

# AANA JOURNAL COURSE

## Update for nurse anesthetists

# 6

\*6 CE Credits

## Cancer: New therapies and new approaches to recurring problems

**Kenneth M. Kirsner, CRNA, MS, JD**  
Houston, Texas

*Caring for patients with cancer presents unique challenges to anesthetists. Chemotherapeutic regimens can cause cardiac, pulmonary, and other complications that will influence the anesthesia provider's care. New surgical techniques, including vertebroplasty, vertebrectomy, radiofrequency ablation of the liver, and sentinel node biopsy, present issues related to the surgical techniques and drugs administered. Recurring problems, including tumors of the airway and cardiac tamponade,*

*continue to present challenges for anesthesia providers. Many patients with cancer who undergo surgery not only have acute pain related to the surgical procedure but also have chronic pain that will influence anesthetic and postoperative pain management. This Journal course discusses new therapies and procedures and approaches to recurring problems in cancer care.*

**Key words:** Cancer, chemotherapy, isosulfan blue, vertebrectomy.

### Objectives

At the completion of this course, the reader should be able to:

1. Discuss the impact of chemotherapeutic agents on the patient undergoing anesthesia.
2. Discuss surgical and interventional radiological procedures for spinal stabilization in patients with cancerous lesions of the spine.
3. Discuss the types of cancer that sentinel node biopsy is used for and the implications of isosulfan blue injection.
4. Discuss the implications of tumors of the upper and lower airway and anesthetic approaches to tumors of the airway.
5. Discuss the anesthetic management of patients with cancer who have cardiac tamponade.

### Introduction

Caring for patients with cancer presents anesthesia providers with special challenges. The disease process and the associated treatments have great importance in anesthetic management. The disease process may cause disturbances in anatomy and physiology that are compounded by the treatment regimens. Medical and sur-

### Eulogy

That swain in Shakespeare, penning ballads  
to his lady's eyebrow: if just once  
he could have seen my sweetheart's breasts,  
he would have written epics. Oh,  
they are so springtime sweet and summer-lilting,  
those twin blossoms, I should have found  
a painter intimate with tender shades  
of pink and cream  
to immortalize their harmony.

Because  
up there on the seventh floor  
they are cutting one of them away,  
the one we touched last week and felt  
the poisoned pearl.  
Now the knives are working, working  
I feel them stabbing through my flesh.  
She will come back gray, remembering  
to smile, the bandages weeping blood,  
her beauty scarred,  
her life saved.

I will love her more  
than yesterday.

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gical treatments for cancer may have effects that influence the patient's health. Chemotherapeutic agents often cause damage to healthy tissues in addition to their cytotoxic action on cancer cells. Surgical techniques may damage adjacent tissues. Drugs and devices used as part of these surgical procedures may influence patients' anesthetic needs. Lesions of the spine frequently cause pain and/or paralysis and vertebral collapse. Vertebroplasty and vertebrectomy are 2 procedures to treat vertebral collapse. Resections of melanoma and breast cancers involve sentinel node biopsy. For sentinel node biopsy, isosulfan blue (Lymphazurin), which has a high rate of allergic reactions, is injected. This article reviews the implications of chemotherapeutic agents and new surgical techniques and some of the implications of the disease process that influence the provision of anesthesia.

### **Chemotherapeutic agents**

Chemotherapeutic agents produce toxic effects on malignant cells, as well as on normal tissues and organs. Anesthesia providers must be aware of the potentially damaging effects of selected chemotherapeutic agents.

Alkylating agents are commonly used chemotherapeutic agents. Alkylating agents act by alkylating cellular DNA, inhibiting cell growth. Alkylating agents are used against rapidly growing tumors and attack all dividing cells. Busulfan, cyclophosphamide, and melphalan all have the potential to produce pulmonary toxic effects. Decreased oxygenation, pleural effusions, and restrictive breathing patterns are all possible. The incidence of pulmonary complications is low, but complications may occur years after the therapy is administered. Chemotherapeutic metabolic breakdown products also may lead to uric acid deposition and neuropathy. Bone marrow suppression also is possible. High-dose cyclophosphamide has been reported to produce pseudocholinesterase deficiency.<sup>1</sup>

Antimetabolites include methotrexate, 5-fluorouracil, and cytosine arabinose. Antimetabolites block the biosynthesis of normal cellular metabolites. They act on more slowly growing tumors than the tumors affected by alkylating agents. Antimetabolites can cause bone marrow suppression, severe nausea, vomiting, diarrhea, and resulting electrolyte imbalances. Methotrexate is associated with serious renal toxic effects in 10% of patients who receive the drug.

