INTRODUCTION

For the last 2 centuries, morphine has been the single most relied-upon drug for the management of acute surgical pain. Fortunately, modern advances in anesthesia and analgesia have revolutionized this pain management approach. Today, multidisciplinary treatment plans have been identified as a principal factor in both modern-day pain control and optimization of recovery after surgery. Despite numerous medical and technological advances, postsurgical pain is often undertreated. An understanding of the physiology and complex, multifaceted nature of pain is necessary to identifying an optimal treatment plan, which often involves multiple therapeutic modalities. This balanced analgesic approach, known as multimodal analgesia, utilizes a combination of opioid and nonopioid analgesics that target different sites of the peripheral and central nervous system. The aim of multimodal analgesia is to optimize postoperative pain control while limiting the total amount of opioid administered to the patient, thereby minimizing adverse drug effects. This chapter will discuss recent advances in pain management and perioperative care that can improve the quality of postoperative recovery and reduce morbidity after major surgery.

PATHWAYS AND TYPES OF PAIN

The transduction of noxious stimuli involves both the peripheral and central nervous systems. It begins with peripheral nociceptors, which transmit signals along peripheral nerves through the dorsal root ganglia (Figure 27-1). Axons of myelinated A and unmyelinated C fibers synapse in the dorsal horn of the spinal cord, and pain signals are transmitted to the thalamus and cerebral sensory cortex via the ascending spinothalamic tracts. Descending modulation of pain is mediated through the dorsal horn neurons. Medications used to manage pain act at specific areas along this pathway to reduce the intensity of the pain experience.

The different types of pain include somatic, visceral, inflammatory-mediated, and neuropathic pain. Each type responds to different treatment modalities; understanding their distinctions will aid in developing specific therapeutic interventions to maximize patient benefit. Optimal pain management requires a careful appraisal of the source of pain, coupled with an appropriate selection of treatments for each patient. Complex pain cases require multimodal as well as interdisciplinary care. Coordination among healthcare providers before, during, and after a surgical procedure is a critical component of successful operative pain management.

Somatic and visceral pain result from stimulation of sensory receptors or nociceptors in response to noxious stimuli; they are distinguished by the location of their receptors and the nerve fibers that are stimulated. Somatic pain receptors are located within the skin and respond to environmental cues such as sharp, focused, painful stimuli. Examples of this type of pain include incisional or cutaneous burn-related pain. Visceral receptors are located in visceral organs (bladder, ureter, small and large bowel, etc) and respond to internal cues such as dilation of the bowel or inflammation from infection. Visceral fibers are slow-conducting unmyelinated C fibers that join autonomic and somatic nerves entering the central nervous system. Visceral pain can either be localized to the site of tissue damage or be sensed at a distant anatomic region from the source of tissue injury, a phenomenon called “referred pain.” Neuropathic pain is related to the sensory perception of pain associated with peripheral or central nerves. Nerve injuries caused by stretching, compression, or cancer invasion are often the precursors to neuropathic pain, and may pose formidable treatment challenges.

Inflammatory mediators have been identified in pain pathways. Substance P, a neurotransmitter...
involved in the perception of pain, is also a mediator in the neuroinflammatory cascade. Interferons and cytokines (interleukin-1, interleukin-6 and tumor necrosis factor-α) are proinflammatory mediators thought to decrease the threshold for pain stimulation and increase the intensity of the response. Interruption of the inflammatory cascade is a potential adjunct for achieving optimal pain control.

**PREOPERATIVE PATIENT ASSESSMENT**

An adequate history and physical examination are critical to identifying the cause of a patient’s pain as well as ensuring that appropriate treatment modalities are employed (Table 27-1). Assessment of pain should include several factors: location, severity, quality, radiation, duration of onset, aggravating and mollifying events, and associated symptoms. The healthcare provider must ascertain whether or not the patient experiences chronic pain or takes chronic medications such as narcotics, non-steroidal antiinflammatory drugs (NSAIDs), anxiolytics, or gabapentin. Patients with chronic pain or history of opioid use or drug abuse may have a tolerance of narcotic-based pain medications and may require substantially greater doses of narcotics than opioid-naive patients. Conversely, others may limit the amount of pain medication they take because of fear of drug dependency.

Acute, severe, and undertreated pain is associated with many adverse systemic effects including increased myocardial oxygen demand, reduced functional residual capacity, hypoxemia, and gastrointestinal ileus. Some patients with severe, poorly controlled operative site pain may develop long-term central sensitization. This condition may serve as the basis for chronic pain syndromes wherein noxious stimuli are accompanied by an exaggerated pain response, or hyperalgesia, and painless stimuli are perceived as painful, a phenomenon known as allodynia.

