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Review Article

Anesthesia for Major Thermal Injury

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Dennis M. Fisher, M.D., Editor

THERMAL injuries cause many complications and deaths. In the United States, approximately 1.25 million persons are treated annually for burns, 50,000 patients are admitted to hospitals, and 5,500 die from major thermal injury. [1] Although many studies have documented a progressive improvement in outcome and survival after major burns, [2-5] management of these patients remains challenging to all involved in their care. Improvements in survival have been attributed to the development of the multidisciplinary burn team, an early aggressive surgical approach to major burns, and improved understanding of the pathophysiologic nature of thermal injuries. [6] This article reviews the literature and describes developments that are relevant to anesthesiologists involved in the care of burn patients.

Classification

Burns are classified according to the total body surface area (TBSA) burned, depth of burn,

and the presence or absence of an inhalational injury. The TBSA burned is calculated using the rule of nines (Figure 1). Whereas the rule of nines accurately predicts the surface area involved in adults, even a modified version appears to underestimate the extent of burn injury in children (Figure 2). [7] Table 1 classifies burn depth and outcomes, and Table 2 gives the definition of a major burn.

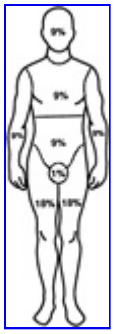


Figure 1

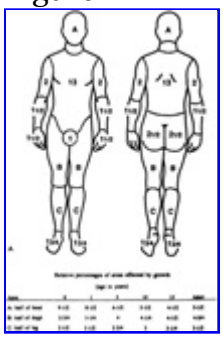


Figure 2

Table 1

Full thickness burns > 10% TBSA
Partial thickness burns > 25% in adults or 20% at extremes of age
Burns involving face, hands, feet, or perineum
Inhalational, chemical, or electrical burns
Burns in patients with serious pre-existing medical disorders
Adapted from the American Burn Association Injury Severity Grading System
TBSA = total body surface area.

Table 2

Pathophysiologic Features and Management of the Patient with Burns

Mediators of Local and Systemic Effects

After a burn injury, mediators released from the burn wound contribute to local inflammation and burn wound edema. [8] Local mediators include oxygen radicals, arachadonic acid metabolites, and complement. In minor burns, the inflammatory process is limited to the wound itself. In major burns, local injury triggers the release of circulating mediators, resulting in a systemic response. This is characterized by hypermetabolism, immune suppression, and the systemic inflammatory response syndrome (Figure 3). Cytokines appear to be the primary mediators of systemic inflammation after burns. [8-11]

Endotoxin is usually detected several days after a burn even in the absence of infection. Endotoxin concentrations correlate with burn size [8] and predict the development of multiple-organ failure and death. [12] Elevated nitric oxide levels may contribute to hemodynamic and immunologic alterations after burn injury. [13]

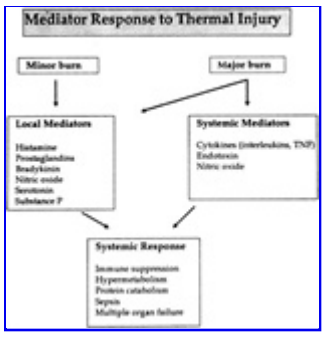


Figure 3

Attempts to modulate the production or block the effects of inflammatory mediators have generally been unsuccessful, and so far these therapies are only experimental (Table 3). [14] The failure to develop a single "silver bullet" to blunt the inflammatory response can probably be attributed to the many mediators that need to be blocked.


Table 3

Cardiovascular Effects

The term burn shock was coined to describe the hypovolemic shock that can occur immediately after a burn. This results primarily from an alteration in microvascular permeability in both normal and burned tissues with resultant leakage of protein-rich fluid from the intravascular compartment to the interstitial compartment. [15-18] Other mechanisms contributing to the transcapillary fluid flux include an increase in intravascular hydrostatic pressure, a decrease in interstitial fluid hydrostatic pressure, and increased interstitial osmotic pressure. [19] Reduced cell membrane adenosine triphosphatase activity in severe burns causes accumulation of intracellular sodium and water, further depleting the intravascular compartment. [20] Significant tissue edema develops in the 12 - 24 h after a major thermal injury as fluid is sequestered in the interstitium of the burn wound and nonburned tissue. Although permeability is increased in nonburned tissue for <24 h, increased permeability persists in burned tissue for >72 h.

In addition to the fluid shifts in the early postburn period, cardiac output is decreased, independent of intravascular volume status. [21-24] Reduced cardiac contractility results from circulating humoral factors, reduced responsiveness to endogenous catecholamines, and

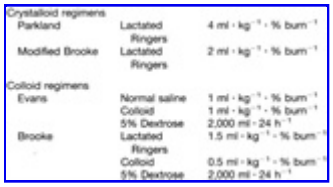
decreased coronary blood flow. Although a specific myocardial depressant factor has not been isolated, humoral factors that decrease cardiac contractility include tumor necrosis factor, [25] oxygen free radicals, [26,27] endothelin-1, [28] and the interleukins. The cardiovascular response to both endogenous and exogenous catecholamines is attenuated after burn because of reduced adrenergic receptor affinity and decreased second messenger production. [29-31] Reduced coronary blood flow in the postburn period may contribute to the decrease in cardiac contractility. [32] The magnitude of cardiac impairment is larger in older patients. [23]

Systemic vascular resistance also increases, coincident with the decrease in cardiac output. [33,34] Nonsurvivors of this initial postburn period have a larger decrease in cardiac output, higher systemic vascular resistance, more metabolic acidosis, and lower oxygen consumption than do survivors. [35]

After successful resuscitation and the first 24-48 h after a burn, the myriad of inflammatory mediators and cytokines released change the cardiovascular response into the classic systemic inflammatory response syndrome, which is manifested by increased cardiac output and reduced systemic vascular resistance and reflects a marked increase in the metabolic rate. [36] The consequences of this are important. The systemic inflammatory response syndrome manifestations are identical to those seen in sepsis, and care must be taken to avoid antibiotic use in the absence of other evidence of systemic infection. In addition, the systemic inflammatory response syndrome is the prime cause of the hypermetabolism manifested by the severely burned patient.

Cardiovascular Resuscitation

The initial aim of cardiovascular resuscitation is to prevent or correct hypovolemia. Many resuscitation formulas have been described with several common features (Table 4). Intravenous fluid is given in proportion to %TBSA burned, and administration is guided by clinical assessment, vital signs, and urine output to determine adequacy of volume replacement. One half the calculated resuscitation fluid requirement for the first 24 h is given in the first 8 h, and the rest is administered during the next 16 h, with the time of injury as the starting point for the calculations.



Crystalloid regimens		
Parkland	Lactated Ringers	4 ml · kg^{-1} · % burn^{-1}
Modified Brooke	Lactated Ringers	2 ml · kg^{-1} · % burn^{-1}
Colloid regimens		
Evans	Normal saline	1 ml · kg^{-1} · % burn^{-1}
	Colloid	1 ml · kg^{-1} · % burn^{-1}
	5% Dextrose	2,000 ml · 24 h^{-1}
Brooke	Lactated Ringers	1.5 ml · kg^{-1} · % burn^{-1}
	Colloid	0.5 ml · kg^{-1} · % burn^{-1}
	5% Dextrose	2,000 ml · 24 h^{-1}

Table 4

Children require special care when both maintenance fluid and fluid losses resulting from burn injury are calculated. Published formulas may underestimate fluid requirements is burned children, especially small patients (<10 kg) and those with large burns (>40% TBSA).

Because infants and small children have high volume-to-surface area ratios, formulas basing fluid requirements on surface area burned and weight may be inaccurate. Furthermore, the amount of fluid calculated for children using standard formulas may be less than their daily maintenance requirements. For children younger than 4 yr, we suggest that fluid replacements be calculated from the formulas and given in addition to the daily maintenance fluid requirements.