The plant alkaloids include vincristine and vinblastine. The major toxic effects of vincristine are on the neurologic system and of vinblastine, on the bone marrow.

Cis-platinum causes myelosuppression and a high incidence of renal toxic effects. It is imperative to exam-

ine renal function and to consider the possible effects of reduced renal function on anesthetic drug administration. Electrolyte balance also must be evaluated.

Antibiotics used as chemotherapeutic agents include doxorubicin (Adriamycin) and daunorubicin (the anthracyclines), bleomycin, and mitomycin C. The anthracyclines may produce cardiac rhythm disturbances, cardiomyopathy, and pump failure. Electrocardiographic changes or dysrhythmias may occur in 40% of patients.<sup>2</sup> Patients who have received these drugs should be examined closely for problems in cardiac function. The toxic effects of doxorubicin may appear early, late, or very late, in relation to drug administration. Patients who have received doxorubicin should be examined closely for signs of cardiac disturbances and congestive heart failure in the preoperative assessment. It is not unreasonable to obtain a preoperative cardiac evaluation, including echocardiography. Monitoring may need to be heightened, possibly including invasive blood pressure and cardiac monitoring.

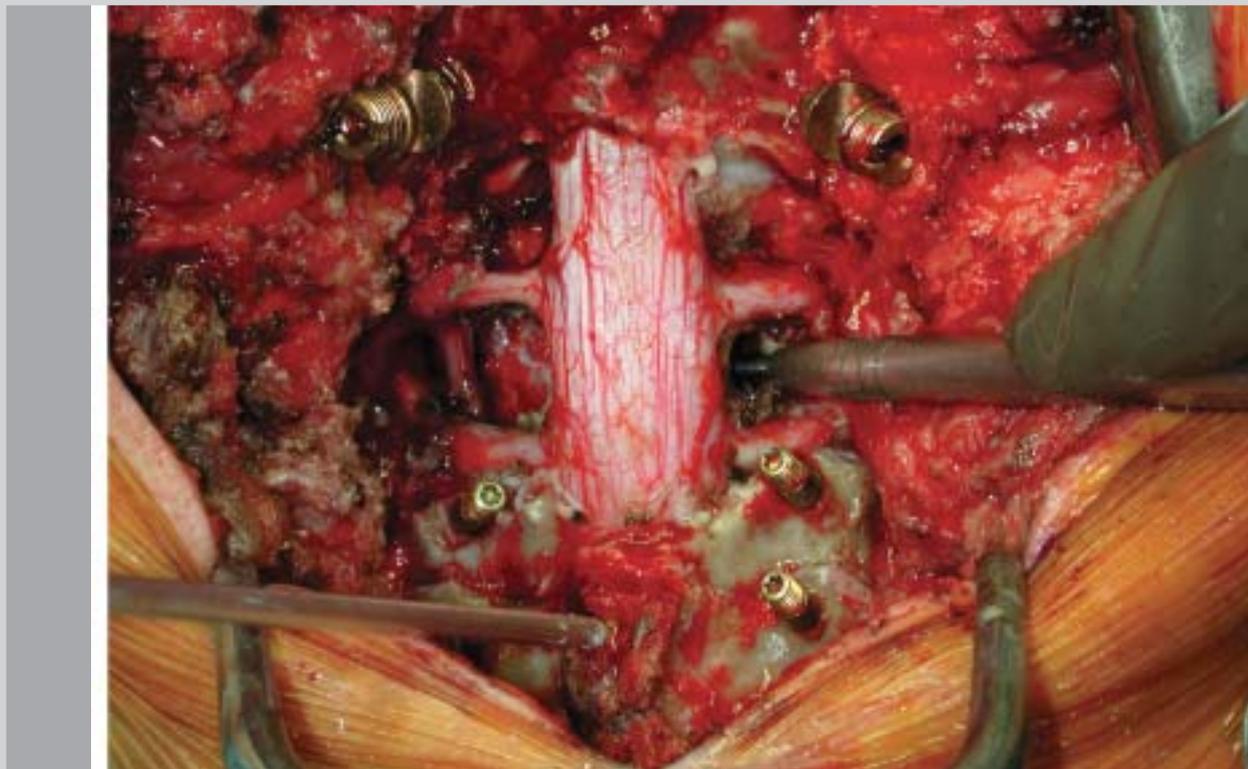
Bleomycin produces pulmonary toxic effects in 5% to 10% of patients receiving the drug; patients receiving bleomycin are at risk for developing postoperative pulmonary insufficiency.<sup>3</sup> Although studies have shown no difference due to the amount of inspired oxygen administered perioperatively,<sup>4</sup> most textbooks of anesthesia indicate that patients receiving bleomycin are especially sensitive to oxygen toxicity and fluid overload,<sup>5</sup> although direct cause and effect is poorly established. The consensus is that the use of the lowest inspired concentration of oxygen compatible with acceptable oxygen saturation of hemoglobin ( $SO_2 > 90\%$ ) should be used. In addition, especially careful management of intravenous fluid administration is important because fluid overload may predispose the patient to the development of acute respiratory distress syndrome during the postoperative period.<sup>5</sup>

