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis* 52: 427, 2011.

[\[PubMed: 21205990\]](#)

27. Flowers CR, Seidenfeld J, Bow EJ et al.: Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol* 31: 794, 2013.

[\[PubMed: 23319691\]](#)

28. Alp S, Akova M: Management of febrile neutropenia in the era of bacterial resistance. *Ther Adv Infect Dis* 1: 37, 2013.

[\[PubMed: 25165543\]](#)

29. Klastersky J, Paesmans M, Rubenstein EB et al.: The Multinational Association for Supportive Care in Cancer risk index: a multinational scoring system for identifying low-risk febrile neutropenic cancer patients. *J Clin Oncol* 18: 3038, 2000.

[\[PubMed: 10944139\]](#)

30. Klastersky J, Paesmans M: The Multinational Association for Supportive Care in Cancer (MASCC) risk index score: 10 years of use for identifying low-risk febrile neutropenic cancer patients. *Support Care Cancer* 21: 1487, 2013.

[\[PubMed: 23443617\]](#)

31. Carmona-Bayonas A, Jiménez-Fonseca P, Virizuela Echaburu J et al.: Prediction of serious complications in patients with seemingly stable febrile neutropenia: validation of the clinical index of stable febrile neutropenia in a prospective cohort of patients from the FINITE study. *J Clin Oncol* 33: 465, 2015.

[\[PubMed: 25559804\]](#)

32. Adelberg DE, Bishop MR: Emergencies related to cancer chemotherapy and hematopoietic stem cell transplantation. *Emerg Med Clin North Am* 27: 311, 2009.

[\[PubMed: 19447314\]](#)

33. Kern WV, Marchetti O, Drgona L et al.: Oral antibiotics for fever in low-risk neutropenic patients with cancer: a double-blind, randomized, multicenter trial comparing single daily [moxifloxacin](#) with twice daily [ciprofloxacin](#) plus amoxicillin/clavulanic acid combination therapy—EORTC infectious diseases group trial XV. *J Clin Oncol* 31: 1149, 2013.

[\[PubMed: 23358983\]](#)

34. Kwaan HC, Bongu A: The hyperviscosity syndromes. *Semin Thromb Hemost* 25: 199, 1999.

[\[PubMed: 10357087\]](#)

35. Adams BD, Baker R, Lopez JA, Spencer S: Myeloproliferative disorders and the hyperviscosity syndrome. *Hematol Oncol Clin North Am* 24: 585, 2010.

[\[PubMed: 20488356\]](#)

36. Stone MJ, Bogen SA: Evidence-based focused review of management of hyperviscosity syndrome. *Blood* 119: 2205, 2012.

[\[PubMed: 22147890\]](#)

37. Ornstein DL, Zacharski LR: Cancer, thrombosis, and anticoagulants. *Curr Opin Pulm Med* 6: 301, 2000.

[\[PubMed: 10912637\]](#)

38. Streiff MB: Diagnosis and initial treatment of venous thromboembolism in patients with cancer. *J Clin Oncol* 27: 4889, 2009.

[\[PubMed: 19738109\]](#)

39. DeLoughery TG: Venous thrombotic emergencies. *Hematol Oncol Clin North Am* 24: 487, 2010.

[\[PubMed: 20488349\]](#)

40. Akl EA, Kahale L, Neumann I et al.: Anticoagulation for the initial treatment of venous thromboembolism in patients with cancer. *Cochrane Database Syst Rev* 6: CD006649, 2014.

[\[PubMed: 24945634\]](#)

41. Lyman GH, Bohlke K, Khorana AA et al.: Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline Update 2014. *J Clin Oncol* 33: 654, 2015.

[\[PubMed: 25605844\]](#)

42. Akl EA, Kahale L, Barba M et al.: Anticoagulation for the long-term treatment of venous thromboembolism in patients with cancer. *Cochrane Database Syst Rev* 7: CD006650, 2014.

[\[PubMed: 25004410\]](#)

43. Basch E, Prestrud AA, Hesketh PJ et al.: Antiemetics: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 29: 4189, 2011. [Erratum in: *J Clin Oncol* 32: 2117, 2014. Dosage error in article text.]
[PubMed: 21947834]
-
44. Jordan K, Gralla R, Jahn F, Molassiotis A: International antiemetic guidelines on chemotherapy induced nausea and vomiting (CINV): content and implementation in daily routine practice. *Eur J Pharmacol* 722: 197, 2014.
[PubMed: 24157984]
-
45. Janelins MC, Tejani MA, Kamen C, Peoples AR, Mustian KM, Morrow GR: Current pharmacotherapy for chemotherapy-induced nausea and vomiting in cancer patients. *Expert Opin Pharmacother* 14: 757, 2013.
[PubMed: 23496347]
-
46. Livshits Z, Rao RB, Smith SW: An approach to chemotherapy-associated toxicity. *Emerg Med Clin North Am* 32: 167, 2014.
[PubMed: 24275174]
-
47. Young JS, Simmons JW: Chemotherapeutic medications and their emergent complications. *Emerg Med Clin North Am* 32: 563, 2014.
[PubMed: 25060250]
-
48. de Wit M, Ortner P, Lipp HP et al.: Management of cytotoxic extravasation: ASORS expert opinion for diagnosis, prevention and treatment. *Onkologie* 36: 127, 2013.
[PubMed: 23486002]
-
49. Langer SW: Dexrazoxane for the treatment of chemotherapy-related side effects. *Cancer Manag Res* 6: 357, 2014.
[PubMed: 25246808]
-

USEFUL WEB RESOURCES

1. American Association for Cancer Research—<http://www.aacr.org>
-

2. American Cancer Society Information for Health Care Professionals—
<http://www.cancer.org/healthy/informationforhealthcareprofessionals/index>

3. American Society of Clinical Oncology—<http://www.asco.org>

4. Multinational Association for Supportive Care in Cancer—<http://www.mascc.org/>

[McGraw Hill](#)

Copyright © McGraw-Hill Education

All rights reserved.

Your IP address is **132.174.255.223**

[Terms of Use](#) • [Privacy Policy](#) • [Notice](#) • [Accessibility](#)

Access Provided by: University of New England
[Silverchair](#)