Crystalloid Formulas. Most burn centers use crystalloid as the primary fluid for burn resuscitation. The Parkland regimen, the most widely used resuscitation formula, administers 4 ml [middle dot] kg^{-1} [middle dot] $\%burn^{-1}$ lactated Ringer's solution over 24 h and aims at a urine output of 1 ml [middle dot] kg^{-1} [middle dot] h^{-1}. [16] If 0.5 ml [middle dot] kg^{-1} [middle dot] h^{-1} urine output is considered adequate, then approximately 3 ml [middle dot] kg^{-1} [middle dot] %burn ($^{-1}$) is recommended. Hypoproteinemia usually develops with purely crystalloid fluid regimens. [16] Burn wound edema is also worse with larger volumes of crystalloid resuscitation fluid. [11]

Colloid Formulas. In the United States, most authorities believe colloid solutions should not be used in the first 24 h because they are no more effective at maintaining intravascular volume than crystalloids. There is abundant evidence that outcome is not influenced by early colloid resuscitation. [11,37,38] In Europe, some resuscitation formulas still include a combination of crystalloid and colloid, [39-42] but the added expense without demonstrable benefit has led to minimal use in the United States. [43,44] The American College of Surgeons Committee on Trauma has advocated that only crystalloid (Parkland or Baxter) formulas be used for all burn resuscitation because of its simplicity, reduced cost, and equivalent outcome.

Hypertonic Saline. Hypertonic saline solutions are effective in treating burn shock. [45-47] Its proponents recommend hypertonic saline solutions for patients with large burns, circumferential extremity burns, or inhalational injury, because the administered fluid volumes are smaller and tissue edema is reduced. However, Huang et al. [48] reported a fourfold increase in renal failure and twofold increase in the number of deaths in patients resuscitated with hypertonic saline solution after major burns compared with those given lactated Ringer's solution. Resuscitation with hypertonic saline solution did not appear to reduce the total resuscitation volume required. Other adverse effects include hypernatremia and intracellular water depletion. Because of these problems, hypertonic saline solutions are used infrequently in most burn centers.

Adequacy of Resuscitation. The usual parameters for guiding fluid resuscitation are vital signs and urine output. Although most patients are treated successfully with this approach, several recent studies have shown advantages to invasive hemodynamic monitoring in adults with serious burns who do not respond as expected to fluid resuscitation. [36,49] In a study of patients with severe burns injuries, Dries and Waxman [49] found no correlation between

clinical parameters (vital signs and urine output) and hemodynamic variables obtained from a pulmonary artery catheter (oxygen consumption and cardiac index). This suggests that vital signs may be normal in patients who are actually hypovolemic. Another study using pulmonary artery catheters documented the hemodynamic profile of patients with major burns. [36] In the initial postburn period, circulatory shock was attributed to hypovolemia, but from the second day, hyperdynamic shock developed with an increase in cardiac index and a marked decrease in systemic vascular resistance. The authors suggest that invasive hemodynamic monitoring is justified in patients with major burns, and the use of inotropes is appropriate in patients unresponsive to fluid loading. [36] Thus pulmonary artery catheterization may be indicated in a few patients who do not respond to fluid resuscitation or belong to a high-risk subgroup, such as those with preexisting cardiac disease. If invasive cardiovascular monitoring is used, whether for initial resuscitation of the patient or for subsequent burn debridement procedures, catheters should be removed as soon as possible to minimize the risk of local and systemic infection.

Burn Resuscitation in Children. Weight-normalized fluid requirements for resuscitation of infants and toddlers with burns are generally larger than for adults. Using a crystalloid resuscitation regimen, about 6 ml [middle dot] kg^{-1} [middle dot] $\%burn^{-1}$ is required to maintain urine output. [50,51] An alternative approach for young children is to provide maintenance fluids in the form of 5% dextrose and 0.45% saline in addition to the resuscitation fluid. However, severely burned children are often hyperglycemic for the first 24 h after injury and consequently may not need glucose during that interval. Colloid replacement sometimes is needed in pediatric burn patients because of the rapid decrease in plasma protein concentration during crystalloid resuscitation. [16]

Failure of Burn Shock Resuscitation. A small percentage of patients fail to respond to conventional resuscitation. These patients frequently have large, deep burns, are at the extremes of age, have an inhalational injury, or preexisting medical conditions. A few centers have indicated that the use of plasma exchange in this group of patients dramatically reduces the fluid needed to maintain hemodynamic stability. [52,53] This technique is not widely used.

Upper Airway Injury

Upper airway injuries result from inhalation of superheated air or steam and toxic compounds found in smoke. [54] Brief exposure of the epiglottis or larynx to either dry air at 300 [degree sign]C or steam at 100 [degree sign]C leads to massive edema and rapid airway obstruction. [55] In children, this may result in macroglossia, epiglottitis, and laryngotracheal bronchitis. Chemical products of combustion such as ammonia, nitrogen dioxide, sulfur dioxide, and chlorine dissolve in the upper airways, forming acids and irritating the mucous membranes of the respiratory tract. Even patients with a mild upper airway injury are at risk for development of progressive airway obstruction as tissue edema develops. Smoke

inhalation injury is described in more detail.

Clinical Features. Stridor is the typical sign of upper airway obstruction. [56,57] If severe, patients may appear dyspneic, use accessory muscles of respiration, and sit upright. Hoarseness and dysphagia are common. The patient may have burns to the face or perioral area, carbonaceous sputum, and oropharyngeal edema. The absence of a facial burn does not rule out a significant upper airway injury.

Several specialized techniques have been used to assess airway burns. Although rarely used in routine clinical practice, flow volume curves can be obtained in about 85% of adult patients and complement the clinical and airway examination. [58] Upper airway obstruction from pharyngeal and laryngeal edema decreases inspiratory flow but not expiratory flow. With more severe injury, both inspiratory and expiratory flow rates may be decreased. Abnormal flow curve patterns often precede visible changes in airway mucosa or diameter. A study examined patients at risk for airway injury using fiberoptic nasopharyngoscopy and flow volume curves to assess the airway. [58] Fifty percent of patients had abnormal curves showing extrathoracic obstruction that correlated with the severity of anatomic change. Direct inspection of the airway using fiberoptic bronchoscopy and nasopharyngoscopy can diagnose anatomic narrowing of the airway. Indications for these more specialized examinations are controversial. Clinical assessment and sometimes direct laryngoscopy by a skilled examiner help the physician make treatment decisions in most situations. [59]

Airway Management

Airway management begins with assessment. The critical information to obtain is the presence of a previous airway abnormality, a current airway injury, and signs of airway obstruction. Once this information is available, the best plan for airway management can be formulated.

An important airway management decision must be made as soon as the patient arrives in the hospital. That is, even if the airway appears normal, should the patient's trachea be intubated prophylactically? Not all airway injuries manifest immediately. Edema associated with massive fluid resuscitation may compromise the airway and make delayed tracheal intubation difficult. Tracheal intubation and muscle paralysis may be necessary to facilitate emergency care and resuscitation, particularly in the presence of other injuries. As a general rule, it is better to tracheally intubate the burn patient early rather than late.

When there is an upper airway injury with signs of airway obstruction, the patient will need rapid tracheal intubation. The best technique and the best location for this vary with the personnel and the institution caring for the patient. However, for patients with markedly abnormal airways, immediate supervised transport of the patient to the operating room may be appropriate. In this location, the anesthesiologist has skilled assistance, a full range of intubation equipment, an anesthetic machine, and the best environment in which to secure the airway surgically should that be necessary.