### **Spinal surgery and percutaneous spinal stabilization**

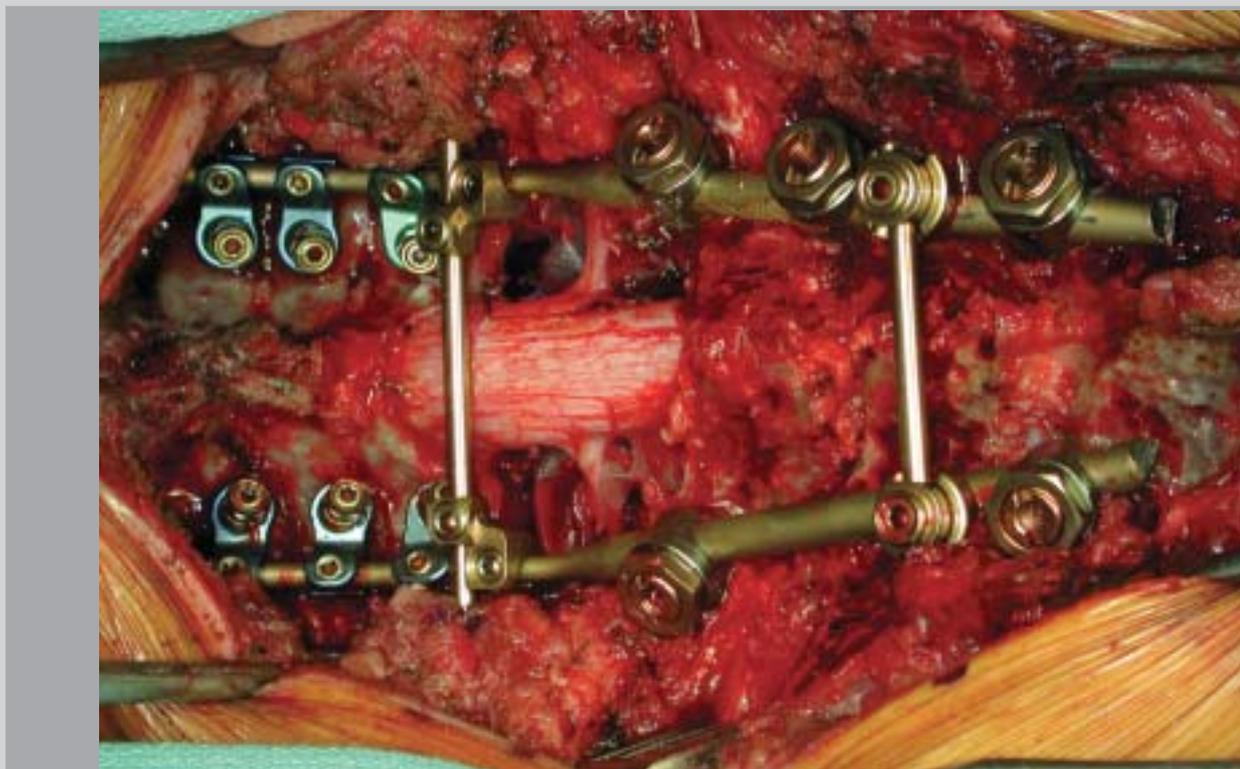
Renal cell carcinoma, breast tumors, melanoma and sarcoma, and lung and prostate tumors may invade the spine. Tumors replace bone tissue, causing collapse of the vertebrae, resulting in pain, weakness, motor dysfunction, and, in severe cases, paralysis. Cervical, thoracic, or lumbar regions may be affected by tumor. Surgical intervention may be required for stabilization of the affected vertebrae. Surgical procedures are palliative, to treat pain and restore neurological function or prevent further loss of function, improving quality of life.<sup>6</sup>