### TABLE 27-1

**PREOPERATIVE MEASURES TO ASSESS AND CONTROL PAIN**

- History and physical examination
  - specifics about pain: location, severity, quality of pain, radiation, onset and duration, aggravating and mollifying factors, and associated symptoms
  - history of chronic pain
  - medications: opioids, NSAIDs, anxiolytics, gabapentin, narcotics, antidepressants
  - history of drug use and abuse
- Patient education and reassurance that pain will be controlled
- Consider anxiolytics: midazolam (1–5 mg) 10 minutes prior to procedure
- Preemptive pain control
  - regional anesthesia with peripheral nerve blocks
  - neuraxial blockade (spinal, lumbar epidural, and thoracic epidural)
  - systemic medications (NSAIDs, opioids)

NSAID: nonsteroidal antiinflammatory drugs

**PAIN CONTROL AT EACH OPERATIVE STAGE**

**Preoperative.** The physiologic response to surgery involves a “sympathetic surge,” a profound activation of the sympathetic nervous system that is thought to contribute toafferent pain signals. This stress response is a well-established sequence of physiologic and molecular events that include fever, tachycardia, tachypnea, hypertension, gastrointestinal ileus, hypercoagulability, protein catabolism, and immunosuppression. Circulating cytokines and neuroendocrine mediators are also involved. The response lasts approximately 3 to 4 days from the time of induction of general anesthesia.

The goal of preemptive pain control is to blunt the physiologic response to surgery as well as to decrease the level of overall pain. Specifically, effective preemptive analgesia reduces the surgical nociceptor input (pain) while simultaneously preventing an ensuing sensitization of the nervous system throughout the perioperative period. The efficacy of preemptive multimodal analgesia depends on the interruption of the transduction ofnoxious stimuli at multiple sites along the pain pathway. Sites targeted by preemptive analgesia include peripheral nociceptors, preganglionic peripheral nerves, the dorsal horn of the spinal cord, and the sensory cortex and limbic system (see Figure 27-1).

Adequate arterial perfusion and partial pressure of oxygen are critical to tissue healing, and vasoconstriction is a threat to normal healing. Measures to control peripheral vasoconstriction should be initiated prior to the operation and include cessation of smoking; controlling fear, pain, and anxiety; correcting hypertension; maintaining normal circulating blood volume; and maintaining normothermia. Preoperative reassurance that pain will be treated aggressively should be a goal of all members of the operative team. Administration of an anxiolytic at least 30 minutes before surgery has been shown to decrease both anxiety and postoperative pain throughout the first postoperative week in a randomized placebo-controlled trial of patients who had outpatient surgery under general anesthesia.

The use of perioperative NSAIDs in preemptive analgesia is preferred over narcotics to limit adverse side effects (nausea, vomiting, urinary retention, cognitive dysfunction, respiratory depression). The use of NSAIDs is often combined with infiltration of the wound with a long-acting local anesthetic (e.g., bupivacaine). Continuation of NSAID analgesia for at least 24 hours after surgery is critical to mitigating the response to a subsequent incision.
surgery is considered essential in order to achieve effective postoperative control of peripheral nociceptive pain. In addition, NSAIDs may achieve a long-term effect by inhibiting sensitization of the central nervous system.

**Intraoperative.** Optimal preemptive pain control involves measures taken prior to the surgical incision, and continues into the postoperative period (Table 27-2). Injection of medications into the subcutaneous tissue underlying the intended incision site reduces postoperative analgesic requirements. Long-acting local anesthetics such as ropivacaine are most commonly used, but ketorolac, tramadol, and morphine have also been used for preincisional analgesia.

Operative site infection is an established potent stimulus for proinflammatory cytokines and chemokines. Prophylactic antibiotics are administered within 60 minutes of incision, re-dosed during major operations, and continued for 24 hours postoperatively. Operations undertaken for infectious etiology, such as abscess, cholecystitis, appendicitis, and diverticulitis, should focus on control of the pathologic source. Infectious complications can be minimized by expeditious surgery; gentle tissue handling; maintenance of normothermia, partial pressure of oxygen, and perfusion pressures; judicious use of antibiotic irrigation; avoidance of fluid overload; and changing gloves and instruments before wound closure. Sympatholytic effects of epidural anesthesia reduce the physiologic stress response to surgery, improve perfusion, reduce hypoxemia, limit blood loss (thereby decreasing transfusion requirements), counteract the prothrombotic state of surgery, and optimize pain control and secondary sensitization.