Tracheal Intubation of the Adult with an Abnormal Airway. With an abnormal airway or upper airway obstruction, the safest way to secure the airway is with the patient awake. Key prerequisites include effective topical anesthesia, proper patient positioning, and supplemental oxygen administration. Intravenous opioid administration is appropriate for the alert patient in pain, but sedatives may worsen airway obstruction and should be used cautiously, if at all. Although the best technique will depend on the operator's expertise, the flexible fiberoptic scope is well suited to this situation. Alternatives include direct laryngoscopy, the laryngeal mask airway, and the Bullard laryngoscope. When general anesthesia is necessary because the patient cannot cooperate, an inhalational induction with spontaneous ventilation may be required before attempts at tracheal intubation.

When the upper airway is badly damaged and endotracheal intubation is not possible, a direct surgical approach to the airway is indicated. Options include a needle cricothyroidotomy, surgical cricothyroidotomy, or tracheostomy; however, because of the high incidence of complications (see below), a surgical airway should be considered only as a last resort.

Tracheal Intubation of the Child with an Abnormal Airway. For children, an inhalational induction with oxygen and a volatile agent before airway manipulation is probably the safest technique. Experience with halothane is extensive, it has proved efficacy in burned children, its potency permits induction of deep levels of anesthesia without compromising oxygenation, and most anesthesiologists are familiar with its use for inhalational induction. Sevoflurane, a new volatile anesthetic with a lower solubility in blood, combined with minimal airway irritation, may offer the advantage of a more rapid induction. [60]

Once the patient is anesthetized, several options are available that depend on the operator's expertise. Pediatric fiberoptic and Bullard laryngoscopes may be useful when direct laryngoscopy is difficult. Both nasal and oral routes for tube passage have their proponents. Although it has not been studied systematically, the laryngeal mask airway may provide a valuable adjunct to maintaining airway patency and as a guide for fiberoptic intubation in patients with severe airway edema.

Although we do not adhere to a rigid protocol, our general practice is to use uncuffed endotracheal tubes in infants and young children. In infants, tubes without a cuff can be of larger diameter, and the narrow cricoid ring usually can provide an adequate seal. However, in larger children, particularly those requiring high inspiratory pressures during mechanical ventilation, we place cuffed endotracheal tubes. The relative safety of using cuffed endotracheal tubes in children has been shown in the operating room [61] and intensive care unit. [62] Postextubation stridor is a recognized complication of long-term tracheal intubation in pediatric burn and trauma patients. [63] It is best to wait until an air leak occurs around the endotracheal tube before tracheal extubation, because this indicates resolution of edema. If there is still no air leak and the patient is deemed ready for tracheal extubation, direct laryngoscopy may be necessary to determine the extent of residual edema. Once extubated, the patient should be closely monitored for progressive airway obstruction

during the subsequent 24 - 48 h.

Tracheal Intubation for Patients with a Normal Airway. In the absence of an airway abnormality, tracheal intubation will usually be achieved using a rapid sequence technique with an intravenous induction agent and a rapidly acting muscle relaxant.

There is general agreement that succinylcholine administration to patients >24 h after burn injury is unsafe. [64-68] After a burn, extrajunctional acetylcholine receptors proliferative in proportion to the magnitude of the burn. [69-73] This results in an exaggerated release of potassium after administration of succinylcholine. Rapid elevations of serum potassium to > 9 mM have been documented and are usually associated with cardiac arrest. Because this process of receptor proliferation takes several days to develop, there is an initial window of safety of unknown duration. Thus conventional wisdom is that administration of succinylcholine is safe only within 24 h of a burn. [74] How long the hyperkalemic response to succinylcholine persists is also unclear. Rocuronium or high doses of other nondepolarizing muscle relaxants (e.g., vecuronium or cisatracurium) are attractive alternatives to succinylcholine.

Long-term Airway Management. Most patients with respiratory failure can be managed with endotracheal intubation. The advantages of tracheostomy include easier oral and tracheal hygiene and easier replacement if the tube is dislodged. But it has some surgical risk, the potential for airway scarring from both the endotracheal tube and tracheotomy, and it leaves a permanent neck scar. The prophylactic use of tracheostomies has been associated with a higher incidence of complications such as pulmonary sepsis, [75,76] but it is not known how many of these tracheostomies were performed through infected burns. With the practice of early excision and neck grafting, infectious complications resulting from tracheostomy may be decreased if the technique is performed after successful neck grafting. When tracheostomies are performed for specific indications such as acute airway loss or long term respiratory failure, the incidence of pulmonary sepsis and death is not increased. However, long-term upper airway sequelae such as tracheal stenosis, tracheoesophageal fistula, and tracheoarterial fistula occur in 28% of these patients. [77]

Smoke Inhalation Injury

The incidence of smoke inhalation injury varies from 5-35% of patients hospitalized with thermal injuries. [78,79] Whereas the mortality rate associated with an isolated inhalational injury is <10%, [80] the addition of an inhalational injury to a cutaneous burn of any size doubles the mortality rate. [81,82]

Smoke inhalation injury is a result of the toxic effects of smoke on both the upper and lower respiratory tract. Chemical products of combustion such as ammonia, nitrogen dioxide, sulfur dioxide, and chlorine combine with water in the respiratory tract, producing strong acids and alkalis. [83,84] For example, sulfur dioxide forms sulfuric acid. These chemical

products induce bronchospasm, edema, and mucous membrane ulceration. Gases such as the oxides of nitrogen, phosgene, hydrochloric acid, and sulfuric acid penetrate more deeply into the respiratory tract, where they damage the alveolar membrane, impair local defenses, and reduce surfactant activity. [84] As a result of inhaling these chemicals, the epithelial lining of the trachea and bronchi becomes necrosed, causing partial or complete airway obstruction and removing an important barrier to infection. [85]

Aldehydes such as acrolein, which are produced by the combustion of cotton, wood, and various synthetic fibers, impair ciliary function and damage mucosal surfaces. This results in edema and mucosal sloughing. At concentrations of only 10 parts per million (ppm), acrolein causes pulmonary edema. [84] Physiologic consequences include increased capillary permeability, increased lung water, and reduced compliance. Lung volumes decrease and airway resistance increases. Progressive worsening of ventilation and perfusion occurs and pulmonary shunting increases. [84]

Clinical Presentation. Certain historical and physical findings predict a high likelihood of an inhalational injury. Patients involved in a closed-space fire or entrapment (such as in a house or automobile) are at high risk for this type of injury. Facial burns, carbonaceous sputum, and respiratory distress are all tell-tale signs. Arterial blood should be analyzed to determine the partial pressure of oxygen, oxygen saturation, carboxyhemoglobin level, and cyanide values. Other investigations that may be necessary include chest radiography, radionucleide lung scans, and fiberoptic bronchoscopy. Sharar and Hudson [59] studied 100 patients with one or more risk factors for inhalational injury and compared clinical and bronchoscopic data for diagnostic accuracy. A 96% incidence of positive bronchoscopic findings was found with the triad of closed-space fire, carboxyhemoglobin levels >10%, and carbonaceous sputum. The incidence decreased to 70% when two of the clinical parameters were present and to <30% if only one clinical finding was present. The authors conclude that history, physical examination, and carboxyhemoglobin measurement are adequate initially, and they recommend that fiberoptic bronchoscopy be reserved for exceptional cases, such as for patients with lobar atelectasis or evidence of debris in a major bronchus. [59] An alternative view is expressed by Masanes et al., [86] who used fiberoptic bronchoscopy to diagnose inhalational injury in 130 burn patients. They confirmed the high sensitivity (0.79) and specificity (0.94) of bronchoscopy by comparing it with histologic findings. They concluded that immediate diagnosis allows prediction of outcome and enables early specific treatment for those with inhalational injuries.