Vertebrectomy is an invasive surgical procedure involving the removal of one or several vertebrae and placement of hardware to maintain spinal stabilization.

**Figure 1.** C6 vertebrectomy with spinal cord exposed



**Figure 2.** C6 vertebrectomy after instrumentation is applied



Patients may have cervical instability related to tumors of the cervical spine (Figures 1 and 2). Awake fiberoptic bronchoscopy, LMA-Fastrach (LMA North America, San Diego, Calif) laryngeal mask airway (LMA; awake or asleep), and laryngoscopy have all been used successfully. Recent literature suggests that the LMA may produce unwanted cervical spine movement in individuals with unstable cervical spines (C. Biddle, oral communication, August 2002). Management should proceed with great care no matter what is done, and alternative airway management plans and tools should always be available.

The anesthesia and surgical teams should jointly determine the airway management approach after assessing the patient's clinical condition and using available diagnostic imaging techniques. Positioning will be dictated by the anatomic location of the spinal tumor. Positioning is managed with a team approach, considering the surgical approach, venous access and monitoring needs, and the duration of the procedure. During cervical and thoracic spine surgical procedures, access to the arms will be nearly impossible once the procedure is begun, so venous and arterial access must be established before the procedure.

Vertebrectomies may entail considerable blood loss, particularly if a large number of vertebrae are involved or if the tumor is highly vascular, such as renal cell tumors. The availability of blood in the operating room and essential equipment facilitating the rapid administration of fluid and blood is essential.

Percutaneous vertebroplasty uses guided imaging to inject polymethylmethacrylate (PMMA) into a collapsed vertebra to restore vertebral height and strength, thus relieving the pain.<sup>7</sup> The procedure was first performed in Europe in 1984 and was performed in the United States about 10 years later. The procedure is performed in the radiology suite or in the operating room, using fluoroscopy. A dye is injected into the fractured or tumor-ridden vertebra, and once the needle is properly located, PMMA is injected, stabilizing the vertebra.

Kyphoplasty is a similar procedure, but the needle has a balloon near the tip. Under fluoroscopy, the needle is inserted into the vertebra. The balloon is inflated, restoring vertebral height. PMMA then is injected, giving support to the vertebra and maintaining the restoration of normal vertebral height.

Complications of the procedure include rib fracture and irritation of the nerve roots. These complications are minor and usually resolve on their own. More serious complications are pneumothorax, fracture of the pedicle, PMMA embolus, spinal cord compression, and increased back pain. Although allergic reactions and hypotension after injection of PMMA are possible, they rarely are seen, perhaps because of the lower volumes of PMMA used and the smaller amounts of blood loss

and fluid shifts for vertebroplasty compared with major open orthopedic surgical procedures.

Vertebroplasty has been performed under general anesthesia and monitored anesthesia care and has been attempted under local anesthesia with intraosseous injection of local anesthetics. The cases attempted under local anesthesia, however, involved patients with osteoporotic fractures, and the local anesthesia was insufficient for 15% of the patients.<sup>8</sup> Most patients who undergo vertebroplasty or kyphoplasty for cancerous lesions are in moderate to severe pain and are unable to lie still in the prone position. While the choice of anesthetic technique is individualized according to a number of factors, a patient's ability to tolerate the positioning for the procedure must be considered.