Meticulous surgical technique and hemostasis are fundamental aspects of postoperative pain control. Blood within the intraperitoneal cavity irritates the peritoneum and causes visceral pain.

### TABLE 27-2

**INTRAOPERATIVE MEASURES BY THE SURGEON TO CONTROL PAIN**

- **Preincision analgesia:** subcutaneous injection prior to operation at incision site, use
  - bupivacaine (10–30 mL of 0.25%),
- **Prevention of infection and systemic inflammatory cascade:** includes
  - preoperative antibiotics 60 minutes prior to incision (appropriate to operation)
  - expeditious surgery
  - gentle tissue handling
  - maintenance of normothermia
  - adequate tissue perfusion (minimizing peripheral vasoconstriction)
  - adequate tissue oxygen partial pressure
  - judicious use of antibiotic irrigation
  - avoidance of fluid overload
  - different gloves, instruments, and possibly gowns prior to closure of incision
- **Meticulous hemostasis:** (avoidance of operative site hematoma), prevents
  - visceral irritation
  - hematoma formation.
- **Intraoperative peritoneal or pleural administration of local anesthetics,** use
  - bupivacaine (15 mL of 0.5% with 1:100,000 epinephrine; 2–5 mL per laparoscopic port site) or ropivacaine (20 mL of 7.5 mg/mL; 4 mL per intercostal space)

Postsurgical hematomas that form in anatomically confined areas such as the groin continually stimulate peripheral nociceptors, resulting in pain that is difficult to control. Unless it is resorbed over time, a pain hematoma may require reoperation for surgical evacuation.

Blockade of afferent pain signals not only blunts pain but also reduces the amount of postoperative narcotic required, ultimately improving the quality of recovery. Intrapleural and intraperitoneal administration of local anesthetic has been shown to control visceral pain better than systemic medication. Recent advances in minimally invasive surgery have translated into smaller surgical incisions, reduced stress response and narcotic requirement, and decreased wound complications, all of which lead to a more rapid postoperative recovery.

**Postoperative.** Parenteral analgesics are commonly administered postoperatively, because patients are often restricted from oral intake after major surgery. However, fast-track rehabilitation is challenging the surgical dogma that restricts oral intake for prolonged periods until passage of flatus or stool has been achieved. Opioid medications (eg, morphine sulfate, fentanyl, Dilaudid [Abbott Laboratories, Abbott Park, Ill]) are among the most common perioperative analgesics administered because of their time-tested efficacy. However, adverse side effects including sedation, nausea, pruritis, and impairment of gastrointestinal motility, make preemptive analgesia an attractive alternative. Multimodal perioperative analgesia using several different drug mechanisms of action facilitates dose reductions in all the pain medications used and early discontinuation of narcotic analgesics, providing better analgesia while minimizing the unwanted side effects of any one drug class.

The method of narcotic delivery impacts the success of pain control. As needed,
nurse-administered medication may result in unacceptable gaps in postoperative analgesia and fail to establish a therapeutic baseline level of pain control. Intravenous patient-controlled anesthesia, which allows timely patient-directed narcotic administration, has a continuous baseline dosing function to limit the peaks of pain intensity in the postoperative period. Multiple studies have documented improved pain outcomes with patient-controlled anesthesia as compared to nurse-titrated medication, but no consensus has been reached about improvements in postoperative complications. Transdermal narcotic administration provides more consistent administration of medication but has a delayed onset of action.

SUMMARY

Comprehensive preoperative assessment by the surgeon and anesthesiologist is the key first step to optimizing operative outcomes. Many perioperative measures fundamental to optimizing patient outcomes are intuitive: gentle tissue handling, minimizing blood loss, preventing hypothermia, administering prophylactic antibiotics within 1 hour of incision, judicious antibiotic irrigation of contaminated sites, minimizing peripheral vasoconstriction, limiting use of drains, ensuring high arterial partial pressure of oxygen, minimizing fluid overload, limiting the physiologic stress response to surgery, and optimizing control of pain.

Emphasis on multidisciplinary approaches to pain management can significantly improve pain care plans beyond pharmacologic measures. Coordination among the primary team, anesthesia, acute pain nursing, pharmacy, mental health, physical and rehabilitative medicine, and the family is a vital component of any inpatient pain care activity. For example, although a dense block of a patient's upper extremity may provide excellent pain relief, if the patient has no motor function in the limb to participate in physical therapy, this modality may not be in the best interest of the patient's overall recovery and health. Effective acute pain management requires the existence of an acute pain service staffed with motivated professionals dedicated to the effective treatment of pain using a multimodal approach.