Management of Smoke Inhalation Injury. Early tracheal intubation may be required for upper airway problems. Smoke inhalation resulting in severe bronchospasm, alveolar damage, or pulmonary edema will necessitate ventilatory support. Although some components of smoke such as carbon monoxide and cyanide may require specific treatment, for the most part management of smoke inhalation injury involves ventilatory support and intensive care. [79,80]

Carbon Monoxide Poisoning

Carbon monoxide is a major component of the smoke produced in most open fires and is responsible for 80% of the deaths associated with smoke inhalation. [87,88] Carbon monoxide is produced by incomplete combustion of carbon-containing compounds such as wood, coal, and gasoline. Carbon monoxide has 250 times more affinity for hemoglobin than oxygen does and produces its toxic effects by displacing oxygen and decreasing the oxygen-carrying capacity of hemoglobin. In addition, carbon monoxide shifts the oxygen dissociation curve to the left, reducing the unloading of oxygen to the tissues. Carbon monoxide also impairs activity of several intracellular enzymes by binding to cytochrome oxidase. [84] These effects cause tissue hypoxia and metabolic acidosis.

Clinical Presentation. Carbon monoxide poisoning should be considered in all victims of enclosed fires. Shusterman et al. [89] found a positive correlation between carboxyhemoglobin levels and the severity of smoke inhalation injury as determined by clinical and radiologic assessment. Symptoms depend on the carboxyhemoglobin level, although it is actually the tissue carbon monoxide level that determines the toxicity of carbon monoxide. With carboxyhemoglobin levels <20%, patients experience headaches, tinnitus, and nausea. At levels between 20 - 40%, patients are weak and drowsy. Carboxyhemoglobin levels >40% cause severe neurologic dysfunction (often permanent) and coma. Cardiac dysrhythmias and brain injury are often fatal when carboxyhemoglobin levels reach 55 - 70%. [90]

Carbon monoxide poisoning is easily diagnosed, based on clinical neurologic findings and the measurement of carboxyhemoglobin levels in the emergency room. The arterial oxygen pressure, pulse oximetry saturation, and arterial oxygen saturation may be normal in the presence of carbon monoxide. Carboxyhemoglobin is read by a pulse oximeter as "saturated" hemoglobin, giving a falsely elevated level of pulse oximetry saturation. [91] Similarly, intravenous mixed venous oxygen sensors overestimate venous oxygen saturation in the presence of carbon monoxide. A cooximeter, which measures the percentage of hemoglobin, oxyhemoglobin, carboxyhemoglobin, and methemoglobin, is needed to obtain an accurate pulse oximetry saturation.

Management. Administration of a fractional concentration of oxygen in inspired gas of 1.0 decreases the half-life of carboxyhemoglobin by nearly a factor of four compared with the half-life when room air is breathed. Elimination of carbon monoxide depends primarily on the alveolar oxygen pressure rather than alveolar ventilation. Therefore, the burn victim should receive oxygen as soon as possible after injury.

The debate continues over the effectiveness of hyperbaric oxygen (HBO) to treat carbon monoxide poisoning. The major question is whether HBO reduces the incidence of delayed neurologic sequelae. Early studies found that 11% of patients with carbon monoxide exposure had gross neuropsychiatric damage during a 3-yr follow-up period. [92] However, a

more recent report indicated that permanent neurologic sequelae ranged from 0.2% to 11%. [93] One review of 115 cases of carbon monoxide poisoning, including 29 resulting from smoke inhalation, reported no correlation between clinical outcomes and carboxyhemoglobin levels and recommended that any patient with neurologic symptoms other than headache and nausea should have HBO regardless of their carboxyhemoglobin level. [94] In a prospective, randomized study of patients who did not lose consciousness, Thom et al. [95] reported that delayed neurologic sequelae could not be predicted based on the patient's clinical history and that HBO significantly decreased the incidence of these sequelae.

In contrast, recent studies have also concluded that HBO is not effective in reducing the incidence of neurologic injury after carbon monoxide poisoning. [96-98] Furthermore, the care of a critically ill patient, often with other injuries in addition to the burn, is difficult in the confined quarters of an HBO chamber.

It is reasonable to conclude that patients with mild exposure (carboxyhemoglobin level <30%) and no neurologic symptoms can be treated with inhalation of a fractional concentration of oxygen in inspired gas of 1.0 via mask or endotracheal tube. Patients who are comatose or have a carboxyhemoglobin level >30% at the time of hospital admission may benefit from HBO. Patients with large burns (>40% TBSA) should be considered for HBO only if there is no delay in the treatment of other more life-threatening problems such as airway compromise or hemodynamic instability. [59]

Cyanide Poisoning

Hydrogen cyanide is produced by burning high nitrogen content plastics such as polyurethane, polyacrylonitrile, and acrocyanate glue found in laminates. Cyanide causes tissue asphyxia by inhibiting intracellular cytochrome oxidase activity, the final step in oxidative phosphorylation, thus preventing mitochondrial oxygen consumption. Cyanide poisoning also arrests the tricarboxylic acid cycle. Affected cells can only generate adenosine triphosphate via anaerobic metabolism, and lactic acidosis results from the anaerobic conversion of pyruvate to lactate.

Clinical Presentation. Cyanide poisoning can be difficult to diagnose. With a concentration of 50 ppm, symptoms include headache, dizziness, tachycardia, and tachypnea. Above 100 ppm, lethargy, seizures, and respiratory failure occur. [84] A history of smoke inhalation should suggest the possibility of cyanide exposure. An anion gap metabolic acidosis that fails to respond to oxygen administration is seen. The mixed venous partial pressure of O_2 is elevated in patients with cyanide poisoning. Plasma lactate levels correlate with cyanide levels and provide an alternative diagnostic tool. [99]

Management. The treatment of cyanide poisoning has generated controversy. A canine study of carbon monoxide and cyanide poisoning concluded that mechanical ventilation alone is

usually adequate treatment; however, persisting blood cyanide and lactic acidosis indicate a need for specific therapy. [100] Cyanide is normally metabolized by hepatic rhodanase to thiocyanate, with thiosulphate as a substrate, but this process is slow. Treatment involves administration of additional thiosulphate to speed hepatic metabolism as well as diversion of cyanide into other metabolic pathways. Nonhepatic metabolic pathways to remove cyanide include the combination of cyanide with methemoglobin and hydroxycobalamin. Methemoglobin levels are increased by administration of nitrites [101]; the resulting methemoglobin combines with cyanide to form cyanomethemoglobin, which effectively neutralizes the cyanide. Although methemoglobin does not transport oxygen, patients tolerate methemoglobin levels of up to 40%, and this can be used to guide therapy.

Sodium thiosulphate administered intravenously enhances hepatic metabolism of cyanide. Kirk et al. [102] studied the effects of a cyanide antidote kit consisting of sodium nitrite and sodium thiosulphate that was administered to patients with signs of cyanide poisoning. Concentrations of cyanide correlated with those of carboxyhemoglobin. The mean peak methemoglobin level was 10%, the mean half-life of cyanide was 3 h, and the highest total non-oxygen-carrying hemoglobin level was 21%. One patient had a marked decrease in blood pressure when sodium nitrite was administered. The authors concluded that the cyanide antidote kit was safe in patients with carbon monoxide and cyanide poisoning but that the effects of methemoglobin formation on oxygen delivery and the extent of cyanomethemoglobin formation needed to be determined.

The combination of carbon monoxide and cyanide poisoning in the burn patient can have potentially lethal effects on oxygen transport and use. Therefore, burn patients should be tested for poisoning and appropriate therapy instituted as soon as possible.