### **Radiofrequency ablation of the liver**

Liver cancers, both primary and metastatic, are common. Relatively few patients have tumors that are amenable to a potentially curative resection by traditional surgical approaches.<sup>9</sup> Radiofrequency ablation uses radiofrequency energy to increase the temperature of the liver tissue greater than 60°C, causing the cells to die in the area around the electrode.

Depending on the size, number, and location of the tumors, the radiofrequency needle electrode may be placed into an unresectable liver tumor percutaneously, laparoscopically, or by an open laparotomy. In the latter case, the rich hepatic blood inflow may act as a heat sink, ie, a coolant to the heated tissue, carrying away the heat like a radiator or cooling blanket and resulting in insufficient heating of the tumor. In those cases, the surgeon will obstruct the hepatic inflow for the duration of the heating.

Complications include pleural effusion, fever, pain, subcutaneous hematoma, subcapsular liver hematoma, hepatic abscess, biliary fistulas, and ventricular fibrillation. Bleeding is infrequent due to the relatively small (15- to 18-gauge) diameter of the radiofrequency needle.

During surgical laparotomy for liver tumors, arterial blood pressure monitoring may be used in addition to routine anesthetic monitoring because the surgical maneuvers may occlude the vena cava, significantly lowering blood pressure. Central venous pressure monitoring is not necessary. As with other liver surgeries, patients are given the smallest amount of fluid needed so that increased pressures in the portal-hepatic system and increased bleeding are prevented.

Radiofrequency ablation also is used for tumors that are difficult to resect or unresectable in locations other than the liver, particularly some bone tumors. Because of the pain caused by the heating of the tissues, general anesthesia is used, even when the needle is inserted percutaneously.

## Sentinel lymph node biopsy

Sentinel node biopsy is a technique used in cancer surgery to identify the lymph nodes into which cancerous lesions drain. It is used in excision of melanomas and in segmental mastectomies for breast cancer. Before the use of sentinel node biopsy, entire lymph node basins were excised to prevent the spread of cancerous cells throughout the body. Rather than excise the entire basin, a combination of a radioactive dye and a blue marker dye are injected at the site of the lesion. The intraoperative identification of lymph nodes containing the injectable dye facilitates the resection of lymph nodes that drain the lesion (Figures 3-6).

Isosulfan blue dye is injected into the cancerous lesion and is quickly drained into the lymphatic system. Allergic reactions may occur following the injections of the dye. According to the manufacturer's package insert, the rate of allergic reactions is 1.5%, ranging from minor reactions to severe anaphylactic reactions.<sup>10</sup> The reactions may be anaphylactic, IgE antibody-mediated reactions or non-IgE antibody-mediated anaphylactoid reactions. The incidence of reactions is higher in cases of breast cancer than in cases of melanoma.<sup>10</sup> This is hypothesized to be because the injection of the dye in melanoma cases is intradermal, but the dye is injected more deeply in breast cancer cases and more rapid absorption occurs. There is debate in the literature about whether prophylactic treatment for anaphylaxis is useful for IgE antibody reactions. However, some authors suggest prophylactic administration of corticosteroids, diphenhydramine, and H<sub>2</sub> blockers before isosulfan blue injection during segmental mastectomies.<sup>11</sup>

Anaphylaxis in anesthetized patients may not manifest with all the signs that occur in awake patients (Table). Hypotension will occur, but other signs such as wheezing and hives may not be present. Hives in cases of anaphylaxis related to the injection of isosulfan blue may appear blue rather than red.<sup>11</sup> Anaphylaxis should be treated as any anaphylactic reaction, with epinephrine, fluids, corticosteroids, and H<sub>2</sub> blockers.

## Recurring anesthetic problems in cancer care

- *Head and neck tumors.* Head and neck tumors are among the anesthesia providers' greatest challenges. In addition to normal variation in the anatomy of the upper airway, tumors in or impinging on the upper airway may produce airway obstruction. Tumors in the pharynx and radiation therapy to the head and neck regions may cause decreases in mobility of the jaw and neck. Tumor and tissues that have been radiated may be more friable than normal tissues, and visualizing the vocal cords may be difficult. Awake fiberoptic intubation or awake tracheostomy may be necessary.