Indirect Respiratory Injury

The lung is at risk in patients with cutaneous burns even in the absence of an inhalational injury. [83] Mechanisms involved include the effects of burn wound mediators on the lung, complications of burn therapy, and infection. Edema occurs in lung that has not been directly injured. Plasma oncotic pressure is decreased through loss of plasma protein in both burned and normal tissue, and pulmonary hypertension is known to occur in the first 24-36 h after burn. These factors dispose the lung to pulmonary edema. [15,83,103-105] Inflammatory mediators such as lipid peroxides, prostanoids, and complement have also been implicated in the development of lung injury. [80]

Patients most at risk for lung injury are those with combined smoke inhalation and severe burns. Initial lung damage is compounded by burn wound manipulation over days and weeks, leading to bacteremia and subsequent pulmonary sepsis in an already compromised tissue bed.

Respiratory Failure

Respiratory failure in burn patients can result from smoke inhalation injury, infection, and the adult respiratory distress syndrome. The occurrence of respiratory failure after thermal injury increases the mortality rate. Inhalational injury increases the incidence of respiratory failure from 5% to 73%. [106] Burn size is also a predictor for the development of pulmonary complications. However, respiratory failure contributes to the risk for death independent of the effects of age and burn size. [106] Respiratory failure often precedes or is a harbinger of multiple-organ failure. [107-109]

Metabolism and Nutrition

A hypermetabolic state develops in proportion to the severity of the burn injury. Early studies suggested that the metabolic rate could double in patients with burns >60% TBSA. [110] Recent studies have shown smaller increases in metabolic rate, and this has been attributed to earlier wound excision and increased use of topical antimicrobial agents, both of which decrease wound bacterial colonization. [111]

Ambient temperature has an important effect on metabolic rate in burn patients. A study of patients with a mean burn size of 44% TBSA showed that patients at thermoneutral ambient temperature (28 - 32 [degree sign]C) had metabolic rates 1.5 times those of nonburned controls. [112] However, when ambient temperature was decreased to 22 - 28 [degree sign]C, the metabolic rate increased in proportion to burn size. Thus ambient temperatures less than the thermoneutral range should be avoided, whether in the burn unit or in the operating room, to minimize further increases in metabolic rate.

Mechanisms postulated to account for the increase in metabolism after burn include release of wound-generated inflammatory mediators, hormone mediators, heat loss, and bacterial translocation from the burn wound or gut. [5,113]

The increase in metabolic rate has implications for nutritional support in the postburn period. In many centers, enteral feeding is started within 4 h of initial resuscitation. Early feeding decreases muscle catabolism and may reduce bacterial translocation through the intestinal mucosa. [113] Adequate pain control, alleviation of anxiety, a thermoneutral environment, and treatment of infection are important steps in limiting catecholamine secretion and thus hypermetabolism, which would divert calories from the healing tissue. [114,115]

Hematologic Effects of Thermal Injury

The effect of burn injury on hematologic parameters and coagulation depends on both the magnitude of injury and the time from injury.

Erythrocytes. Immediately after injury, the hematocrit level increases as noncellular fluid translocates into the interstitium. Despite large resuscitative fluid volumes, the hematocrit

level remains increased during the first 48 h and cannot be used as a meaningful parameter of resuscitation. Unless there are associated injuries, or preexisting anemia, erythrocyte transfusion is rarely, if ever, indicated during resuscitation.

A well characterized anemia of burns occurs during the weeks of care. [116] Some erythrocyte loss is obviously due to bleeding from wounds, from blood sampling for laboratory tests, and during operations. In addition, however, there is a shortened erythrocyte half-life. In part this can be related to erythrocyte damage during the heating injury and in part to circulating factors (the burn erythrocyte half-life returns to normal when they are administered to people who are not burned). [117]

Data regarding the response to erythropoetin, both exogenous and endogenous, are conflicting. The marrow can respond with reticulocytosis, but the response is inadequate considering the elevated levels of erythropoetin found in response to the burn anemia.

Most patients with moderate burns will not need blood transfusions. Because of our use of tourniquets during excision of extremity burns, and the acceptance of lower hemoglobin concentrations in burn patients, erythrocyte requirements in our burn center are only one fifth of what they were 10 yr ago. [118] Patients undergoing burn excision and grafting who are otherwise healthy will tolerate a hematocrit of 20% without problems and will replenish their erythrocyte mass easily with iron supplementation.

Platelets. During resuscitation of patients with moderate and severe burns, the platelet count usually decreases. Some decrease is dilutional, but the largest decrease results from the formation of microaggregates in the skin and smoke-damaged lung. The platelet count returns to a normal level by the end of the first week and remains at this level unless sepsis or multiple-system organ failure occurs. [119] Bleeding from thrombocytopenia is rare. If blood loss during operation is limited to less than one blood volume, platelet transfusions usually are not necessary. Frequent platelet transfusions lead to antibody formation and ineffectiveness of further transfusions if they are needed.

Coagulation. After major burns, both the thrombotic and fibrinolytic mechanisms are activated. [116,119] In general, clotting factors decrease, both from dilution and from some consumption as damaged capillaries, venules, and arterioles coagulate in the skin. Disseminated intravascular coagulation is a rare but devastating complication of massive burn injury for patients with fourth degree burns involving structures deep to the skin and subcutaneous tissue. Later, postburn thrombogenicity returns due to a decrease in antithrombin III, protein C, and protein S levels. This can cause venous thrombosis and pulmonary embolism. During this period, all patients with major burns need thromboembolism prophylaxis, such as the subcutaneous administration of low-dose heparin.

Renal Function

The incidence of acute renal failure in burned patients varies from 0.5% to 38%, depending primarily on the severity of the burn. [120,121] The associated mortality rate is consistently high (73 - 100%). Renal impairment results from reduced renal blood flow secondary to hypovolemia and decreased cardiac output. Increased levels of catecholamines, angiotensin, aldosterone, and vasopressin cause systemic vasoconstriction and can contribute to renal impairment. [122] Other mechanisms for renal failure include the nephrotoxic effects of drugs, myoglobin, and sepsis. [123]

During the hypermetabolic phase of burn healing, elevated cardiac output increases renal blood flow. The consequent increase in glomerular filtration can alter the pharmacokinetics of drugs excreted by the kidneys. For example, some renally excreted antibiotics (e.g., cephalosporins and aminoglycosides) will be cleared more rapidly and will not be at therapeutic blood levels if administered according to a normal (i.e., that for an unburned patient) dose regimen. [124] However, tubular function and creatinine clearance may be decreased despite increased renal blood flow. [123] The end result is that interpatient variability in renal function is large in burned patients.

Other Pathophysiologic Effects of Major Burns

Immune function is impaired and the presence of the devitalized tissue in the burn wound places the burn patient at considerable risk for both wound infection and systemic sepsis. Treatment with topical antimicrobial creams has decreased the incidence of burn wound sepsis, at least in the first 2 weeks after a burn. A strict aseptic technique is required for all vascular cannulation procedures and burn wound contact. Gastric mucosal stress ulceration occurs with major burns [125,126] and may be minimized by enteral feeding. Our practice is to start enteral feeding early and to administer sucralfate or histamine receptor blocker therapy. After burn injury, the clearance of cimetidine [127] but not ranitidine [128] is increased. Table 5 summarizes the pathophysiologic effects of thermal injury.