The anesthesia provider and surgeon must carefully

**Figure 3. Surgeon injecting isosulfan blue into melanoma on arm**



**Figure 4. The blue color spreads around the lesion.**

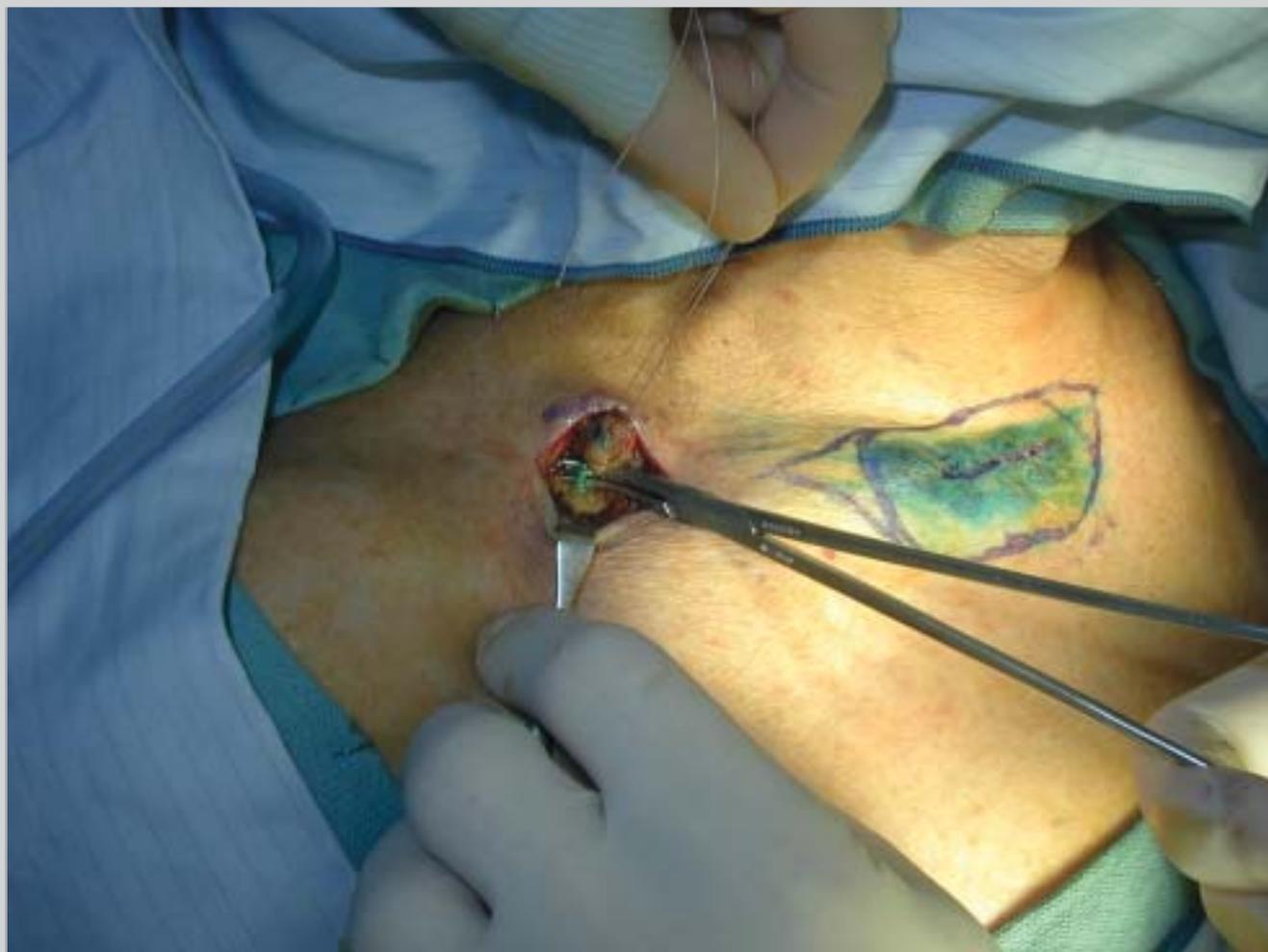


**Figure 5. Continued spread**



assess the airway and collaborate to develop a plan of care. Careful assessment of the airway, both indirect laryngoscopy by the surgeon and assessment by the anesthesia provider, are essential. The routine airway assessments made, such as hyoid-mental distance and range of motion of the neck, may be insufficient in

**Figure 6.** A melanoma injected below the clavicular area; the blue spread to the lymphatic channel is shown



**Table.** Signs of anaphylaxis in anesthetized patients

<b>Signs</b>	<b>Present under general anesthesia</b>
Flushing, erythema, and urticaria	May be present, but may appear gray or blue
Wheezing and increased airway pressure	May be present, but frequently absent due to bronchodilating effects of inhalation anesthetics
Bradycardia then tachycardia	Frequently present
Hypotension	Frequently present; may be the only sign of anaphylaxis
Dysrhythmias	May be present

patients with head or neck tumors or previous surgeries or radiation therapy in the head or neck region. Administration of topical anesthesia and visualizing the airway with a laryngoscope while the patient is awake will allow the anesthetist to determine whether visualization of the larynx is possible before inducing general anesthesia. The surgeon should be present at induction in case an emergency tracheostomy is necessary.

Tumors of the head and neck may be difficult for the

surgeon to separate from the vascular structures of the neck. Discussion of the extension of the tumor with the surgeon is imperative. Access to blood and blood products may be necessary, along with sufficient intravenous access.

Lower airway tumors, in the lower airway, mediastinum, or thorax, present a different challenge to the anesthetist. Tumors may grow in the airway, restricting airflow. Mediastinal tumors, including enlarged lymph

nodes, lymphomas, and large thyroid masses, while outside the airway, can press on the trachea, resulting in tracheal deviation. A severe tracheal deviation can make visualization of the vocal cords and intubation difficult.

Assessment of the patient begins with careful physical assessment. Difficulty breathing, wheezing, inability to lie flat, and tracheal deviation must be noted. Pulmonary function tests, chest radiographs, computed tomography scans, and magnetic resonance imaging should be reviewed to see the extent of the tumor and airway compromise. As with tumors of the upper airway, the surgical and anesthetic teams should discuss findings and plans before the procedure to ensure the best approach for the patient.

When formulating the anesthetic plan, the unique problem of lower airway obstruction must be considered. When the lumen of one area of the trachea or bronchi is narrowed relative to the surrounding area, positive pressure ventilation may have deleterious effects. The narrowing may be caused by tumor growing in the airway or by tumor impinging on the wall of the airway, thus narrowing the lumen at that point.

The narrowest point in a tube with a fluid flowing through it will have the lowest pressure at the narrowest point (Figure 7). Thus, positive pressure ventilation will tend to narrow the trachea or bronchus with the constriction even more in what is referred to as the ball-valve effect. If more pressure is used to compensate for difficulty ventilating, the pressure at the constriction will continue to decrease, narrowing the constriction even more.

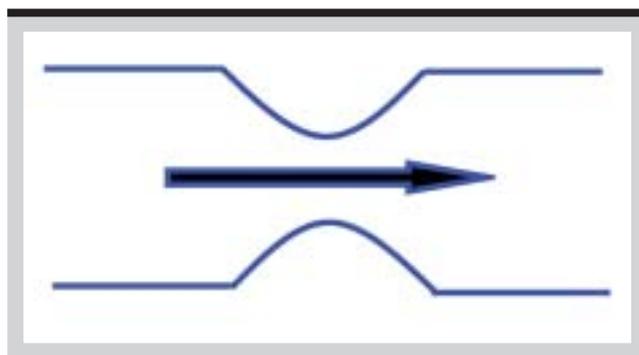
For this reason, spontaneous ventilation often is used in procedures for bronchial or tracheal stent placement, laser resection of bronchial or tracheal tumors, and other procedures when compression of the lower airway compression is an issue.

Spontaneous ventilation can be carried out using a facemask or an LMA. For bronchoscopy and stent placement, the entire procedure may be performed using the LMA. Fiberoptic intubation also may be used with the patient awake and breathing spontaneously.

For laser resections of tumors in the airway, jet ventilation often is used. The surgeon inserts a metal cannula between the sessions of laser resection. During laser resection, the cannula is removed and patient is not ventilated.