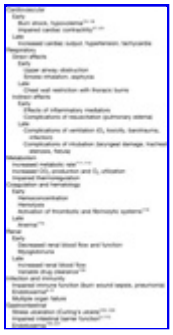


Table 5

Pharmacology in Burns

Pharmacokinetic Effects. The pathophysiologic changes occurring after thermal injury alter

pharmacokinetic parameters such as absorption, bioavailability, protein binding, volume of distribution, and clearance. [129] The extent of these changes depends on the magnitude of injury and the time between injury and drug administration. [130]

In the acute phase after a burn, organ blood flow is reduced because of hypovolemia and decreased cardiac output. Drugs administered by routes other than intravenously are likely to show delayed absorption. [131]

Plasma albumin concentrations decrease and [Greek small letter alpha] 1 acid glycoprotein levels increase. Plasma protein binding of albumin-bound drugs such as benzodiazepines is decreased, resulting in an increase in the free fraction and thus a larger volume of distribution for the drug. [132] However, because most anesthetic drugs are not highly protein bound, and because the hemodynamic changes with burns are so marked, the effect of protein binding on the pharmacologic effects of anesthetics is minimal. In addition, fluid loss to the burn wound and edema elsewhere can decrease plasma concentrations of many drugs below those expected in the unburned patient.

After the initial resuscitation phase, cardiac output increases as the hypermetabolic state develops. This increases blood flow to the kidneys and liver with increased drug clearance. [133] However, there is wide patient-to-patient variability in renal and hepatic function after burns, so drug therapy must be tailored to each patient. [123,130]

Pharmacodynamic Changes. Changes in the drug-receptor interaction are common after burns and appear to account for many of the clinically important alterations in anesthetic pharmacology.

The Burn Wound and Its Management

Natural History of the Burn Wound

First-degree and superficial second-degree burns heal spontaneously. Deep partial-thickness burns require more than 3 weeks to heal spontaneously and may have poor functional and cosmetic outcomes. Full-thickness burns require excision with subsequent skin grafting. [134] In the past, most full-thickness and all deep partial-thickness burns were treated expectantly: Eschar was permitted to slough spontaneously or was removed surgically after a period of conservative management. The open wounds were then permitted to granulate. Once healthy granulation tissue covered the wound, split-thickness, meshed skin grafts were applied. This process occurred over weeks to months in major burns and was associated with a high mortality rate from infection.

Now the approach to burn wound care is more aggressive. Topical antimicrobial therapy has reduced burn wound infections, at least in the first 2 weeks, and techniques to harvest skin have improved. Understanding of the systemic effects of the burn wound has increased, and

new alternatives are available for temporary skin coverage after burn excision (e.g., cultured epithelial cells and synthetic "skin").

Burn Wound Excision

Although the timing and extent of burn wound excision are still debated, there has been a shift toward earlier excision and grafting. [4,134-138] The most widely used approach involves an initial 48-h period of patient stabilization, followed by excision and grafting of the burn. Operations are often limited to about 20% of body surface, but with multiple operating teams and use of tourniquets, larger areas can be excised without materially increasing operative time or the need for blood transfusion. These procedures are repeated every 2 days until the burn wound excision is completed. The surgical technique uses tangential excision, in which eschar is shaved from the burn until a viable plane of tissue is reached. This procedure can result in massive blood loss. [139] For third- and fourth-degree burns, a more complete tissue removal is needed (i.e., fascial excision, en mass removal of the eschar). In general, we find that blood loss is less with this technique.

The approach of early excision, with the first operation performed in the first several days after a burn, appears to decrease the mortality rate [4,135,138] and shorten the hospital stay. [135,137,138,140] Several recent developments offer alternatives for the management of patients with extensive burn injuries. Artificial skin substitutes such as Integra (Integra LifeSciences Corporation, Plainsboro, NJ) show promise. [141] Integra is composed of a bilaminate membrane of chondroitin sulfate. The outer silicone layer closes the wound, and the inner layer establishes a vascular supply. The outer layer is removed after 2 weeks and replaced with thin autologous skin grafts. The deep layer provides some structural support to the thin graft. Because only a thin graft is required, the donor site may be harvested more frequently. Another product is an acellular dermal matrix that provides support to a thin skin graft applied at the same time. [142] Use of cultured human keratinocytes was initially promising, but recent results show that they do not provide good skin coverage and they are expensive. [143]

Another promising technique uses wound growth factors to accelerate burn wound and donor site healing. Results with recombinant human growth hormone have been encouraging, especially in children. [144-147]

Anesthesia for Excision and Grafting

Preoperative Assessment and Preparation

Successful anesthesia for excision and grafting of a burn requires planning (Table 6). The patient's age and %TBSA provide an index of the patient's likely physiologic condition. Knowledge about the patient's current cardiorespiratory status is important when planning for intraoperative monitoring. Similarly, the extent of the burn wound excision allows the

physician to determine vascular access and blood product requirements. To prevent intraoperative hypothermia, the operating room should be warm (approximately 28 [degree sign]C) before the patient's entry. Forced air warming devices are less effective in the patient with a large %TBSA because the area of the burn and donor skin sites must remain exposed. Location of burns and donor skin sites indicate the need for special positioning, for repositioning the patient during operation, or both.


Premedication
Provide adequate analgesia
Brief period of fasting
Vascular access
Establish large-bore intravenous access
Consider invasive monitoring
Securing the airway
Consider alternatives to direct laryngoscopy
Consider awake intubation if neck or facial contractures present
Ventilation
Hypermetabolism increases minute ventilation requirement
Parenteral alimentation increases minute ventilation requirement
Smoke inhalation/ARDS may necessitate ICU-type ventilator
Fluids and blood
Blood loss can be rapid during excision
Check coagulation status
Temperature regulation
Warm all fluids and keep operating room warm
Selection of anesthetic
Include opioids with all techniques
Catecholamine levels are increased (endogenous and exogenous)
Muscle relaxants
Avoid succinylcholine
Resistance to nondepolarizing muscle relaxants
Recovery
Opioid requirements are large
ARDS = adult respiratory distress syndrome.

Table 6

Airway assessment follows the usual bedside inspection and chart review. Mallampati class, thyromental distance, and head and neck mobility should be assessed. The presence of facial burns can make ventilation difficult by face mask. Edema, scarring, or contracture formation may limit mouth opening and neck mobility.

Preoperative fasting guidelines have been modified in burn patients for several reasons. Achieving adequate caloric intake in patients with major burns is difficult and nutritional support is frequently supplemented by nasogastric tube feedings, so minimizing the fasting period before operation is beneficial. Our practice in tracheally intubated patients is not to discontinue enteral feeding before operation; in unintubated patients, we stop feeding 4 h before surgery. This improves preoperative nutrition without apparently increasing the risk for aspiration. [148] One study has shown that gastric acid production is decreased rather than increased in the immediate postburn period. [149] Persons at high risk for aspiration can be treated with histamine receptor antagonists, metoclopramide, and antacids. Current analgesic requirements should be noted and a plan for postoperative analgesia discussed with the patient and parents or guardians of pediatric patients.

Monitoring

Monitoring for major burn excision or debridement is based on a knowledge of the patient's medical condition and the extent of the surgery. The electrocardiogram may be done from burned surfaces using needle electrodes or surgical staples to which an alligator clip is attached. Standard electrocardigram pads may be placed under a dependent part of the body; although they may not adhere well, they will provide a satisfactory electrocardigraphic signal in most cases. Reflectance pulse oximetry may offer advantages over standard transmission oximetry if skin sites for monitoring are limited. [150] Alternate sites for

standard oximeter probes, such as the ear, nose, or tongue may also may be used.

Arterial pressure should be monitored invasively for any large debridement. Those patients with more extensive burns, coexisting medical conditions, or complications of their burns may benefit from central venous access, a pulmonary artery catheter, or both. Insertion of invasive monitors through burned tissue sometimes is required. Temperature monitoring is essential because hypothermia is common and difficult to prevent. The operating room ambient temperature should be >28 [degree sign]C and all topical and intravenous fluids warmed. When possible, nonoperative sites should be covered and forced air warming devices used. Urine output should be measured. Neuromuscular function should be monitored in those patients in whom muscle relaxants are to be used.

Vascular Access

Securing adequate venous access is a prerequisite to burn excision and grafting procedures. For most cases, a minimum of two large-bore peripheral intravenous lines or one peripheral and one central line should be used. These can be difficult to place. Small-bore peripheral veins can be dilated to a larger gauge using kits designed for this purpose. Central venous access using a pulmonary artery catheter introducer provides an excellent route for rapid fluid administration with the added advantage of easy placement of central venous or pulmonary artery catheters. The internal jugular vein and subclavian vein are used most commonly for central access, but femoral vessels are an alternate site if burns are present around the neck. [151] An ultrasound probe that allows for localization of vessels has been useful to aid placement of central catheters in patients in whom access is difficult. [152] Intravenous lines should be connected to high-efficiency fluid warmers with the ability to infuse large volumes rapidly. When possible, blood should be administered rapidly through peripheral, rather than central, intravenous lines to minimize potential adverse effects on the heart caused by metabolic changes in stored blood products.

Airway Management

Acute airway problems are usually addressed before the patient arrives in the operating room for burn debridement. In those patients with major burns or an inhalational injury, the trachea may already be intubated. In the unintubated patient, preoperative identification of an abnormal airway should be an indication for an awake intubation in those patients who can tolerate the procedure. For the child with an abnormal airway, tracheal intubation after an inhalational induction with oxygen and a volatile agent may be the best option.

The patient with a normal airway with no risk of aspiration can be managed by a conventional intravenous induction followed by paralysis with a nondepolarizing muscle relaxant. The dose of muscle relaxant needed in burned patients is larger than in unburned patients. Securing the endotracheal tube can be difficult in the presence of facial burns. Use of a circumferential tie around the patient's head, securing the tube with wire to a tooth, or

dental arch bar stabilization of the tube can provide secure fixation that would otherwise be difficult to obtain. [153]

General Anesthesia

General anesthesia with the combination of an opioid, muscle relaxant, and a volatile agent is the most widely used technique for burn excision and grafting. With the obvious stipulation that succinylcholine be avoided, the selection of anesthetic agents is not a critical factor for most burn wound excisions.

Nondepolarizing Muscle Relaxants. Patients with thermal injury are resistant to the action of nondepolarizing muscle relaxants (NDMR; Figure 4). [71,154] This effect takes up to a week to manifest and may be observed for as long as 18 months after the burn had healed. Marked resistance to NDMRs only occurs when the burn is >30% TBSA. [154] Pharmacokinetic alterations do not explain this resistance, and a pharmacodynamic explanation has been proposed. [69-71] Burn injury appears to cause acetylcholine receptors in muscle to proliferate under the burn and at sites distant from the burn injury. [71-73] An increase in acetylcholine receptors is usually associated with resistance to NDMR and increased sensitivity to depolarizing muscle relaxants. Pavlin et al. [section] showed that acetylcholine receptors increase with as small as a 2% TBSA burn injury. Kim et al. [73] showed that local irritation or inflammation of muscle can upregulate acetylcholine receptors and that the presence of an NDMR can accentuate this upregulation. The resistance to NDMRs implies that the burned patient will require larger than normal doses of NDMR to achieve a desired effect and that the duration of action will be shorter than normal.

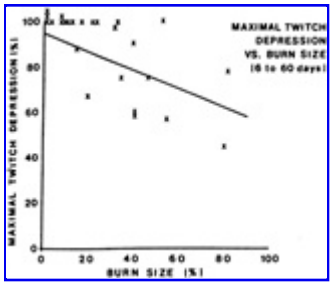


Figure 4

Anesthetic Agents. The choice of volatile agent does not appear to influence outcome from anesthesia for burn surgery. Experience with halothane, enflurane, and isoflurane is extensive, but the selection of a particular agent need not be influenced by the presence of a burn injury. Because of its rapid onset and lack of pungency, sevoflurane may offer advantages as an agent for inhaled induction of anesthesia in children or adults with abnormal airways. [60] There is no evidence that repeated halothane anesthesia in pediatric burn patients predisposes them to halothane-induced hepatotoxicity. In hyperdynamic burned patients, enflurane and isoflurane similarly decrease cardiac output and oxygen consumption. However, the reductions parallel one another so that the oxygen supply to the

tissues remains sufficient to meet demand. [155]

Various intravenous agents have been given successfully to burn patients. Ketamine offers the advantage of stable hemodynamics and analgesia and has been used extensively as the primary agent for both general anesthesia and analgesia for burn dressing changes (see below). Its major drawback is its tendency to produce dysphoric reactions. In the hemodynamically unstable patient, etomidate is a reasonable alternative to ketamine to induce anesthesia. In patients who are adequately volume resuscitated and not septic, thiopental or propofol are acceptable induction agents and are commonly used at our institution.

Regardless of the choice of induction or maintenance agent, the need to administer supplemental opioids is important. Burn patients experience intense pain and usually require large doses of opioids to remain comfortable, even in the absence of movement or surgical procedures. Furthermore, because they routinely receive opioids as a part of their daily care, they become tolerant to these drugs. To prevent the patient from awakening in pain and to determine an adequate dose of opioids, we often permit the patient whose trachea will likely be extubated to breathe spontaneously toward the end of the excision and grafting procedure. The concentration of volatile agent is gradually decreased while opioids are administered to keep the adult patient's respiratory rate in the range of 15 - 20 breaths/min.

Ventilation. Mechanical ventilation is required for patients with more extensive burns, inhalational injury, or respiratory complications. Patients with a lung injury have a substantial increase in dead space ventilation, so that end-tidal carbon dioxide may not correlate well with arterial carbon dioxide levels. [156,157] Therefore, arterial blood gases should be measured frequently. In addition, carbon dioxide production increases secondary to the increased basal metabolic rate and administration of intravenous alimentation. These changes combine to increase the patient's minute ventilation requirement markedly. For some patients with very abnormal gas exchange (e.g., in patients with minute ventilation >15 1/min, peak inspiratory pressures >50 cm H_2O, or both), the standard anesthesia ventilator may be inadequate and use of an intensive care ventilator may be necessary. [158] Patients with pneumonia or adult respiratory distress syndrome may require frequent endotracheal tube suctioning and bronchodilator therapy.

Regional Anesthesia

There are several indications for regional anesthesia for burn surgery, either alone or combined with general anesthesia, but these are limited primarily to the patient with small burns. For the patient having surgery below the umbilicus, a lumbar epidural or caudal anesthetic can provide excellent postoperative analgesia. An epidural catheter technique offers the advantage of prolonged postoperative analgesia. Extensive debridement with the potential for massive blood loss is a relative contraindication to epidural local anesthetic use

during operation, but epidural opioids can be used. Probably the greatest limitation to the use of regional techniques is the extent of the surgical field; most patients with major burns will have multiple injuries or need skin harvested from areas too extensive to be easily blocked by a regional technique. In addition, regional techniques should not be performed through burned tissue because of the potential for infection to spread.

Blood Loss during Burn Excision

Blood loss during burn wound excision and grafting can be massive, and blood should be readily available before extensive burn excision is initiated. [139] Mann et al. [118] documented blood loss and transfusion requirements in patients with >10% TBSA requiring surgery. In 1990, their patients experienced a mean blood loss of 0.23 ml for each square centimeter of surface area excised, and the average amount of blood transfused was 20 ml/%burn. On average, a patient with a 50% burn required only 1,000 ml blood. These figures are a significant improvement compared with their 1980 experience, and the change is attributed to the use of limb tourniquets during burn wound excision and a more restrictive transfusion policy. However, recent studies [159,160] have reported much larger transfusion requirements. Housinger et al. [159] reported a mean blood loss of 2.8% of a patient's blood volume for each %TBSA excised.