- **Cardiac tamponade.** Cardiac tamponade is a frequent complication of cancer and cancer therapies. While chronic cardiac tamponade is withstood more easily than acute cardiac tamponade caused by trauma, eventually the same problems occur: tachypnea, tachycardia, and jugular venous distention. The diagnosis usually is made by echocardiography, although electrocardiography and chest radiographs also assist in the diagnosis.

**Figure 7.** The narrowest point is also the point with the lowest pressure. As the speed of the gases traveling past the constriction increases, the pressure is lowered.



Cardiac effusion and tamponade are treated by pericardiocentesis or pericardial window. The anesthesia team and the surgical team must coordinate the sequence of events. If the patient's hemodynamic condition is stable, general anesthesia may be induced before surgery. Anesthesia may be induced with the patient in a head-up position. Hemodynamic monitoring lines, including an arterial line, should be placed before induction. Ketamine and etomidate are the preferred induction agents. Agents that depress myocardial function, such as propofol and thiopental sodium, should be avoided.

Patients in unstable condition or who have hemodynamic compromise should undergo pericardiocentesis or pericardial window under local anesthesia. The procedure will have to be performed with the patient sitting up at a 30° to 45° angle. Once the pericardium is entered and the effusion is drained, the patient's condition should rapidly stabilize, and general anesthesia can be safely induced (Figures 8 and 9).

- **Pain.** Many patients with cancer have chronic pain. It is essential that their pain be treated throughout the perioperative period.<sup>12</sup> Patients taking oral opioids need to have them replaced with a substitute during the preoperative period when oral intake is restricted. Short-acting opioids such as fentanyl and sufentanil may be appropriate intraoperatively; however, their relatively short half-lives will result in decreased opioid blood levels. The early reinstatement of long-acting opioids is important in avoiding the reemergence of severe pain.

A recent case of mine illustrates the consideration that must be given to chronic pain. The patient was a 39-year-old, 53-kg woman with breast cancer with metastasis to her femurs and lumbar, thoracic, and cervical spine. The chronic pain service had been consulted, and she was receiving oral hydromorphone, fentanyl patches, fentanyl lollipops for breakthrough pain, and antidepressants. The patient had a pathologic fracture of her femur and required a removal of a previously placed

**Figure 8.** Tachycardia and pulsus paradoxus due to pericardial effusion



**Figure 9.** Same case after the pericardial window was made and general anesthesia was induced, showing the decrease in pulse rate and resolution of pulsus paradoxus



intramedullary rod, followed by hemiarthroplasty.

The patient had several fentanyl patches on her skin at the time of surgery and had taken hydromorphone with sips of water before arrival at the hospital. Anesthesia was induced with propofol and sufentanil and a sufentanil drip at 0.5 µg/kg per hour was started along with 5% to 7% inhaled desflurane. Approximately 90 minutes after induction, her heart rate and blood pressure increased substantially, and 6 mg of hydromorphone was administered. The sufentanil was increased to 1 µg/kg per hour, and a hydromorphone drip of 5 mg/h was begun. Additional doses of hydromorphone were administered for increases in blood pressure and

heart rate. A total of 300 µg of sufentanil and 46 mg of hydromorphone had been administered during the 5 hours and 13 minutes of surgery. Despite the massive amounts of opioids, the patient breathed spontaneously and was extubated immediately after closure of the wound. Another 10 mg of hydromorphone was administered after extubation and another 4 mg on arrival in the postanesthesia care unit. The chronic pain service was notified, and her postoperative pain management continued under their direction.

While the multidimensional and complex nature of pain control for patients with cancer is beyond the scope of this article, we must keep in mind that this facet of cancer care cannot be ignored and that treatment of pain with opioids is not rendered unnecessary by the administration of anesthetic agents or routine amounts of short-acting opioids. The psychological and physiological effects of pain on patients with cancer are critical factors that cannot be ignored any more than hydration, nutrition, or any other aspect of care.

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#### AUTHOR

Kenneth M. Kirsner, CRNA, MS, JD, is a staff nurse anesthetist at the University of Texas M.D. Anderson Cancer Center, Houston, Tex.