Intraoperative tourniquet use on burned extremities reduces overall blood loss [119] and also decreases the rate of loss, making intraoperative hypovolemia less likely. Some centers use postoperative compression dressings after excision and grafting to reduce blood loss. [161] Topical epinephrine has also been used to reduce blood loss during excision and grafting procedures. [162] We have found that application of bandages soaked in 1:10,000 epinephrine after excision of burned skin is effective in producing a bloodless surface for placement of skin grafts. Although extremely high levels of catecholamines in the blood have been measured with this technique, sup [double vertical bar] complications such as dysrhythmias are uncommon. After burn injury, cardiovascular responses to catecholamines are attenuated because of a reduced affinity of the B-adrenergic receptor for ligands and decreased second messenger production. [31] This may explain the minimal changes in blood pressure and heart rate observed after topical administration of such high concentrations of epinephrine.

If blood loss is excessive, it is prudent to analyze the patient's hematologic status regularly. Platelets or coagulation factors may need to be replaced. Although the extent of surgical operation is intentionally limited in many centers to one volume of blood lost, replacement exceeding one blood volume may be an indication for a coagulation assessment with particular attention to thrombocytopenia. [163] After excision and grafting of burns, coagulation factors and platelets return to baseline values more rapidly in burned than in unburned patients. [164]

Recovery

Patients requiring large volumes of fluid during operation are at risk for developing considerable soft-tissue edema. If the patient has been prone to or if there is significant facial edema after operation, tracheal extubation probably should be delayed until this resolves. Generous administration of opioids during operation is necessary to control pain on emergence from anesthesia. Benzodiazepines can be a useful adjunct to analgesic medication. Meperidine sometimes is beneficial to treat immediate postoperative shivering while improving patient comfort and reducing pain associated with excess movement. [165]

Management of Burn Pain

Severe pain is an inevitable consequence of a major burn injury, [129,166] and analgesic requirements are frequently underestimated. [166] Burn patients require frequent wound excision and grafting, dressings changes, and physical therapy. Anxiety and depression are common components in a major burn and can decrease the pain threshold. Unfounded concerns about opioid overdose and addiction have limited drug administration in the past. [167,168] Pain management should be based on an understanding of the types of burn pain (acute, or procedure-related pain versus background, or baseline pain), frequent patient assessment by an acute pain service team, and the development of protocols to address problems such as breakthrough pain. [167]

Analgesia for Burn Procedures

Opioids. High-dose opioids are needed to manage pain associated with burn procedures, and morphine is currently the most widely used drug. Partial agonist and agonist-antagonist combinations have been used, but their efficacy is limited by a ceiling effect. [166] Meperidine has been used in burned patients, but prolonged administration is limited by the potential for accumulation of the toxic metabolite normeperidine, so long-term meperidine administration is not recommended.

The intravenous route is preferred to administer opioids early in the course of a burn or after burn wound debridement. During the resuscitation phase of a burn, absorption from intramuscular sites may be erratic and too slow for rapid paid control. Once the patient is tolerating enteral feeding, opioid administration can continue by this route.

The pharmacokinetic parameters of morphine in burn patients have been studied and the results are inconsistent. Furman et al. [169] reported a decrease in the volume of distribution and clearance and an increase in the terminal elimination half-life of morphine in burn patients within 2 weeks of injury. Two other studies found that morphine pharmacokinetics were similar in burned and unburned adults. [170,171] Pharmacodynamic changes at opioid receptors have been suggested to explain the apparent tolerance to opioids seen after

thermal injury. [169] However, Silbert et al. [172] found that opioid analgesic potency is actually increased acutely after burn injuries for opioids acting at [micro sign], [Greek small letter kappa], and [Greek small letter delta] receptors. Peripheral antinociceptive mechanisms are also being examined. Local production of endogenous opioids in burn wounds produces some analgesia in burn patients, but not nearly enough to mitigate the need for additional exogenous opioids. [173]

The key concepts are that severe pain is common and patient responses vary, so individual titration to effect and frequent reassessment are important. Furthermore, most burned patients rapidly develop tolerance to opioids. There is no evidence that the incidence of opioid addiction in burn patients is more common than in other acutely ill patients. Patient-controlled analgesia appears to be the ideal method for opioid administration for acute or procedure-related pain. Its safety and efficacy in burns has been documented for both children [174] and adults. [175,176]

Non-opioid Analgesia. Ketamine has been used extensively in the management of burn patients, especially in the context of burn dressing changes, for which its beneficial properties are most useful. [177,178] Ketamine activates the sympathetic nervous system and usually increases blood pressure. Respiratory depression is minimal. Irving and Butt [179] describe the use of ketamine in pediatric burn surgery. However, significant side effects can occur, [180,181] and ketamine is best used with supervision by an anesthesiologist. [166] Ketamine also produces prolonged sedation that interferes with the patient's ability to resume oral intake.

Nitrous oxide with oxygen has been used effectively for analgesia during burn wound dressing changes. However, scavenging of the gas when administered outside of an operating room (such as in a Hubbard tank room) is problematic. [182,183] If nitrous oxide is administered with opioids, the patient may be induced into a state of general anesthesia with profound respiratory depression.

The efficacy of general anesthesia administered by an anesthesiologist for procedures on a burn intensive care unit has been documented. [184] General anesthesia for extensive burn debridement may also be more efficacious than subanesthetic doses of sedatives and analgesics. [185]

For minor pain, we recommend use of analgesics such as acetaminophen. Nonsteroidal anti-inflammatory drugs have antiplatelet effects and may not be appropriate for patients who require extensive excision and grafting procedures. In addition, burn patients can also manifest the nephrotoxic effects of nonsteroidal anti-inflammatory drugs. [186] Opioids and benzodiazepines can be used successfully together if patients are anxious. Patient monitoring must be appropriate to the level of sedation.

Background (Baseline) Pain

Burn injuries cause significant persistent background pain during the entire recovery period. [187,188] This continuous background pain may be mediated by increased nociceptor sensitivity secondary to the action of inflammatory mediators from the burn wound, such as serotonin, histamine, and prostaglandins. Interestingly, total pain perception is proportional to the magnitude of the burn during the first week only. [189] Thereafter, it varies widely among individual patients regardless of of the burn magnitude, length of time since injury, and sociodemographic characteristics of the patients. [189]

Morphine is the most widely studied medication to treat background pain. The oral route for administration is the most appropriate beyond the initial resuscitation phase. [171] After oral administration to the burned patient, the plasma morphine concentration peaks at 30 min and the terminal half-life is 3 h. With a continuous-release morphine preparation, the plasma concentration peaks at 1.4 h with a terminal half-life of 14.7 h. Oral morphine sulfate thus can be used for breakthrough pain and morphine continuous release (on a 8- to 12-h schedule) for background pain. [190]

Pain may persist in burned areas long after burns have healed. [191] Failure of opioids to control pain may be due to the development of a neuropathic component of the pain. This has been described in both acute [192] and chronic [191] burns. Management can be difficult, with various options available. Patients with chronic pain may respond to physical therapy, behavioral therapy, and various drugs (e.g., methadone, [193] antidepressants, anti-convulsants, and intravenous lidocaine). [194] A detailed description of the management of these patients is beyond the scope of this article. Referral of the patient to a pain medicine specialist may be indicated.

Conclusions

Providing anesthesia care to burned patients is challenging, but it can be satisfying when the anesthesiologist is successful in taking a severely ill patient through a devastating, deforming, painful, and emotionally stressful process. Training and experience in providing anesthesia care for patients with burns should be complemented by familiarity with advances in related fields. The competent and informed anesthesiologist is a valuable member of the burn team and is encouraged to participate fully in caring for burned patients.

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